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In this issue

DONOR-THEMED ISSUE

From donor motivation to donor vigilance

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Vox Sanguinis

EDITORIAL

Themed issue – focusing on donor assessment, motivation and vigilance

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Blood donors are irreplaceable, and donor research is foundational to safe and sufficient blood supplies around the world. In recognition of increasing emphasis on such research, this issue of *Vox Sanguinis* focuses on donor assessment, donor motivation and donor vigilance. There was considerable interest in submitting articles for this issue. We selected eleven articles originating from Europe, North America, Australia and Africa, including four multi-country articles that span diverse aspects of these three subjects. We briefly summarize salient events and activities and highlight the articles in this special issue.

Historical reflections

Until the emergence of HIV, donor assessment was a much simpler process than it is today. There were questions about general health, known and presumed risk factors for infections such as syphilis and hepatitis, as well as biometric measurements such as body temperature and haemoglobin. Donors were encouraged to eat before donating and offered rest and refreshments post-donation to reduce the chance of vasovagal reactions (fainting). These steps were generally based on 'common' knowledge rather than evidence-based donor studies. Donor assessment took on a whole new meaning when it was realized that HIV was transmissible by blood transfusion. In the United States, the FDA required specific donor education relating to HIV/AIDS and specific sexual risk questions [1]. Most Western countries implemented similar questions, but risk reduction was presumed rather than quantified, and post-implementation monitoring was very basic. Expectations of governments, patient groups and blood operators themselves to effectively monitor safety increased research activity. Donor testing methods incrementally improved along with safety. As new, potentially transfusion-transmissible infectious threats emerged such as vCJD, chikungunya virus, West Nile virus, and Zika virus, as well as non-infectious concerns such as TRALI and iron deficiency, research and increasingly quantitative risk assessment were used to inform policy decisions.

While donor vigilance (i.e. safeguarding donor health) has always been important, there has been a gradual increase in research activity, with greater intensity in the last decade. Three areas stand out. Recognition of the need to standardize definitions of donor reactions in order to effectively monitor them and compare was recognized, and led to development of definitions (ISBT2014). Interventions to reduce risk of donor reactions, especially vasovagal reactions, such as pre-donation water and salty snacks and practicing applied muscle tension during donation have been hypothesized and tested. Donor iron levels and the impact of donation frequency have been an area of intense investigation leading to improvements in donor information, changes in the interdonation interval, ferritin testing (often for risk groups of donors) and recommendations for iron supplementation for at-risk donors.

Recent focus of donor assessment

After many years of incrementally adding to new donor eligibility criteria, we now find ourselves questioning the value of some. With current testing for transfusion-transmissible infections, the risk for most is vanishingly small and changing societal values demand evidence-based justification for deferral. No deferral has been more controversial than the lifetime deferral for men who have sex with men (MSM). Implemented at a time before universal HIV testing commenced when there was urgency to act and regulatory/public support, the benefit was presumed. However, once deferral criteria are implemented, defining the risk posed by their relaxation or removal is complex and often leads to 'policy inertia'. This issue contains several articles addressing this challenge. To demonstrate the safety profile of the UK's then 12-month MSM deferral policy, Davison et al analysed rates of HIV as well as HBV, HCV and syphilis pre- and post-implementation of a 12-month deferral for MSM showing that there were no significant changes post-implementation. They also used a large online survey to measure non-compliance (i.e. failure to declare MSM in the past 12 months), reporting high compliance, with only about 0.6% of men non-compliant. Research to measure donor compliance has

become increasingly an expectation of policymakers both pre- and post-implementation of donor criteria. In Australia, Hoad et al questioned the utility in temporary deferral of donors post-endoscopy. They evaluated incidence of HIV, HCV and HBV among donors who returned after being temporarily deferred for endoscopy, showing zero incidence. These results were used as part of the evidence in an application to their regulator to remove the deferral, which was subsequently approved. A report by Mikkelsen et al describes how the TRANSPOSE study sought to bring European countries together to consider common donor criteria. This reflects growing recognition of the need for evidence-based approaches to donor management, while recognizing that the local epidemiology may mean that some criteria should not/cannot be standardized. Their article highlights the difficulty of coordinating between jurisdictions and achieving consensus.

Current trends in donor vigilance

This issue features an International Forum by Goldman et al describing a survey of risk mitigation strategies employed in different countries to reduce vasovagal reactions in whole blood donors. All countries provide information to donors, most offer water before and after donating, and some have special provisions for first-time donors. Interestingly, many undertook some form of evaluation to inform policies. Most surveyed countries have some form of donor vigilance, at least for moderate and severe reactions and reported using ISBT2014 or similar criteria. However, a second article by Mikkelsen et al from the TRANSPOSE study suggested that there is still work to be done in this regard. They reported that a different selection of European countries were not all using standardized definitions. An article by Crowder et al surveyed US blood donors pre- and post-implementation of an enhanced post-donation instruction sheet. Their results suggest that donors remembered items of immediate relevance, but less about problems that may develop. This has important implications for adverse events, particularly rare but serious events occurring after leaving collection areas, such as motor vehicle accidents.

Research into motivation to donate blood has been increasing and remains a priority as recruitment and retention continues to challenge blood centres [2]. There is an ethical obligation to provide appropriate care for donors, but the potential impact of donor adverse events on continued donation behaviour is not inconsequential and often stated as an operational benefit of reducing reaction rates [3]. In this issue, three studies give a different perspective. Thijsen et al assessed the impact of recruiting Australian first-time donors directly into plasma apheresis donation rather than the usual start in whole blood donation. They report that while first-time plasma donors have marginally higher vasovagal reactions and phlebotomy injuries, interestingly donor retention was not affected. Thorpe et al present a qualitative study of Australian lapsed plasma donors aimed to understand why they stopped donating. Adverse experiences were often not related, rather life events and concerns about eligibility and safety. Interestingly, some still see themselves as plasma donors and intend to donate again. These two articles provide important pointers given that many countries are expanding their source plasma programs to meet demand for plasma-derived products. In a cross-sectional survey of first-time blood donors in Ghana by Asamoah-Akuoko et al, concerns about reactions also had little to do with intention to return. Practical matters such as access to a collection site and advertising/reminders were positive predictors, whereas concerns about how the blood donation will be managed and discomfort with receiving test results were negative predictors pertinent to the sub-Saharan African setting.

Future directions

Until 2020, donor research has been focused almost exclusively on informing policy in blood collection agencies. There are a few notable exceptions such as the work by Murphy and colleagues, which monitored HTLV-positive donors biannually starting in 1992 to understand outcomes of the infection [4]. In the United States, the concept of blood donor collection sites functioning to provide a health check and reference centre has been around for a number of years, but the emphasis has been more as a donor recruitment incentive than providing a public health service. In this issue, a report by Hughes et al describes basic health indicators of blood donors to assess cardiovascular risk in young otherwise healthy individuals in the United States. They report that nearly half were overweight, more than half had high blood pressure, and over 6% had elevated cholesterol levels. Although the measurements were taken to evaluate donors for donation, and cholesterol as a recruitment incentive, their analysis demonstrates how donor data currently collected could contribute to public health knowledge. In a survey of the ISBT Transfusion Transmitted Infectious Diseases Working Party, with the sudden onset of the COVID-19 pandemic donor studies sprang up almost overnight around the world to estimate seroprevalence (see O'Brien et al). The objective was primarily to inform public health policy. Millions of leftover blood samples from donations usually discarded were more than a rare opportunity; for many countries, they were the only viable approach, particularly given the urgency to launch such studies. In 2020, for the first time we see

assessment of some donor health indices conducted primarily to inform public health, rather than donor policy. We believe that this represents a turning point in the role of blood donor research, and expect that it will continue beyond the COVID-19 pandemic.

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ORIGINAL PAPER

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Blood donation by men who have sex with men: using evidence to change policy

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Background In 2011 in the United Kingdom (UK), excluding Northern Ireland, the deferral of men who have sex with men (MSM) changed from lifetime to 12 months. We describe MSM who donated before and after this to inform further policy reviews.

Materials and Methods Characteristics and sexual behaviours of donors identifying as male from routine surveillance are described. Rates of infections are compared pre- and post-implementation of a 12-month deferral. Donors are compared with screen negative male donors responding to a large-scale survey during 2013/2014.

Results Comparing the five years pre- and post-change, the rate of confirmed positives for markers of HBV, HCV, HIV and syphilis decreased by 6·9% from 14·1 to 13·1/100 000 donations. The rate of recent infections was unchanged (1·72/100 000). Of 22 776 survey responses identifying as male, MSM disclosed sex between men over 12 months ago giving 99·35% compliance among male donors. Two-thirds of the 72 non-compliant MSM reported one to two partners and one-third had no new partners within 12 months. The most commonly reported reason for non-compliance from MSM both positive and negative for infection was 'not important to declare' (37·2% and 40·7%). Test seeking was rare (9·3% and 2·1%).

Conclusion Compliance with the 12-month MSM deferral policy was very high. The very low rates of infections post-change demonstrated the effectiveness of the policy. These data were an important part of the 2017 review of all sexual behaviour deferrals.

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Introduction

In the UK, the minimum requirements for blood donation policy are set out in the UK Blood Safety and Quality Regulations (BSQR) 2005 and translated into law from the European Union Directives 2004/33/EU [1,2]. This states that there is a requirement for permanent deferral of 'persons whose sexual behaviour puts them at high risk of acquiring severe infectious diseases that can be transmitted by blood'; the definition of high-risk sexual behaviour is open to interpretation thus there is potential for change. The policies to fulfil these requirements are determined by government ministers upon the advice of the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO), an independent expert committee.

Men who have sex with men (MSM) are significantly and disproportionately affected by HIV, and, since the

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early 1980s were permanently excluded from blood donation by all four UK blood services to minimize transfusion transmitted HIV (TT-HIV) [3,4]. Despite improvements in test sensitivity and knowledge of blood-borne viral infections, a policy review in 2006 concluded there were insufficient data about how a change to policy may impact on safety particularly in relation to donor compliance, that is respecting the policy. As a result, no changes were recommended, but work was commissioned to assess the extent of MSM donating blood despite being asked not to, that is the level of MSM compliance with the permanent deferral [5].

This work among a sample of gay, bisexual and other MSM in the general population identified good compliance with the permanent deferral with 89% reporting not donating since becoming ineligible and 97·5% not donated in the last year. A change was welcomed among responders; preference was for an individualized risk assessment, but the complexity was recognized, and a 12-month deferral since last sex with a man was favoured over 5 years [5]. These data prompted a further policy review. In 2010, SaBTO assessed the impact of a 12-month deferral of MSM, and a 12-month deferral for commercial sex workers (CSW). Of importance were the calculations that demonstrated a change from a permanent to a 12-month deferral for MSM was expected to have a negligible impact on HIV residual risk (RR); the key assumption was that the high compliance with the permanent deferral would be unchanged under a 12-month deferral [6]. The review also included an analysis of the epidemiology of infections in donors and the general population, testing performance, operational issues, and consideration of the ethics and equity of the deferrals for MSM and CSW [7,8]. The outcome was a recommendation by SaBTO to change to a 12-month deferral for MSM [9]. This was accepted by government and implemented by the blood services in England, Wales and Scotland in 2011. Northern Ireland followed in 2016 on the basis that the change had not impacted on the safety of the supply.

While the expected impact of the change on HIV RR was reassuring, the assumptions about compliance were based on limited information. Thus, as part of their recommendation to change the MSM deferral, SaBTO requested an assessment of compliance with all donor section criteria relating to infectious disease risk, and robust surveillance of positive donors. Surveillance was already in place, but to assess compliance, Public Health England (PHE) on behalf of the four UK blood services undertook a large–scale, unlinked, anonymous, web-based survey of screen negative blood donors. The Northern Ireland Blood Transfusion service (NIBTS) was included but the lifetime deferral of MSM remained in place at this time.

Following implementation of the 2011 recommendations, lobbying by those maintaining policy inequity continued, and the deferral was criticized as over-cautious. In response, at the end of 2016, the UK government asked SaBTO to review the donor selection guidelines again. The scope of this review was broader and considered policies relating to MSM, CSW, other higher risk sexual partners, skin piercing, injecting drug use and endoscopy. Here, we describe information about MSM donating blood in the UK that was provided to SaBTO. This includes a comparison of male donors with confirmed markers of infection for the five years before and after the 12-month deferral policy, and an analysis of responses from males to the 2013/14 UK blood donor survey of negative donors [10]. Findings from the survey were extrapolated to the UK donor population to estimate the number of MSM donors in 2014 and their rate of compliance. MSM identified in the survey were described, including some information about their sexual behaviour.

Methods

Data sources

Positive blood donors from surveillance

Surveillance data are collected by NHSBT/PHE Epidemiology Unit for donations tested by the four UK blood services [11]. Data include donations tested by donor type (first-time and repeat) and details of those with confirmed markers of infection. A demographic breakdown is provided by NHSBT annually and applied to all donations tested in the UK. For donors with confirmed markers of infection, the microbiology results, details of previous donations, and clinical and behavioural risk information collected at post-test discussion (PTD) are passed to the surveillance scheme. Where possible, donors identified at the PTD as non-compliant are asked why they came to donate and did not disclose this information. From the information provided, the surveillance team categorize positive donors according to their most probable source of infection; males who report oral or anal sex between men (SBM) are classified MSM. Infections are assigned by the unit as recently acquired if there was a previous negative donation within 12 months, or if HBV NAT pick up and/or acute HBV is indicated by confirmatory tests, or if HIV NAT pick up, or HIV avidity test indicated acquired in the last 4–5 months or if HCV NAT pick up. For syphilis, the clinical history is also reviewed, along with a previous negative donation within 12 months and/or IgM-positive treponema result.

All male blood donors with confirmed markers of hepatitis B (HBV), hepatitis C (HCV), HIV and syphilis between 2007 and 2016 were extracted from the surveillance database. For NHSBT MSM repeat donors with recently acquired infection, the details of previous donations were determined from the national donor management system PULSE (Savant.co.uk).

Negative donors from the UK blood donor survey

The UK blood donor survey was a large-scale, unlinked anonymous, web-based survey of screen negative blood donors undertaken by Public Health England (PHE), on behalf of the four UK blood services, between November 2013 and October 2014 [10]. In brief, 65 439 (29%) donors responded to the survey, which included 18 054 first-time donors. Demographic information included gender, age, ethnic group, country of birth, level of education, first language spoken and area of residence. Many of the survey questions were asked in the same format as on the donor health check (DHC) form. Responders who disclosed behaviours or characteristics that may have resulted in a deferral if declared at the time of donation that is, did not meet the donor selection guidelines, were identified as non-compliant. Towards the end of the survey, these participants were asked why they had not reported the information at donation by selecting all that applied from a list of reasons (i.e. multiple reasons if appropriate) or to give an alternative response in free text. The survey also asked the number of sexual partners, number of new sexual partners and history of sexually transmitted infection (STI). The Research Governance Coordinator at HPA's R&D Office (part of PHE since 1st April 2013) considered this survey to be service evaluation and formal ethical approval was not required.

Analysis

From surveillance, UK male donors with confirmed markers of infection were compared for the five years pre- and post-change (2007–2011 v 2012–2016). Annual rates of confirmed markers of infection were calculated per 100 000 donations from male donors. Differences in proportions pre- and post-change were investigated using chi-squared and Fisher's exact, trends in rates were investigated using Poisson regression.

From the UK blood donor survey database, responses from donors identifying as male were extracted. Donors reporting ever having had oral or anal sex with another man were classified as MSM; those reporting sex within 12 months (MSM < 12), or more than 12 months (MSM > 12) were identified. All MSM < 12 were determined non-compliant with the current MSM deferral criterion. For this analysis, all MSM > 12 were determined compliant, including MSM > 12 from Northern Ireland Blood Transfusion Service (NIBTS) even though at the time of the survey all MSM were permanently excluded from blood donation. The demographic characteristics of MSM < 12 and MSM > 12 were compare, and the sexual behaviours of MSM < 12 were described.

The reasons for non-compliance collected in both data sources were reviewed. The responses from the negative donors in the donor survey were aligned with the main categories reported for the infected donors in the routine surveillance and their distributions were compared.

Estimating the number of MSM donating blood in the UK under a 12-month deferral and the rate of compliance

The proportion of male survey responders who were MSM, MSM < 12 and MSM > 12 were calculated among all, first-time and repeat donors and adjusted to allow for differences in the age, gender, ethnicity and donor type between responders and all blood donors in 2014. Weights to do this were derived from the number of NHSBT donors as the only available source and stratified by age group (17–24, 25–34, 35–44, 45+), gender, ethnicity (white, non-white) and donor type. The adjusted proportions were applied with 95% confidence intervals (95% CI) to the estimated number of males donating in the UK during 2014 to give the estimated total number of MSM ($_t$MSM), estimated total number of MSM < 12 ($_t$MSM < 12) and estimated total number of MSM >12 ($_t$MSM > 12) donating.

The rate of compliance with MSM 12-month deferral was estimated among all male donors and among MSM donors as follows:

$$\text{Complaince among MSM donors}(\%) = \frac{{}_t\text{MSM} - {}_t\text{MSM}{<}12}{{}_t\text{MSM}} \times 100$$

$$\text{Complaince among male donors}(\%) = \frac{N\,\text{male donors} - {}_t\text{MSM}{<}12}{N\,\text{male donors}} \times 100$$

Results

Male donors positive for markers of HBV, HCV, HIV or syphilis

The number of donations from male donors tested and confirmed positive in the UK fell from 6 678 147 and 940 in 2007–2011 to 5 301 592 and 695 in 2012–2016 (Table 1). This represents a small decrease in rate (6·9%)

Table 1 Blood donations from male donors with confirmed markers for HBV, HCV, HIV or syphilis and recently acquired infections by the probable exposure categories of men who have sex with men (MSM), non-MSM and not known in the UK, 2007-2016

	UK 2007–2011								UK 2012–2016								MSM 2007–2011 v 2012–2016	Totals 2007–2011 v 2012–2016
	MSM		Non-MSM		Not known		Total		MSM		Non-MSM		Not known		Total			
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	Fisher's exact *P*=	Chi-square *P*=
Donations tested							6 678 147								5 301 592			
Confirmed	56	6·0	615	65·4	269	28·6	940	100·0	59	8·5	420	60·4	216	31·1	695	100·0		
Rate/100 000							14·1								13·1			
Donor type																		
First-time	25	44·6	525	85·4	215	35·0	765	81·4	31	52·5	367	87·4	169	78·2	567	81·6	0·255	0·918
Repeat	31	55·4	90	14·6	54	8·8	175	18·6	28	47·5	53	12·6	47	21·8	128	18·4		
Confirmed markers of																		
HBV	3	5·4	258	42·0	66	10·7	327	34·8	4	6·8	186	44·3	50	23·1	240	34·5	0·097	0·009
HCV	1	1·8	177	28·8	61	9·9	239	25·4	1	1·7	98	23·3	53	24·5	152	21·9		
HIV	32	57·1	44	7·2	6	1·0	82	8·7	21	35·6	16	3·8	4	1·9	41	5·9		
Syphilis	20	35·7	136	22·1	136	22·1	292	31·1	33	55·9	120	28·6	109	50·5	262	37·7		
Recent infections	20	17·4	58	50·4	37	32·2	115	100·0	27	29·7	43	47·3	21	23·1	91	100·0		
Rate/100 000							1·7								1·7			
Donor type																		
First-time	3	15·0	17	29·3	15	40·5	35	30·4	5	18·5	20	46·5	7	33·3	32	35·2	0·535	0·472
Repeat	17	85·0	41	70·7	22	59·5	80	69·6	22	81·5	23	53·5	14	66·7	59	64·8		
Evidence of recent																		
HBV[a]	2	10·0	10	17·2	4	10·8	16	13·9	3	11·1	2	4·7	4	19·0	9	9·9	0·914	0·633
HCV	0	0·0	1	1·7	1	2·7	2	1·7	0	0·0	2	4·7	1	4·8	3	3·3		
HIV[b]	8	40·0	16	27·6	3	8·1	27	23·5	12	44·4	4	9·3	1	4·8	17	18·7		
Syphilis	10	50·0	31	53·4	29	78·4	70	60·9	12	44·4	35	81·4	15	71·4	62	68·1		
Age group years																		
17–24	3	15·0	13	22·4	10	27·0	26	22·6	10	37·0	8	18·6	4	19·0	22	24·2	0·056	0·038
25–34	8	40·0	11	19·0	6	16·2	25	21·7	3	11·1	10	23·3	5	23·8	18	19·8		
35–44	6	30·0	20	34·5	13	35·1	39	33·9	4	14·8	12	27·9	0	0·0	16	17·6		
45–54	2	10·0	9	15·5	6	16·2	17	14·8	5	18·5	13	30·2	5	23·8	23	25·3		
55 years and over	1	5·0	5	8·6	2	5·4	8	7·0	5	18·5	0	0·0	7	33·3	12	13·2		
Ethnicity																		
White British	17	85·0	47	81·0	29	78·4	93	80·9	22	81·5	28	65·1	14	66·7	64	70·3	0·219	0·29
White other	3	15·0	2	3·4	3	8·1	8	7·0	1	3·7	7	16·3	4	19·0	12	13·2		
Mixed other	0	0·0	9	15·5	4	10·8	13	11·3	3	11·1	8	18·6	2	9·5	13	14·3		
Not known	0	0·0	0	0·0	1	2·7	1	0·9	1	3·7	0	0·0	1	4·8	2	2·2		

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Table 1 (Continued)

	UK 2007–2011								UK 2012–2016								MSM 2007–2011 v 2012–2016		Totals 2007–2011 v 2012–2016	
	MSM		Non-MSM		Not known		Total		MSM		Non-MSM		Not known		Total					
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	Fisher's exact *P*=		Chi-square *P*=	
Place of birth																				
UK	16	80·0	43	74·1	21	56·8	80	69·6	20	74·1	24	55·8	15	71·4	59	64·8	0·358		0·421	
Outside UK	3	15·0	9	15·5	3	8·1	15	13·0	2	7·4	11	25·6	5	23·8	18	19·8				
Not known	1	5·0	6	10·3	13	35·1	20	17·4	5	18·5	8	18·6	1	4·8	14	15·4				
Compliant																				
Yes	0	0·0	48	82·8	0	0·0	48	41·7	1	3·7	40	93·0	0	0·0	41	45·1	1·000		0·299	
No	20	100·0	9	15·5	0	0·0	29	25·2	24	88·9	2	4·7	0	0·0	26	28·6				
Not known	0	0·0	4	6·9	37	100·0	41	35·7	2	7·4	1	2·3	21	100·0	24	26·4				

[a]Includes one HBV and HIV co-infection.
[b]Includes one syphilis and HIV co-infection.

from 14·1 to 13·1/100 000 donations tested when comparing the five years before and after the 2011 change. Pre-change, 56 (6·0%) donors with confirmed markers were assigned MSM, increasing to 59 post-change (8·5%). For MSM, the most common markers were for HIV and syphilis; post-change there was some evidence ($P = 0·097$) of a decrease in the proportion of MSM with markers of HIV (57·1% v 35·6%) and an increase in syphilis (35·7% v 55·9%). In comparison, for non-MSM the most common marker was for HBV, accounting for 42·0% and 44·3% for both periods; markers of HIV were detected at very low levels at 7·2% and 3·8%, respectively.

The number of recently acquired infections among donations from males fell post-change from 115 to 91; however, the rate was unchanged at 1·7/100 000. (Table 1). For both periods, most recent infections in MSM and non-MSM were HIV and syphilis, in repeat donors, of white British ethnicity and born in the UK, with some evidence of difference in age following the change in deferral as the proportion aged over 45 years increased ($P = 0·038$). Pre-change, 20 donors (17·4%) were assigned MSM, compared to 27 post-change (29·7%). The characteristics of MSM with recently acquired infections were generally similar to non-MSM. There was no change after the 12-month deferral except for an increase in the proportion of MSM with markers of infection among younger (17–24) and older (45 plus) age groups that approached significance ($P = 0·056$).

For MSM donors with recently acquired infection, 24 of 27 (88·9%) were not compliant with the 12-month deferral (Table 1). One MSM donor with recently acquired HBV disclosed no other risk information other than SBM over 12 months prior and hence was categorized as compliant with the deferral. There was not enough information to determine compliance for the remaining two. For non-compliant MSM, 21 were repeat donors who had given an average of 23 previous donations overall, ranging from 2 to 70, a further one from Northern Ireland was excluded as no data were available. Among these 21, 16 (76·2%) had donated under the lifetime deferral, three disclosed SBM before 2012 at their post-test discussions suggesting likely prior non-compliance. Nine reported no SBM before 2012, suggesting no prior non-compliance. No information about SBM pre-2012 was available for the remaining four.

Annual rates of confirmed markers and recently acquired infections among all males per 100 000 donations from male donors, and MSM per 100 000 donations from male donors between 2007 and 2016 were steady across all years (Fig. 1).

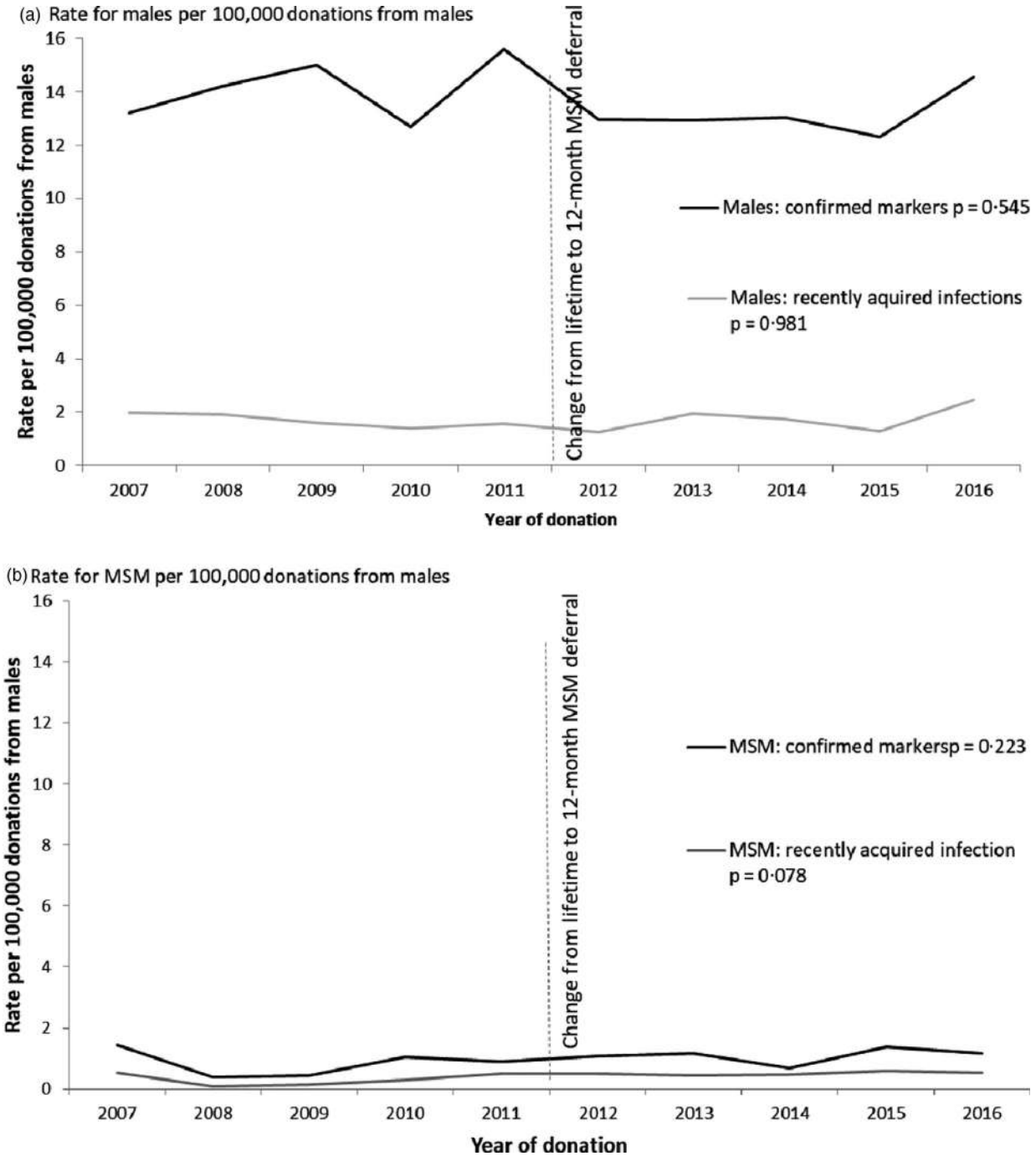

Fig. 1 The annual rates of confirmed markers and recently acquired infections for (a) all males, and (b) MSM, among donations from male donors between 2007 and 2016.

Men who have sex with men in the UK blood donor survey

Of 65 439 responses to the UK Blood Donor Survey, 34·8% (22 776/65 439) identified as male (Fig. 2). Donors who did not respond to the question 'Before your last donation, did you ever have sex?' were excluded from further analysis (711). Among the remaining males who reported 'Yes', 1·1% (253/18 577) reported oral or anal sex with a man at some time in

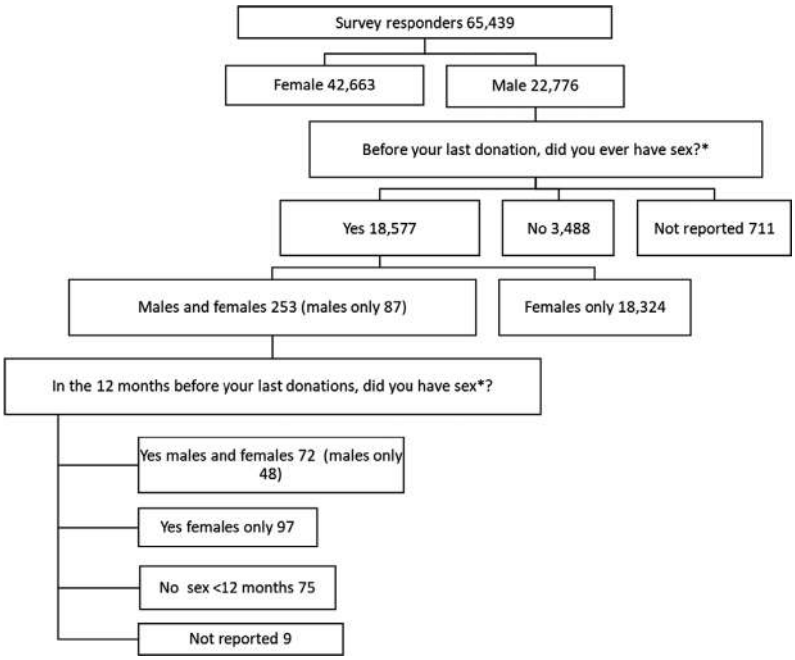

Fig. 2 Response to the sex questions of UK Blood Donor Survey by those identifying as male.

the past (120 first-time and 133 repeat donors) and classified MSM.

Of the 253 MSM, most were NHSBT donors, aged less than 45 years and educated beyond 16 years of age (Table 2). Half were repeat donors, and almost all were of white ethnicity, born in the UK and spoke English as their first language. There were 181 MSM >12 (71·5%) and 72 MSM <12; there were no differences in the characteristics between these two groups, except for a significantly higher proportion of MSM >12 with English as their first language for first-time donors (97·8% v 82·8%, $P = 0·009$) and donors overall (98·3% v 90·3%, $P = 0·007$), and some evidence ($P = 0·08$) of a difference in age with a greater proportion of MSM >12 in older groups.

Among the 72 MSM <12, two-thirds reported 1-2 partners in previous 12 months and a third reported no new partners; significantly greater proportions of both were seen among donors with exclusively male partners than those reporting both male and female (78·3% v 42·3%, $P = 0·003$, and 50·0% v 11·5%, $P < 0·001$) (Table 3). Similar behaviours were reported from first-time and repeat donors. Around 1 in 10 MSM <12 reported ever having been diagnosed with a sexually transmitted infection.

The estimated number of compliant and non-compliant MSM donors in the UK

The adjusted proportions of MSM, MSM <12 and MSM >12 among males were applied to the estimated number of male donors in the UK in 2014 to give 8196 MSM (95%CI 6913–9711), of whom 3030 (95% CI 2253–4073) were MSM <12 and 5165 (95% CI 4196 to 6356) were MSM >12 (Table 4). All males except MSM <12 were considered compliant with the 12-month MSM deferral including four from NIBTS which at the time still had a permanent deferral. Thus, among UK male blood donors, compliance was estimated to be 99·35% (95% CI 99·33% to 99·37%).

Reasons for non-compliance given by MSM donors

Reasons for non-compliant MSM not declaring their risk at donation were given by 91·7% (66/72) in the donor survey and 44·8% (43/96) of positive donors from surveillance (Table 5). Among both groups, the most common response was 'Not important to declare' (37·2% and 40·7%). Test seeking was rare (9·3% and 2·1%). From the donor survey, non-compliant MSM who reported exclusively male partners were less likely to report 'too embarrassed/didn't want anyone to know' than MSM who had had male and female partners.

Discussion

Assessing UK blood donor surveillance data for the five years before and after implementation in 2011 of a 12-month deferral policy for MSM revealed no significant impact on the rate of confirmed markers of HBV, HCV, HIV and syphilis, or of recently acquired infections. The

Table 2 The characteristics of men who have sex with men (MSM) responders to the UK blood donor survey

	First-time donors			Repeat donors			All			Total
	MSM < 12 *N* (%)	MSM > 12 *N* (%)		MSM < 12 *N* (%)	MSM > 12 *N* (%)		MSM < 12 *N* (%)	MSM > 12 *N* (%)		All *N* (%)
Total	**29 (100.0)**	**91 (100.0)**	**Fisher's exact *P*=**	**43 (100.0)**	**90 (100.0)**	**Fisher's exact *P*=**	**72 (100.0)**	**181 (100.0)**	**Fisher's exact *P*=**	**253 (100.0)**
Blood service										
England	27 (93·1)	82 (90·1)	1·00	34 (79·1)	72 (80·0)	0·79	61 (84·7)	154 (85·1)	0·67	215 (85·0)
Scotland	2 (6·9)	8 (8·8)		6 (14·0)	10 (11·1)		8 (11·1)	18 (9·9)		26 (10·3)
Northern Ireland	0 (0·0)	1 (1·1)		0 (0·0)	3 (3·3)		0 (0·0)	4 (2·2)		4 (1·6)
Wales	0 (0·0)	0 (0·0)		3 (7·0)	5 (5·6)		3 (4·2)	5 (2·8)		8 (3·2)
Age group										
17–24	17 (58·6)	45 (49·5)	0·80	10 (23·3)	12 (13·3)	0·08	27 (37·5)	57 (31·5)	0·50	84 (33·2)
25–34	6 (20·7)	23 (25·3)		11 (25·6)	11 (12·2)		17 (23·6)	34 (18·8)		51 (20·2)
35–44	3 (10·3)	10 (11·0)		8 (18·6)	16 (17·8)		11 (15·3)	26 (14·4)		37 (14·6)
45–54	3 (10·3)	8 (8·8)		7 (16·3)	28 (31·1)		10 (13·9)	36 (19·9)		46 (18·2)
55 years and over	0 (0·0)	5 (5·5)		7 (16·3)	23 (25·6)		7 (9·7)	28 (15·5)		35 (13·8)
Education										
Beyond 16	19 (65·5)	67 (73·6)	0·51	39 (90·7)	82 (91·1)	1·00	58 (80·6)	149 (82·3)	0·80	207 (72·3)
Equivalent to 16	10 (34·5)	23 (25·3)		4 (9·3)	8 (8·9)		14 (19·4)	31 (17·1)		45 (24·2)
None	0 (0·0)	1 (1·1)		0 (0·0)	0 (0·0)		0 (0·0)	1 (0·6)		1 (3·1)
Not known	0 (0·0)	0 (0·0)		0 (0·0)	0 (0·0)		0 (0·0)	0 (0·0)		0 (0·4)
Ethnic group										
White	26 (89·7)	85 (93·4)	0·55	42 (97·7)	89 (98·9)	0·54	68 (94·4)	174 (96·1)	0·63	242 (96·6)
Non white	3 (10·3)	5 (5·5)		1 (2·3)	1 (1·1)		4 (5·6)	6 (3·3)		10 (3·1)
Not known	0 (0·0)	1 (1·1)		0 (0·0)	0 (0·0)		0 (0·0)	1 (0·6)		1 (0·3)
Place of birth										
Born UK	23 (79·3)	80 (87·9)	0·36	41 (95·3)	84 (93·3)	1·00	64 (88·9)	164 (90·6)	0·65	228 (93·3)
Born outside UK	6 (20·7)	11 (12·1)		2 (4·7)	6 (6·7)		8 (11·1)	17 (9·4)		25 (6·6)
Not known	0 (0·0)	0 (0·0)		0 (0·0)	0 (0·0)		0 (0·0)	0 (0·0)		0 (0·1)
Language										
English-speaking	24 (82·8)	89 (97·8)	0·009	41 (95·3)	89 (98·9)	0·24	65 (90·3)	178 (98·3)	0·007	243 (97·3)
Other	5 (17·2)	2 (2·2)		2 (4·7)	1 (1·1)		7 (9·7)	3 (1·7)		10 (2·7)

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Table 3 The characteristics of men who have sex with men (MSM) responders to the UK blood donor survey who had had sex with a man within 12 months (non-compliant) by donor type

	First-time donors			Repeat donors			All donors			Total
Gender of partners	**Male only**	**Male and female**	**Fisher's exact**	**Male only**	**Male and female**	**Fisher's exact**	**Male only**	**Male and female**	**Fisher's exact**	**All**
Total	***N* (%)**	***N* (%)**	***P***	***N* (%)**	***N* (%)**	***P***	***N* (%)**	***N* (%)**	***P***	***N* (%)**
	16 (55.2)	**13 (44.8)**		**30 (69.8)**	**13 (30.2)**		**46 (63.9)**	**26 (36.1)**		**72 (100.0)**
Number partners 12 months										
1–2	13 (81·3)	5 (38·5)	0·045	23 (76·7)	6 (46·2)	0·084	36 (78·3)	11 (42·3)	0·003	47 (65·3)
3–5	2 (12·5)	6 (46·2)		4 (13·3)	5 (38·5)		6 (13·0)	11 (42·3)		17 (23·6)
6–10	1 (6·3)	1 (7·7)		3 (10·0)	1 (7·7)		4 (8·7)	2 (7·7)		6 (8·3)
10+	0 (0·0)	1 (7·7)		0 (0·0)	1 (7·7)		0 (0·0)	2 (7·7)		2 (2·8)
Number NEW partner 12 months										
0	7 (43·8)	1 (7·7)	0·01	16 (53·3)	2 (15·4)	0·05	23 (50·0)	3 (11·5)	<0·001	26 (36·1)
1–2	3 (18·8)	0 (0·0)		6 (20·0)	3 (23·1)		9 (19·6)	3 (11·5)		12 (16·7)
2+	6 (37·5)	12 (92·3)		8 (26·7)	8 (61·5)		14 (30·4)	20 (76·9)		34 (47·2)
One or more sexually transmitted infection										
Yes	1 (6·3)	1 (7·7)	1·00	4 (13·3)	2 (15·4)	1·00	5 (10·9)	3 (11·5)	1·00	8 (11·5)
No or not reported	15 (93·8)	12 (92·3)		26 (86·7)	11 (84·6)		41 (89·1)	23 (88·5)		64 (88·5)

Table 4 The number of compliant and non-compliant men who have sex with men (MSM) donating blood in the UK in 2014 estimated from male responders to the UK blood donor survey

	Sex ever (where reported)			Sex between men (SBM)		
s	Total	No	Yes	Yes	Over 12-months (MSM > 12)	Less 12-months (MSM < 12)
Male donor survey responders	22 065	3488	18 577	253	181	72
Observed %		15·8%	84·2%	1·1%	0·8%	0·3%
Adjusted %		17·5%	82·5%	1·8%	1·1%	0·6%
(95% CI)			(81·6–83·4)	(1·5–2·1)	(0·9–1·4)	(0·5–0·9)
Est. donors (467 087 x adjusted %)			385 311	8196	5165	3030
(95% CI)			(381 137–389 325)	(6913–9711)	(4196–6356)	(2253–4073)
First-time donors						
Male donor survey responders	5338	1080	4258	120	91	29
Observed %		20·2%	79·8%	2·2%	1·7%	0·5%
Adjusted %		23·9%	76·1%	2·4%	1·8%	0·6%
(95% CI)			(74·8–77·4)	(2·0–2·9)	(1·4–2·2)	(0·4–0·9)
Est. donors (65 704 x adjusted %)			50 012	1576	1176	400
(95% CI)			(49 149–50 843)	(1302–1906)	(943–1466)	(272–588)
Repeat donors						
Male donor survey responders	16727	2408	14 319	133	90	43
Observed %		14·4%	85·6%	0·8%	0·5%	0·3%
Adjusted %		15·3%	84·7%	1·5%	0·9%	0·7%
(95% CI)			(83·6–85·8)	(1·2–1·9)	(0·6–1·2)	(0·5–1·0)
Est. donors (401 383 x adjusted %)			340 124	6132	3472	2660
(95% CI)			(335 603–344 387)	(4812–7807)	(2518–4783)	(1834–3856)

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Table 5 Reasons for non-compliance reported by positive and negative donors classified as men who have sex with men (MSM)

Positive donors		Negative donors			
Responses from positive donors disclosed at post-test discussion and reported to surveillance	All	Male and female partnerss	Exclusively male partners	All	Responses from negative donors disclosed on the donor survey
Not important to declare	16 (37·2%)	21 (37·5%)	36 (42·9%)	57 (40·7%)	Donations are tested so it doesn't matter,my risk is low or zero, I didn't think it was important
Embarrassment or privacy issue	8 (18·6%)	13 (23·2%)	23 (6·0%)	19 (13·6%)	I was too embarrassed , I didn't want anyone to know
Lack of understanding/awareness	6 (14·0%)	14 (25·0%)	19 (22·6%)	33 (23·6%)	I did but was told I could not donate, It was more than 12 months ago, Not asked, I didn't understand the question, forgot, not between donations
Test seeking	4 (9·3%)	2 (3·6%)	1 (1·2%)	3 (2·1%)	I wanted to be tested for infection
Other	9 (20·9%)	5 (8·9%)	15 (17·9%)	20 (14·3%)	Other -free text
		1 (1·8%)	7 (8·3%)	8 (5·7%)	Prefer not to say
Total	43 (100%)	56 (100%)	84 (100%)	140 (100%)	Total[a]

[a]One hundred forty responses from 66 non-compliant donors.

large-scale survey of negative blood donors provided, for the first-time, an estimate of the number of MSM donating blood in the UK and showed a very high compliance (99·35%) with the deferral. These data provided reassuring evidence that the MSM 12-month deferral question was appropriately applied by almost all male donors and were an important consideration when reviewing these donor selection criteria again in the 2017 SaBTO review. [12] The number of recently acquired infections and the extent of sex between men formed the basis of the calculations that provided evidence that a 3-month deferral would not impact on residual risk of undetected infections entering the blood supply. The outcome of the review was to recommend a further change in MSM donor selection policy and for others with increased risk sexual partners, from 12-month deferral to 3 months. This was implemented in November 2017 in the UK, excluding Northern Ireland, and surveillance continued to closely monitor the impact.

Donors with confirmed markers assigned MSM accounted for a similar proportion of males both before and after the change to a 12-month deferral, but the proportion with recently acquired infections increased by 12%. This was mostly due to HIV and syphilis and could be of concern to HIV window period risk; however, this was an increase of four infections across five years, representing a small change on an already low number. Similarly, there was no trend in rate of confirmed markers, or those with recent infections, among donations from MSM donors across the 5 years before and after the change. As infections in MSM donors are detected each year at very low levels, particularly those which are recently acquired, it was necessary to group all the markers together in order to increase the likelihood of detecting an impact of the 12-month MSM deferral on the trend among male donors. However, grouping infections by donor subgroups rather than virus type obscures any differences between them. The characteristics of MSM with recently acquired infections (mostly HIV and syphilis) didn't alter significantly after the change, except for some evidence of increasing age. This could reflect changes seen in HIV transmission by age groups in the general population; while declines in first-time diagnosis have been reported across all age groups there was less decline in males over 50 years [13].

Importantly, there was no significant increase in recently acquired infections in MSM donating for the first time. Furthermore, most of the repeat MSM donors with recently acquired infection had donated before under the permanent deferral. Although past sex between men (i.e. non-compliance) cannot be assumed in these males, it does suggest that these MSM with recently acquired infections did not come to donate because of the policy change.

The very high level of compliance with a 12-month MSM deferral estimated here among males was also confirmed in Australia at 99·7% and France at 99·3%, and 99·6% in Canada under a 5-year deferral [14–16] The same trend for lower compliance in first-time donors than repeat has also been reported [17–19]. Canada undertook a compliance survey both pre and post-implementation of their 5-year deferral, and they showed compliance

improved under the time-limited deferral. While theoretically this is plausible if the newly implemented criteria are more acceptable to MSM, it cannot be assumed. Previously published estimates for compliance in the UK of 95% and 89% under a lifetime deferral would suggest this could be the case [5,6]. However, although derived from the best available data at the time, these estimates are not directly comparable with the national representative sample of males known to have given blood that were surveyed here.

From the survey, it was estimated that 1·8% of male donors in 2014 were MSM. This is lower than the estimated 5·5% of males who are MSM in the general population, which is at least in part because of the selection criteria and MSM appropriately self-deferring.[20]

Despite the very high level of compliance under the 12-month deferral, 72 non-compliant MSM were identified in the survey. Since we did not survey MSM who had had sex between men <12 months and had not donated, we could not assess factors associated with compliance. However, we did find that compliant and non-compliant MSM who responded to the survey were generally similar except for a significantly lower proportion of non-compliant MSM who had English as their main language compared to compliant MSM (90·3% vs. 98·3%, $P = 0{\cdot}007$). Not having English as a first language does not necessarily reflect a poorer understanding of donor information or donor selection so may not be associated with compliance. There was some suggestion that among repeat donors non-compliant MSM were younger than compliant, although not statistically significant.

A closer look at the sexual behaviour of MSM who had had sex within 12 months from the donor survey revealed generally lower risk behaviours with most donors having only one to two partners, and few having a new partner. A third, however, reported both male and female partners in the last 12 months, which is considered high given that a general population survey reported a quarter of MSM had a female partner at some point throughout their lifetime [21]. Furthermore, almost all these donors reported a new partner suggesting potentially riskier sexual behaviour among bisexual males donating. When asked about non-compliance, there was more embarrassment reported in this group, possibly as they may not identify as gay or bisexual. This could mean there are more bisexual males responding to the survey who were still unable to disclose sex between men despite the anonymous nature of the survey and were categorized as heterosexuals.

The most common reasons for non-compliance in positive and negative MSM donors related to either self-perception of low risk or intentional non-disclosure because they didn't want to be turned away. The former included those who reported exclusive partnerships, said they were HIV negative, or discounted any potential risk as donations are tested. The latter included donors who were too embarrassed to declare sex between men or had been told by others that if they did, they would not be allowed to donate. Test seeking was rare in both donor groups, a finding supported by others published in a meta-analysis of motivation for donation which found 4·3% donors reported donating for a test [22].

Limitations

Male responders were under represented in the donor survey, and while efforts were made to adjust responses to the whole donor population, only data for NHSBT were available. Also, despite the anonymous nature of the questionnaire, non-compliance may be under-reported if donors still felt unable to accurately disclose their sexual history, particularly sex within 12 months, which has been suggested by others to be associated with a wish or need to provide socially desirable answers, or if the format of the survey was perceived as not being completely anonymous [14]. Similarly, MSM among positive donors may be have been under identified if the donors were unwilling to disclose SBM at the post-test discussion. For some donors, disclosure may have improved since removal of the lifetime deferral, although this may not be the case for donors who remain ineligible.

Conclusion

A very high rate of compliance of males with 12-month MSM deferral, and the very low rates of infection that were maintained post-change demonstrates the effectiveness of the policy. For many years the only data about MSM who donated blood was limited to positive donors, albeit a key source. However, for the first time in the UK our anonymous survey provided information about negative MSM who donate blood and characteristics of those who did and did not comply. Among non-compliant donors, despite identifying some higher risk behaviours, two-thirds were potentially lower risk based on low numbers of sexual partners, potentially supporting the merits of exploring such a question in future policy reviews. Non-compliance, even at the very low level detected in the UK, can pose a threat if the donor is unaware of their partners risk and should be minimized. While factors associated with non-compliance could not be investigated, reasons for non-compliance have been identified and ways to address this including supporting donors to recognize their own risk and facilitating disclosure should be explored.

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Conflict of interest

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Authorship

All authors contributed to the survey design. NA gave statistical and analysis advice. KD performed the analysis and wrote the manuscript with the support of the other authors. All authors provided feedback on the manuscript.

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ORIGINAL PAPER

Offering new and returned donors the option to give plasma: implications for donor retention and donor adverse events

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Background and Objectives In 2018, Australian Red Cross Lifeblood changed its plasmapheresis eligibility criteria to allow donors to donate plasma without the requirement of a prior successful whole blood donation. This study evaluated the impact of this policy change on donor retention and donor safety.

Materials and Methods All donors who had attempted to give their first plasma or whole blood donation from January to June 2018 were included in this retrospective cohort study. Donor characteristics and adverse events were analysed for this index donation, and the cohort was followed for 18 months to analyse time to return, subsequent donation frequency and predictors of return.

Results Male and younger donors provided a significantly greater proportion of first donation plasma than females and older donors. New donors who gave plasma had the highest rate of donor adverse events, including vasovagal reactions and phlebotomy injuries. Nevertheless, donor retention was not affected, with more new donors returning and at a greater subsequent donation frequency after a plasma donation compared to new donors donating whole blood. First-time plasma donors who had previously donated whole blood, however, had greater and quicker rates of return, and more subsequent donations.

Conclusion Offering new donors the option to give plasma had a positive effect on donor return and subsequent donation frequency. Removing the requirement of a prior whole blood donation is a viable way to increase plasma collections although the combined effect of new donor status and plasmapheresis procedure on adverse event risk needs to be considered.

Key words: blood donation, donor adverse events, plasmapheresis, retention, whole blood.

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Introduction

Blood collection agencies worldwide are faced with changing demands for blood products. While the demand for red cells has declined over the years due to medical advancements and improvements in patient blood management, the demand for plasma-derived products has steadily increased [1]. As a result, Australian Red Cross Lifeblood (Lifeblood) has changed its focus from primarily collecting whole blood to recruiting donors to donate plasma via apheresis to increase plasma collections [2].

Recruitment for plasma predominately occurs through whole blood donation [3]. In many countries, donors are required to give at least one successful whole blood donation before attempting plasmapheresis. This requirement is to ensure donor suitability for apheresis donation and to minimize the risk of adverse events. The plasmapheresis procedure takes approximately four times as long as a whole blood donation and includes the process of

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returning the donor's red cells, with anticoagulant and, in Australia, with saline compensation. Due to the complexity of the procedure, the donor consent process is longer in duration and more extensive as donors are at risk of experiencing apheresis-specific adverse events, such as citrate reactions and infiltration, and are at an increased risk of haematomas, caused by red cells infiltrating the soft tissues during the return phase of the procedure [4].

To adapt to the change in demand for different blood products, Lifeblood assessed the feasibility, tolerability and acceptability of offering new donors the option to donate plasmapheresis in a cluster randomized, stepwedged trial in 2016–17 (ACTRN12616001307493). The aim of this trial was to address a gap in knowledge regarding the safety and donor acceptance of first-appointment plasma donations as few blood collection agencies allow new donors to give plasmapheresis. The study demonstrated that donating plasma at their first donation appointment did not negatively affect donation satisfaction, donor return within 6 months, or the rate of vasovagal reactions compared to new donors who gave whole blood.

As a result of this trial and the establishment of two plasma only collection centres, Lifeblood changed its eligibility criteria for plasmapheresis in January 2018 to allow donors to give a plasmapheresis donation without requiring them to have given whole blood in the last 2 years (see Table 1). This change also allows donors who return following a prolonged period of lapse (i.e. more than 24 months since last donation) to donate plasma. In this study, we evaluated the impact of this policy change on donor retention and donor safety. Specifically, we compared donor return rates over an 18-month period and donor adverse event rates for all first-time plasma and whole blood donors to determine whether there are any differences between those who donated whole blood recently prior to giving their first plasma donation, and new and returned donors who were offered to go direct to plasma. This information will provide insights into optimizing plasma collections while ensuring donor safety.

Materials and methods

Study population

Following ethical approval, donation and demographic information on a cohort of all donors who had attended their first whole blood or plasma donation (i.e. index donation) from 1 January 2018 to 30 June 2018 was extracted from the Lifeblood database. Donations given for therapeutic reasons or by donors who were deferred from all donation types for the entire 18-month study period were excluded. In addition, donations given by donors aged less than 18 years were removed as the minimum age for blood donation was increased to 18 years on 14 January 2018 preventing many from returning for a subsequent donation.

Additional exclusion criteria were applied based on prior donation experience. Between 26 May 2003 and 13 November 2006, Lifeblood merged its different state-level software platforms into one national blood management system. Donations made prior to the merger were captured as 'legacy donations' with no distinction recorded based on phlebotomy type. Therefore, for the purposes of this study, first-time plasma donors with a legacy donation count (n = 2661; 0·04%) were excluded from the study as we were unable to determine whether they had previously donated plasma. Further, donors who had participated in the initial feasibility, tolerability and acceptability trial (ACTRN12616001307493) that offered new donors the option to donate plasma by apheresis were also excluded.

Based on their donation history, donors were categorized as: (1) *First-time whole blood new donor* – someone who made their first whole blood donation in the study period with no prior donations, (2) *First-time plasma new donor* – someone who made their first plasma donation in the study period with no prior whole blood donations, (3) *First-time plasma regular donor* – someone who made their first plasma donation in the study period AND who had donated whole blood within the last 24 months, and (4) *First-time plasma returned donor* – someone who made their first plasma donation in the study period AND who had donated whole blood more than 24 months ago. The second and last category are a result of the changes made to the plasma eligibility criteria, with new and previously lapsed whole blood donors being able to donate plasma for the first-time.

Donor recruitment and retention strategies

In 2018, individuals are able to make a plasma or whole blood donation appointment either via telephone or through the Lifeblood website. On the day of their appointment, donors may be asked to change their donation type based on the centre's daily collection target. Potential donors to be converted to plasma are identified based on their blood group, with the order of preference being AB-Positive, B-Positive, A-Positive and O-Positive. If the donor agrees to a plasma donation, veins on both arms are checked for apheresis suitability and, if found suitable, the donor then proceeds to donate plasma. No different weight or height eligibility criteria are applied to donate plasma or whole blood. The target collection volume for all first-time plasma donors is set at 13% of their estimated total blood volume.

Table 1 Demographic and donation characteristics in first-time plasma and whole blood donors[a]

Characteristic	First-time whole blood new donor	First-time plasma		
		New donor	Regular donor	Returned donor
n (%)	34 252 (56·0)	5919 (9·7)	18 629 (30·5)	2352 (3·8)
Age (years)	33·0 ± 12·4	31·6 ± 11·9	33·3 ± 13·1	32·3 ± 10·6
18–29 years	16 826 (49·1)	3203 (54·1)	9313 (50·0)	1189 (50·6)
30–49 years	13 063 (38·1)	2108 (35·6)	6574 (35·3)	956 (40·6)
50–70 years	4363 (12·7)	608 (10·3)	2742 (14·7)	207 (8·8)
Gender				
Female	19 778 (57·7)	3126 (52·8)	10 720 (57·5)	1464 (62·2)
Male	14 474 (42·3)	2793 (47·2)	7909 (42·5)	888 (37·8)
Blood group				
O-Negative	2798 (8·2)	338 (5·7)	1541 (8·3)	69 (2·9)
Other	31 454 (91·8)	5581 (94·3)	17 088 (91·7)	2283 (97·1)
Collection site type				
Static	26 637 (77·8)	5837 (98·6)	18 085 (97·1)	2308 (98·1)
Mobile	7615 (22·2)	82 (1·4)	544 (2·9)	44 (1·9)
Prior donation count	-	-	4·1 ± 5·1	3·3 ± 3·2
Donation outcome				
Completed	33 028 (96·4)	5209 (88·0)	16 908 (90·8)	2100 (89·3)
Aborted	1224 (3·6)	710 (12·0)	1721 (9·2)	252 (10·7)
Donor adverse events	3024 (8·8)	726 (12·9)	1845 (9·9)	252 (10·7)
Vasovagal reaction	2760 (8·1)	524 (8·9)	1102 (5·9)	175 (7·4)
Loss of consciousness	167 (0·5)	45 (0·8)	66 (0·4)	12 (0·5)
Citrate reaction	n/a	133 (2·2)	464 (2·5)	46 (2·0)
Phlebotomy injury	288 (0·8)	140 (2·4)	364 (2·0)	41 (1·7)
Other event	16 (0·0)	9 (0·2)	39 (0·2)	5 (0·2)

[a]Data are reported as frequency (%) or mean (standard deviation).

With regards to retention strategies, all donors who have donated plasma or whole blood for the first time receive a thank you email the following day and an SMS within three weeks notifying them that their donation has been sent to a specific hospital (whole blood donors) or turned into a life-saving treatment (plasma). After six weeks, donors receive an educational email informing them of their optimal donation for their blood type. Donors with an O-Negative blood type will be asked to continue donating whole blood, while donors with a B-Positive or AB-Positive are asked to continue donating plasma. Donors with any other blood type will receive a message that their blood is versatile and Lifeblood may ask them to donate either whole blood or plasma. All donors continue to receive reminders at the same time points, with the only difference being messaging around the ideal donation type for their blood group.

Data

Lifeblood data on donor age, sex, blood type, donation outcome and donation history were extracted for the cohort. Further, donor adverse event information was extracted for the index donation. Donor adverse events were categorized using the Standard for Surveillance of Complications Related to Blood Donation [4] as either vasovagal reaction, phlebotomy injury (including haematoma, painful arm, and arterial puncture), citrate reaction (plasma donations only) or other (including haemolysis, allergic reaction and chest pain).

The cohort was followed for 18 months to track subsequent donations. Return date was defined as being the next time the donor presented to donate, regardless of whether they were eligible to donate or made a successful donation. Subsequent donation counts were calculated as the number of blood collections (including whole blood, plasma and platelets) made after the index donation within 18 months only for those who returned. Subsequent plasma donation counts included only subsequent plasma collections.

To determine time taken to return, we accounted for the mandatory recovery period between donation types (84 days for whole blood donations and 14 days for plasma donations). The date the donor was considered

eligible to return was calculated by adding the mandatory recovery period to the index donation date. Time taken to return was then calculated by subtracting the eligibility date from the return date, which was limited to 12 months after becoming eligible due to the available follow-up data.

Statistical analyses

Analyses were performed using statistical software (Stata Statistical Software: Release 15, StataCorp LLC, College Station, TX). Donor and donation characteristics were described by means (±standard deviation) for continuous variables, and by totals (percentages) for categorical variables. Univariate differences were examined using chi-square goodness of fit, logistic regression and one-way analysis of variance (ANOVA), with significant effects further examined using post hoc Tukey's HSD tests to determine where significant differences occurred between groups. Multivariate logistic regression was used to evaluate the association between new donor donation type and return with 18 months, and new donor donation type and the occurrence of a vasovagal reaction at index. Univariate survival analysis was performed to examine the return behaviour of the different donor groups through Kaplan–Meier survival curves and log-rank tests. Multivariate Cox proportional hazards models were fitted to the data to determine predictors of return within 12 months of being eligible for new donors only, and any donors who did not return were censored at the end of the follow-up period. Sex (male/female), blood type (O-Negative/other), donation outcome (completed/aborted), the occurrence of a donor adverse event at index donation (yes/no), and whether any temporary deferrals were applied after the index donation (yes/no) was entered as categorical variables, and age as a continuous variable in the models. All findings were considered significant at P values less than 0·05.

Results

A total of 61 152 first-time whole blood and plasma donations were included in this study. The cohort comprised of 34 252 (56%) first-time whole blood new donors, 5919 (10%) first-time plasma new donors, 18 629 (30%) first-time plasma regular donors and 2352 (4%) first-time plasma returned donors. An overview of sample characteristics is presented in Table 1.

Demographic and donation characteristics

Among new donors, the majority donated whole blood (34 252; 85%) as opposed to plasma (5919; 15%). The first-time plasma new donor group had a significantly greater proportion of males, $\chi^2(1) = 50{\cdot}0$, $P < 0{\cdot}01$, and were significantly younger than the first-time whole blood new donor group, $t(40\ 169) = 8{\cdot}4$, $P < 0{\cdot}01$.

Out of all first-time plasma donors, the majority were regular donors (18 629; 69%), followed by new donors (5919; 22%), and returned donors (2352; 9%). Although females overall provided the greatest proportion of first-time plasma donations, we observed differences across the three first-time plasma groups. There was a significantly greater proportion of males in new donors than regular donors, $\chi^2(1) = 40{\cdot}9$, $P < 0{\cdot}01$, and returned donors, $\chi^2(1) = 60{\cdot}6$, $P < 0{\cdot}01$ and a significantly greater proportion of males in regular donors than returned donors, $\chi^2(1) = 18{\cdot}9$, $P < 0{\cdot}01$. A one-way ANOVA showed that there was a statistically significant difference in age between the first-time plasma groups, $F(3,29\ 368) = 84.15$, $P < 0{\cdot}01$. A Tukey post hoc test revealed that regular donors were significantly older than both new and returned donors (all P's $< 0{\cdot}01$), with the age of new donors and returned donors not significantly differing ($P = 0{\cdot}07$).

Donor adverse event rates

The overall rate of donor adverse events was 13% in first-time plasma new donors, 11% in first-time plasma returned donors, 10% in first-time plasma regular donors and 9% in first-time whole blood new donors, $\chi^2(3) = 101{\cdot}7$, $p < 0{\cdot}01$. Compared to first-time plasma new donors, first-time plasma returned donors (OR: 0·81, 95%CI: 0·70–0·94), first-time plasma regular donors (OR: 0·74, 95%CI: 0·68–0·81), and first-time whole blood new donors (OR: 0·66, 95%CI: 0·60–0·71) had lower odds of experiencing a donor adverse event.

Focusing specifically on vasovagal reactions, first-time whole blood new donors (OR: 0·90, 95%CI 0·82–1·00), first-time plasma regular donors (OR: 0·65, 95%CI: 0·58–0·72) and first-time plasma returned donors (OR: 0·83, 95%CI: 0·69–0·99) had reduced odds of experiencing a reaction compared to first-time plasma new donors. Examining only reactions with a reported loss of consciousness, first-time whole blood new donors (OR: 0·64, 95%CI: 0·46–0·89) and first-time plasma regular donors (OR: 0·46, 95%CI: 0·32–0·68) also had lower odds of experiencing a loss of consciousness compared to first-time plasma new donors.

As gender, age and donor experience are a known risk factors for vasovagal reactions and differences in gender and age were observed between the new donor groups, we further investigated differences for new male and female donors separately adjusting for age (see Table 2). For males donating plasma, the odds of experiencing a vasovagal reaction were 1·17 times greater (OR: 1·17,

Table 2 Donor adverse event rates and odds ratios for new donors giving whole blood or plasma by gender[a]

	Male			Female		
	Plasma	Whole blood	OR (95% CI)	Plasma	Whole blood	OR (95% CI)
Donor adverse events	288 (10·3)	981 (6·8)	1·51 (1·31–1·73)[b]	474 (15·2)	2043 (10·3)	1·52 (1·36–1·69)[b]
Vasovagal reaction	211 (7·6)	895 (6·2)	1·17 (1·00–1·37)[b]	313 (10·0)	1865 (9·4)	1·04 (0·91–1·18)
Loss of consciousness	28 (1·0)	66 (0·5)	2·05 (1·32–3·21)[b]	17 (0·5)	101 (0·5)	1·04 (0·62–1·74)
Citrate reaction	30 (1·1)	n/a	n/a	103 (3·3)	n/a	n/a
Phlebotomy injury	60 (2·1)	93 (0·6)	3·38 (2·43–4·69)[b]	80 (2·6)	195 (1·0)	2·64 (2·03–3·43)[b]

[a]Data are reported as frequency (%) or odds ratio (95% confidence interval).
[b]$P < 0·05$.

95%CI: 1·00–1·37) and the odds of experiencing a loss of consciousness were 2.05 times greater (OR: 2·05, 95%CI: 1·32–3·21) than those who donated whole blood. The result for new female donors was not statistically significant for either vasovagal reaction (10·0% vs. 9·4%; OR: 1·04, 95%CI: 0·91–1·18) or loss of consciousness only (0·5% vs. 0·5%; OR: 1·04, 95%CI: 0·62–1·74).

Phlebotomy injuries were more prevalent in plasma (1·7–2·4%) than whole blood (0·8%) donors. Among new donors only, the odds of having a phlebotomy-related injury were 2.86 times greater when donating plasma compared to whole blood (OR: 2·86, 95%CI: 2·33–3·50). This increase in odds was observed for both male (OR: 3·38, 95%CI: 2·43–4·69) and female first-time donors (OR: 2·64, 95%CI: 2·03–3·43). On the other hand, no significant differences were found in phlebotomy injuries or in citrate reactions between the plasma groups.

Effect on return behaviour

Table 3 displays the rates of return within 18 months after a first plasma or whole blood donation by study group. The highest rate of return was observed in first-time plasma regular donors (82%), followed by first-time plasma returned donors (71%), first-time plasma new donors (69%) and first-time whole blood new donors (67%), $\chi^2(3) = 1·3e + 03$, $P < 0·01$. When examining the two new donor groups only and adjusting for age, gender, blood type, donation outcome and the occurrence of a donor adverse event, we found that the odds of first-time plasma new donors returning were 1·19 times greater than the odds for first-time whole blood new donors (OR: 1·19, 95%CI: 1·12-1·26).

Among those who returned, significant differences were observed in the proportion of donors returning to donate plasma, $\chi^2(3) = 8·1e + 03$, $P < 0·01$, the average number of subsequent total donations, $F(3,44\ 077) = 952·4$, $P < 0·01$, and subsequent plasma donations, $F(3,44\ 077) = 1704·3$, $P < 0·01$. The greatest proportion of donors returning to donate plasma was observed among first-time plasma returned donors (75%), followed by first-time plasma new donors (69%) and first-time plasma regular donors (65%). First-time plasma donors who had been regular whole-blood donors gave the highest subsequent donation counts, with an average of 5·4 (±5·3) subsequent total donations and 4·1 (±5·0) subsequent plasma donations. A Tukey HSD test, corrected for multiple comparisons, showed that all groups differed significantly from each other in subsequent total and plasma donations (all P's < 0·01), except for first-time plasma new donors and return donors in their subsequent plasma donation counts ($P = 0·38$). In particular,

Table 3 Return behaviour within 18 months by study group[a]

	Number of returned	Returned to donate plasma	Subsequent total donations[b]	Subsequent plasma donations[b]
First-time whole blood				
New donor	23 108 (67·5)	5463 (15·9)	3·1 ± 3·1	1·2 ± 2·9
First-time plasma				
New donor	4055 (68·5)	2786 (47·1)	4·5 ± 5·1	3·7 ± 4·9
Regular donor	15 243 (81·8)	9841 (52·8)	5·4 ± 5·3	4·1 ± 5·0
Returned donor	1675 (71·2)	1248 (53·1)	4·2 ± 4·5	3·6 ± 4·4

[a]Data are reported as frequency (%) or mean (standard deviation).
[b]Data reported only for those who returned to donate again.

new donors donating plasma gave more subsequent donations than new donors donating whole blood (4·5 vs. 3·1, $P < 0·01$) and more subsequent plasma donations (3·7 vs. 1·2, $P < 0·01$).

Time taken to return

A Kaplan–Meier survival curve was used to further investigate time to return over 12 months for first-time whole blood and plasma donors after becoming eligible to return to donate again (see Fig. 1). A log-rank test showed significant differences between the study groups, $\chi^2(3) = 1850·9$, $P < 0·01$. Of those who returned after the mandatory recovery period, first-time whole blood new donors took the least amount of time to return (mean, 61·5 days; median, 14 days), followed by first-time plasma regular donors (mean, 67·0 days; median, 35 days), first-time plasma new donors (mean, 79·3 days; median, 40 days) and first-time plasma returned donors (mean, 84·9 days; median, 42 days). All groups differed significantly from each other, except first-time plasma returned donors and first-time plasma new donors ($P = 0·14$).

Predictors of return among new donors

Predictors of the probability of return within 12 months were further investigating in new donors only using Cox regression to determine the effect of the policy change on new donors (see Table 4). Among both new donors who donated plasma and those who donated whole blood, being older (plasma and whole blood HR: 1·01) or having an O-Negative blood type (plasma HR: 1·23; whole blood HR: 1·48) significantly increased the likelihood of return, while not completing the donation (plasma HR: 0·67 whole blood HR: 0·65) or experiencing an adverse event (plasma HR: 0·83; whole blood HR: 0·64) decreased the likelihood of return. New donors who donated whole blood were also less likely to return if they received a temporary deferral (HR: 0·48) while being more likely to return if they donated at a mobile collection site (HR: 1·08). Finally, new donors who donated plasma were less likely to return if they were male (HR: 0·93).

Discussion

Due to increasing demand for plasma, changes were made to first-time plasma eligibility criteria with the aim of increasing the number of plasma collections in Australia. In our evaluation, we found that changing the criteria did not have negative effects on the rate of donor return. Further, first-time plasma new donors gave a greater number of subsequent plasma donations in the next 18 months than first-time whole blood new donors. These findings demonstrate that allowing new and previously lapsed donors to donate plasma is an effective strategy to increase plasma collections.

While we did not observe a negative effect of the policy change on donor retention, differences were observed in the rate of donor adverse events between the study groups. New donors were at a greater risk of experiencing a vasovagal reaction and a phlebotomy injury when donating plasma compared to whole blood. The latter is unsurprising as the longer duration time, draw and return

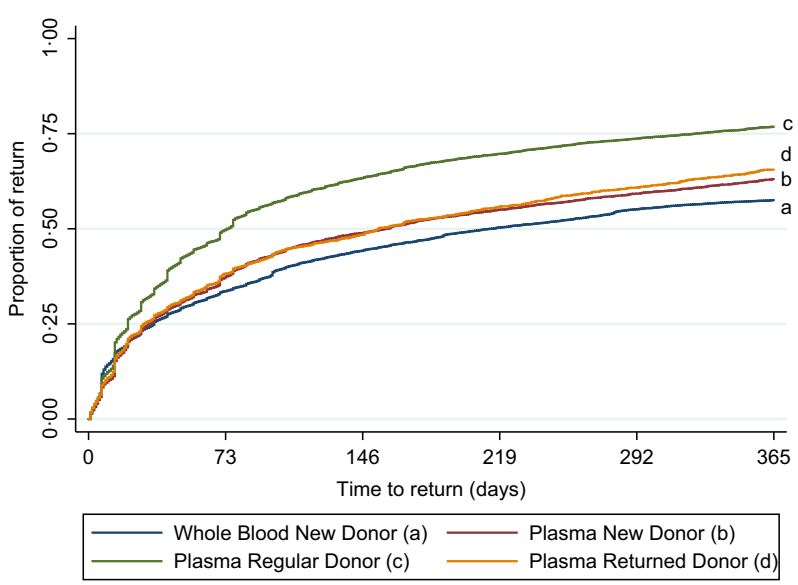

Fig. 1 Time taken to return within 12 months for first-time plasma and whole blood donors by study group [see additional file]. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 4 Hazard ratios for new donor return within 12 months

	Whole blood		Plasma	
Characteristic	**HR**	**95% CI**	**HR**	**95% CI**
Age (in years)	1·01	1·01–1·02[a]	1·01	1·01–1·01[a]
Male	0·97	0·94–1·00	0·93	0·87–0·99[a]
O-Negative	1·48	1·40–1·56[a]	1·23	1·07–1·41[a]
Mobile site type	1·08	1·05–1·12[a]	-	-
Donation aborted	0·65	0·57–0·74[a]	0·67	0·58–0·78[a]
Donor adverse event	0·64	0·59–0·69[a]	0·83	0·73–0·96[a]
Temporary deferral	0·48	0·34–0·69[a]	0·88	0·76–1·00

[a] $P < 0·05$.

cycles, use of anticoagulant and saline compensation increases the risk of phlebotomy injuries [4,5]. No significant differences were found in the rate of injuries or citrate reactions between the first-time plasma groups, indicating that new or previously lapsed donors were not at an increased risk of a phlebotomy injury or citrate reactions during plasmapheresis compared with experienced and recent donors.

Meanwhile, the highest rate of vasovagal reactions was observed in the first-time plasma new donor group, with new male donors being at a greater risk of experiencing a reaction when donating plasma compared to whole blood. This finding differs from the feasibility trial, which may be attributed to sample size differences (808 vs 5919 first-time plasma new donors) and the exclusion of donors aged less than 30 years in the feasibility study which resulted in an older study population compared to our cohort (mean age 43·2 years vs. 31·6 years). Further, while the observed rate of loss of consciousness was low, we did observe that first-time plasma new donors were at a greater risk than first-time whole blood new donors and first-time plasma regular donors. However, a knowledge gap currently exists on how to reduce the risk of vasovagal reactions in plasmapheresis [6]. First-time donors have described feeling anxious when confronted with the donation equipment and procedure, such as the cold sensation of the red cell return and the yellow colour of the plasma bag [7], and donors identify (the idea of) red cell return as a significant barrier to plasma donor recruitment *and* retention [8]. Despite the differences in donation experience, no studies have yet been published on strategies to prevent these reactions from occurring specifically in plasmapheresis donations. Addressing vasovagal reactions in plasmapheresis is an important issue for future research.

One of the key objectives of this evaluation was to examine the potential effect of a recent prior whole blood donation on subsequent donation behaviour. We found that first-time plasma regular donors had a higher rate of return, gave more subsequent donations and returned quicker than those going straight to plasma. This difference in return rate may be attributed to a greater proportion of regular donors returning to whole blood: while approximately half of all three first-time plasma donor groups returned to donate plasma again, a further 23% of regular donors returned to whole blood compared to 16% of new donors and 14% of returned donors. While it may be attributed to the effect of a recent donation experience which is a known predictor of return [9], it may also be that regular donors were able to compare their first plasma donation to a (more recent) whole blood donation experience. Bagot and colleagues [10] found that plasma donors who had lapsed back to whole blood were deterred by the required time and effort to donate plasma compared to whole blood. Therefore, regular donors may have made a more informed decision to convert back to whole blood, and that this was key to their retention. Donors without a (recent) whole blood donation may perceive any kind of donation as a costly behaviour and may not be able to differentiate between donation types. A better understanding is needed of first-time new plasma donor return and additional studies should be undertaken with this unique cohort to identify why new donors decide to continue to donate plasma or lapse.

Focusing on new donors, we found a greater proportion of males and younger donors donating plasma at their first donation appointment. This could potentially be attributed to staff targeting male donors, who they perceive as being more suited to plasmapheresis, or to males reporting a greater number of risky behaviours, such as travel, which prevent donors from giving whole blood. Similarly, Hirani and colleagues [11] found poorer vein suitability for blood donation among females compared to males. Therefore, more males may have been converted to plasma in our cohort based on vein quality. On the other hand, similar predictors of return were found between the two new donor groups; being older, and having an O-Negative blood type, a donor adverse event, and early termination of the donation procedure affected the likelihood of return within 12 months for both first-time plasma new donors and first-time whole blood new donors. However, a known deterrent to continued donation, being temporarily deferred from donation, was not found to discourage first-time plasma new donors. Further, while first-time plasma new donors had a greater subsequent donation count compared to first-time whole blood new donors, this may be attributed to a shorter donation interval for plasma (14 days) compared to whole blood (84 days) and not the donor's motivation to continue to donate.

In sum, offering new donors the option to give plasma did not affect donor return compared to those who

donated whole blood. Our evaluation extended the results from the feasibility, tolerability and acceptability trial to a national blood donor population, and we did not observe that early plasma conversion was a deterrent to continued donation. Removing the requirement of a prior whole blood donation is a viable way to increase plasma collections although the heightened risk of adverse events due to the combined effect of being a new donor and donating plasma needs to be considered. Our learnings may be useful to organizations collecting convalescent plasma from individuals with no prior blood donation experience.

Conflict of interests

The authors declare that they have no conflicts of interest relevant to the manuscript submitted to VOX SANGUINIS.

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ORIGINAL PAPER

Gone, but haven't forgotten: insights on plasmapheresis donation from lapsed donors

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Vox Sanguinis

Background and Objectives Blood Collection Agencies in several countries have implemented strategies to increase the number of plasmapheresis collections. Despite this, a sizable minority of plasma donors lapse from donation each year, with little research conducted on this topic. An understanding of the plasma donation experience from the perspective of lapsed donors, insights into why they stopped donating and their views on returning to donate may provide opportunities to intervene to increase the retention and reactivation of plasma donors.

Materials and Methods A qualitative approach was used in this study, with 17 lapsed plasma donors (no plasma donation for at least 13 months) interviewed. A purposive recruitment strategy was used to obtain a sample with diversity in gender (47% men), age (M = 36·2 years, SD = 13·6) and donation experience (M = 9·2 years, SD = 9·6). Semi-structured, narrative interviews were conducted, with participants describing their plasma donation careers chronologically from first donation to most recent.

Results The majority of participants described at least some aspect of the plasma donation procedure as unpleasant. However, adverse experiences were only attributed to lapsing in a minority of cases, with other participants reporting significant life events, perceived ineligibility and concerns about the safety of the procedure as the reason why they lapsed.

Conclusion It is common for lapsed plasma donors to intend to donate again in the future. Recommendations are given for strategies to address barriers to returning, noting the potential role of tailored education and support.

Key words: donors, lapse, plasmapheresis, retention.

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Introduction

Increasing the number of plasmapheresis donations is a priority for Blood Collection Agencies (BCA) committed to voluntary non-remunerated (VNR) donation. A declining need for red blood cells coupled with a strengthening demand for plasma for fractionation has led to a strong focus on moving whole blood donors to plasmapheresis and retaining donors within those panels. Retaining repeat donors is more cost effective than recruiting new donors. Further, repeat donors have fewer health risks than first-time donors and are less likely to be deferred from donating [1]. However, analyses show that the yearly attrition rate for the plasmapheresis panel in Australia is 40%, with approximately one-third lapsing back to whole blood and the remaining two-thirds lapsing from donating altogether [2]. Preventing accidental lapse from plasmapheresis and reactivating lapsed donors represent a timely, efficient and cost-effective approach to increasing the supply of plasma-derived products.

Most research on donor lapse is specific to whole-blood donation. Having a medical issue, a negative physical experience, inconvenience and time constraints have been identified as reasons for either lapsing from, or stopping,

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whole-blood donation [3–6]. Increasingly, research findings suggest that deterrents to donation, and reasons for lapsing from whole-blood donation, differ by gender, life-stage and country of donation [6–7]. Piersma and colleagues (2019) investigated the relationship between key life course-related events and donor lapse among whole-blood donors in the Netherlands and Denmark [7–8]. They reported that, among Danish donors, having a child and losing a job were associated with a greater risk of lapse, while in the Netherlands, starting a new job was associated with lapse. The authors also found that difficulty planning a donation, decreasing perceived health status and knowing fewer other donors partially explained why donors were more likely to lapse.

It remains unclear whether plasmapheresis donors lapse for similar reasons and at the same life stages. In a Canadian study, in comparison with whole-blood donors, current apheresis donors were more likely to nominate time constraints related to leisure activities and difficulties accessing a blood drive as deterrents to donation, while apheresis donors who had reduced their donation frequency were more likely to nominate reasons such as time constraints due to work or study, and difficulty accessing a blood drive [3]. These findings suggest that difficulties fitting donation into their lives are common deterrents to being an ongoing plasmapheresis donor. An earlier focus group study reported that deterrents to plasma donation differed between donors who had lapsed from donation altogether and those who had returned to donate whole blood. The former expressed lower levels of motivation and commitment to donation and were more likely to have experienced physical discomfort, such as difficulty finding a vein, during a donation [9]. Both those who lapsed altogether and those who lapsed to whole blood indicated that plasma donation was a costly behaviour in terms of the time and effort required.

More research is required to understand whether there are factors specific to donating plasma, in the context of donors' careers and life events, that contribute to donor lapse. Research is also required to enable BCAs to assist donors in overcoming barriers to ongoing plasma donation and minimise common triggers to donor lapse. This research explored lapsed plasma donors' experiences of donating plasma, reasons for not having donated recently and views about donating plasma again.

Materials and methods

A lapsed plasma donor was defined as someone who had previously made at least one plasma donation but had not donated plasma for more than 12 months prior to participation in the study. They were further classified into short-term lapsed (no plasma donation in 13-24 months) and long-term lapsed (no plasma donation in >24 months), following the categories used by Australian Red Cross Lifeblood. Given that few studies have explored the perspectives of lapsed plasmapheresis donors on their donation experience, and in the context of their individual life events and donation careers, a qualitative approach was considered the most appropriate method to facilitate in-depth understanding from the donor perspective [10].

The conceptual framework for the interviews and coding was derived from known reasons for lapsing from the whole blood and plasma literature, as well as insights into the influence of life-course factors on reasons for lapsing from donation [3,7,8]. A critical realist, interpretive approach was used, combined with deductive and inductive coding [11].

Selection and recruitment

This study was approved by the Australian Red Cross Lifeblood (formally known as the Blood Service) Ethics Committee. Donors aged 18-65 years, who had last successfully donated plasma more than 12 months ago, who were not currently deferred from plasmapheresis and who had a valid email address and phone number, were eligible to participate. To obtain a broad range of perspectives, we recruited participants with diversity in age, gender and donation experience (see Table 1.)

Contact details of eligible donors were extracted from Lifeblood's database, stratified on the basis of age group, sex and duration of lapse. Up to two call attempts were made and a voice message was left if the donor could not be reached. Two hundred and six donors were called at least once, with 59 donors answering. Of these, 37 agreed to participate. In total, 17 donors completed an interview with the remainder not answering the phone at the time of their scheduled interview appointment. A comparison of those who completed interviews and those who agreed to participate but did not complete an interview showed that they did not differ on gender ($\chi^2 = 0{\cdot}032$, $P = 0{\cdot}56$), age or length of donation career (all $t > 1{\cdot}39$, $ps > 0{\cdot}06$).

Interview procedure

Interviews were semi-structured and narrative, with participants asked to discuss their plasma donation careers chronologically from when they started donating plasma until the present. The opening question was 'Can you tell me how you first started donating plasma?', with the interviewer also asking participants about their experience of donating plasma and the last time they donated plasma [12–13]. An interview schedule guided the

Table 1 Donor characteristics by donor status

Characteristic	All donors (n = 17)	Lapsed: plasma only (n = 7; 41·2%)	Lapsed: whole blood and plasma (n = 10; 58·8%)
Age	36·2 (±13·6)	33·3 (±11·3)	38·2 (±15·3)
Sex			
Male	8 (47·0%)	5 (29·4)	3 (17·6%)
Female	9 (53·0%)	2 (11·8)	7 (41·2%)
Years as a donor	9·2 (±9·6)	9·0 (±5·0)	9·0 (±12.1)
Lapsed from plasma 13–24 months	15 (88·2%)	7 (41·2%)	8 (47·0%)
Lapsed from plasma >24 months	2 (11·8%)	0 (0%)	2 (11·8%)

interviews, to ensure that key questions were covered in each interview. Each interview lasted approximately 30 min with verbal consent obtained from each participant immediately prior to the interview. All interviews were recorded and transcribed verbatim and checked for inconsistences. Thematic saturation was determined to have been achieved after 10 interviews; seven additional interviews were conducted to ensure adequate data were obtained from all groups of interest.

Analysis

Two researchers (RT and LN) independently coded the first three transcripts using pre-identified categories derived from the literature, such as known reasons why blood donors lapse, the research aims and interview schedule [11]. New categories were also identified during this process. Double coding was conducted to ensure the identified categories made sense to both researchers, the categories were adequately defined, data were appropriately fitted into these categories, and to agree on a working coding framework [11]. The remaining transcripts were coded in NVivo 11 (QSR International) using this framework. Any new categories identified during this process were added to the coding framework [11].

Findings

Becoming a plasmapheresis donor

Three participants had donated plasma as their first donation, while the remaining 14 had been converted to plasma donation from whole blood. Of the latter, two were deferred from whole-blood donation, and another two were influenced by friends or family to donate plasma. The remainder had been informed by staff about the demand for plasma and the value of donating plasma or that plasmapheresis was the preferred donation for their blood type.

Donating plasma: donor reflections on the procedure

When asked to reflect upon their prior plasma donations, fewer than half the participants (n = 7) recalled the plasmapheresis procedure as positive or uneventful. Of the seven, those who had previously donated whole blood indicated that, aside from taking longer, they did not find donating plasma different from donating whole blood.

The remaining 10 participants indicated that they found one or more aspects of the plasmapheresis procedure physically unpleasant. These aspects were raised by participants during discussions about their experiences of donating plasma and were not directly mentioned as reasons for not donating plasma.

Several participants commented on the overall procedure being unpleasant; for example, the donor needing to actively monitor the progress of their donations on the apheresis machine and take steps to adjust their blood pressure in order to retain the flow. These donors indicated that they found this aspect of apheresis donation to be 'a bit more physically intensive', or that they were not certain whether they understood 'the readings on the machine' and were concerned about whether they would 'prolong the actual donation' by not pumping at the correct time.

Other participants indicated that specific elements of the procedure were unpleasant or difficult. For example, two donors said that the return of red cells was slow and/or difficult, and sometimes interrupted, and as a result the donation took longer. These donors believed that the difficulties were related to them having small veins:

> Actually, I normally have a bad experience, because I have a very tiny vein, so I hardly get any blood out, so it was always really slow, and I always had to squeeze really hard to get a little bit out. (P14, Female, 30–39 years)

This participant refers to having a 'bad experience' while donating plasma as the norm for her, suggesting

that she had experienced a difficult red-cell return on more than one donation.

Other aspects of plasmapheresis perceived by participants as unpleasant were the return of red cells feeling uncomfortable, feeling cold during the donation and having a citrate reaction. These donors indicated that even when the apheresis procedure works properly, being an ongoing plasma donor requires acceptance of some discomfort and a degree of adjustment to the procedure:

> I thoroughly enjoy giving plasma. How do I say that. That's not really exactly right. I certainly get the funny metallic taste in my mouth. . .Yes, you can feel the blood going back in when the cycle reverses, and you can feel the cells being literally pushed back in. It is cold, but it's actually understanding what plasma produces that actually makes me go back. Does that make sense? (P05, Male, 50–65 years)

Interestingly, this donor explains that, despite finding plasmapheresis physically uncomfortable, he finds donating plasma to be a positive experience and attributes this to understanding the uses of donated plasma. Other participants in this group said that they had continued to donate, despite finding the procedure uncomfortable, because of information given to them by staff about the uses of plasma, and having received adequate explanations from staff about the procedure before making their first plasma donation. These donors believed that knowing what to expect helped them tolerate the uncomfortable or unexpected aspects of apheresis and persist with donation:

> The nurse told me how it's processed outside of the body and then the red blood cells are returned. . .– it was pretty uncomfortable the first few times, but as long as they're cluing people in to what they might experience, then people don't get shocked, because they think oh, it's just happening to me, is something wrong? (Participant 3, male, 20-29 years)

Lapsing from plasma donation

When discussing their status as donors, most participants considered themselves to be current plasma donors despite not having donated for at least 13 months. Nevertheless, all mentioned one or more events or circumstances that contributed to them not having donated plasma recently. These were a change in circumstances or a significant life-event *(n* = 10), change in eligibility to donate plasma (*n* = 5), having a negative donation experience (*n* = 5), concerns about the safety of the apheresis procedure (*n* = 2),institutional reasons, such as staff implying that the demand for plasma is low and asking donors to donate whole blood (*n* = 2), and concerns about their health (*n* = 1). These will be discussed in detail in the following sections.

Change in circumstances or life-event

The majority of participants (*n* = 10) noted that a changed circumstance, including moving house, starting a new job, getting married, raising children, changing work hours and studying full time had contributed to donation becoming inconvenient. For example, some donors had moved away from their usual donor centre and had not had time to establish where their closest centre was or simply could not find a convenient location to donate. For one woman, this move was associated with retiring to a regional area further away from a donor centre. Others found that donating had become more difficult to fit into their lives due to changed work or study hours. The reasons given by these donors for not having donated recently were not directly related to plasmapheresis and may also have disrupted a whole-blood donation routine. However, it was notable that four of these 10 participants had also raised negative aspects of plasmapheresis donation.

> I moved back to Melbourne, with two kids and new work, and things happening, that [donating] just hadn't occurred to me yet. . . (Participant 13, male, 30-39 years)

Two participants who had been converted to donate plasma from whole blood indicated they had chosen to continue donating whole blood instead of plasma because of the convenience of donating at a mobile unit that visited their current workplaces regularly, which only allows for whole blood donation. While they could also donate plasma at a fixed donation centre in between whole blood donations, they were concerned that this practice would disrupt their whole-blood donation routines:

> . . .Apparently if you donate the plasma outside of the schedule of the whole blood, it can shift your whole blood forward. I enjoy not having to go out of my way all that much to donate whole blood, because the bus comes to work, it's convenient. So I try and manage it around the whole blood. (Participant 10, male, 20–29 years)

These examples suggest that donating may become less convenient for donors at particular stages of their lives and that changes in donation behaviour are not necessarily related to changes in motivation.

Perceived ineligibility

While all participants were eligible to donate at the time of the interviews, five indicated that a previous change in their eligibility to donate plasma resulted in an interruption to their donation routine. Specifically, they mentioned being deferred for a tattoo, being pregnant, having an adverse event, being concerned about their health and being asked to obtain clearance from a medical practitioner prior to donating again. Some of these donors were uncertain when or if they were eligible to return to donate. One participant had self-deferred because of a concern of the impact of donating upon her health and was waiting for medical test results before deciding whether to return to donate.

Having a negative donation experience

When asked to discuss why they had not donated plasma recently, five participants reported physical side-effects experienced during or after their last plasma donations. These participants recalled experiencing extreme tiredness post-donation, haematoma, citrate reactions, vasovagal reactions (VVR) and delayed bleeding. Of these donors, one was a first-time plasma donor. The donor who experienced the VVR said that he had been advised to donate whole blood for his next couple of donations before donating plasma again, while the donor who experienced the citrate response indicated that staff had advised her not to donate plasma again. Neither donor was officially deferred from donating plasma at time of interview. The donor who experienced delayed bleeding remained unaware of the cause, and while she expressed willingness to return to donate, she remained concerned that a re-occurrence of these symptoms would interfere with her work or caring for her children.

> During it and the whole process was fine, afterwards not so much which is why it's made it very tricky to go back. Because afterwards my arm wouldn't stop bleeding. (P16, Female, 40–49 years)

Concerns about the safety of the procedure

Two participants expressed concerns about the safety of the plasmapheresis procedure and indicated that these concerns were an ongoing deterrent to returning to donate plasma. Both indicated that they were unsure about the safety of having blood returned to them, and one also questioned the impact of frequent plasma donation on their general well-being. This donor commented that he would like to see evidence for the safety of the two-weekly minimum inter-donation period. Similarly, one of the donors who expressed concerns about the safety of the return of red cells recalled being given information about plasma by centre staff but felt that this was not enough for her to be sure about the safety. As a result, she preferred to donate whole blood:

> When you donate your plasma, your blood goes through a machine and coming back to your body. I'm not sure that the machine is single use. The part that my blood going inside and coming out, is that just for me? (Participant 4, female, 30-39)

This donor explained that she had donated plasma twice and had not considered the safety aspect until after the donation when she was at home. For that reason, she had not discussed her safety concerns with staff while at the donor centre.

Institutional reasons

Two donors (both O-positive) explained that they did not actively decide to stop donating plasma; however, staff had suggested that the demand for plasma was low at that time and indicated a preference for them to give whole blood at their subsequent donations:

> Last time I went in...they told me that they needed more whole blood...At the moment, they said there's no major demand for plasma, so if I could just keep giving whole blood every three months, they're happy enough for that...that's why I haven't returned to it [plasmapheresis], on the grounds that they didn't want it. (Participant 1, male, 30–39)

Returning to donate plasma

The majority of participants expressed a desire to return to donate plasma, and four noted that receiving a phone call from the researchers acted as a prompt for them to return to donate. Those who wanted to return indicated that their original reasons for donating were still relevant. Of the 59 donors who were invited to participate in the study but declined, 18 booked appointments to donate either plasma or whole blood after receiving the phone call. Other participants acknowledged that while they would like to return to donate, the circumstances contributing to them lapsing were still relevant. For example, the donors who lapsed because of changes in circumstances noted that time and availability remained barriers to returning:

> I know where the centre is, but I haven't had the time to do anything yet. I just have to work out a time. I feel like I want to go back, but haven't got

> the time, because I think I want to be more settled. (Participant 14, female, 30–39)

In contrast, those who had lapsed through being asked to donate whole blood or because of safety concerns indicated they were unlikely to return to donate plasma unless they received information from the BCA that either to allayed their concerns about safety or explained that plasma was needed and why.

Similarly, those who had stopped donating plasma because of physical side-effects at their last donation or health concerns indicated that these events remained either temporary or permanent barriers to returning to donate plasma. Some were considering changing their donation practice in response to their perception that their previous donation schedule was too taxing; for example, returning to whole-blood donation or donating plasma less frequently. Two participants indicated that they wanted to improve their physical condition before returning to donate plasma. While neither was unwell or ineligible to donate, they expressed a belief that they needed to improve their health or fitness because donating plasma was physically taxing and they wanted to be able to donate plasma successfully:

> I'll try to wait till I'm tip-top and got some spare time (Participant 8, male, 20–29 years)

Discussion

This paper presented the findings of interviews with 17 plasmapheresis donors in Australia who had not made a plasma donation for at least 13 months. Our interviews with these lapsed plasma donors explored their past experiences of donating plasma, the influences on their lapse and their views on returning to donate plasma. This approach provides insights into how lapsed donors view their relationship with donating and can help inform when and how to intervene to prevent lapse or to reactive lapsed donors.

Participants tended to view themselves as current plasma donors despite not having donated plasma for over a year. As such, it seems that self-identity as a donor is not tied to recency of donation and this may be important for BCAs to recognise when designing communication strategies for use with this cohort of donors. This finding also suggests that lengthy donation breaks may not always be related to changes in motivation. Rather, and consistent with previous research [5,7–8], as donors transition through different life stages, particularly moving house, changing jobs or having children, routines may be disrupted and donating plasma may become inconvenient and difficult to prioritise. Perceived (in)convenience is a recognised barrier to retention [6], and these data suggest that this can also impact the decision of which product to donate, particularly given the additional time requirements of plasmapheresis. The attachment of donors whose motivation remains but whose behaviour has been disrupted by life events is perhaps 'stickier' than other donors who lapse from plasmapheresis. As such, this group may be relatively easier to reactivate in the longer term whether the BCA acts to maintain their connections with these donors.

As has been reported for whole-blood donors, temporary health concerns and perceived ineligibility due to previous deferrals disrupted donation practices [1,14–16]. Concerns about the ongoing safety of the process had similar effects. For these donors, events associated with their plasmapheresis experience had impacted their fundamental motivation to donate. Identifying the reason for lapse, therefore, may be critical for BCAs to target their approach to reactivation. As shown in the current study, some donors simply need an additional reminder (such as an invitation to participate in a study) in order to return. Others will require more from the BCA in terms of assurances. Additional research is required to determine whether and under which circumstances lapsed donors return.

It is possible that some participants did not intend to return to donate plasma, despite indicating to the interviewer that they did. For example, a number of participants noted that plasmapheresis is not always pleasant, and these perceptions may have deterred them from returning even if they did not report this when asked for their reasons for not donating. In other studies, lapsed plasma donors cited negative physical experiences while donating as deterrents to donating plasma [9,17–18]. Research with lapsed donors has found that they are less likely to return if they perceive the costs to be too high [12]. Perhaps the combination of discomfort and inconvenience led some donors in the current study to appraise plasma donation as too costly at present [12].

Our findings indicate that when donors understand the apheresis procedure, know what to expect, and understand the uses of plasma, they are less likely to be concerned or anxious about any physical sensations that do occur. Other studies have noted the importance of donor centre staff providing reassurance and explanation to first-time plasma donors, or those considering plasma donation [4,9,12,19–20]. In our study, concerns about the procedure were raised by experienced as well as first-time donors, indicating BCAs should provide ongoing opportunities for donors to access information and ask questions to allay concerns and normalise any adverse experiences [21]. Such support may facilitate continued donation.

Our study supports recommendations for BCAs to communicate clearly with donors about their preferred

donation type when the organisation collects both whole blood and plasma [18]. Donors converted from whole blood to plasma with the explanation that plasma is more in demand are unlikely to return to donate whole blood if they cannot or no longer wish to donate plasma, unless this request is accompanied by an explanation from staff about the need for both products [21]. Similarly, plasma donors asked to donate whole blood on occasion need to be told that their preferred donation type on the day may change depending upon inventory needs, to reduce the risk of them lapsing from the plasma panel.

Our findings are limited by the small sample size and low response rate (27%), which may be expected in a study of people no longer actively engaged in donation; however, we did reach thematic saturation. Our sample is not representative and there is a possibility that those who chose to participate in this study were more positively disposed towards future plasma donation than those who did not agree to be interviewed. Despite this concern, the findings from this study challenge the traditional view of the 'lapsed' donor and indicate that there are opportunities to retain plasma donors, through improved communication, education and support, and to reactivate many of these donors when they have not presented for a period of time.

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Conflict of interests

The authors declare no conflict of interests.

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ORIGINAL PAPER

Characterization of health issues in young first-time blood donors

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Vox Sanguinis

Abstract

Background and objectives Blood donors, especially young donors, are considered a healthy segment of the population. We sought to identify medical issues that may warrant medical referral in young first-time blood donors.

Materials and methods A retrospective cohort study was performed in first-time donors ages 16–22 who presented in a system of nineteen regional United States blood centres over 10 years. Donor health attributes characterized include body mass index, blood pressure, total cholesterol and pre-donation haemoglobin. Using standardized definitions, overweight and obese body mass, hypertension, elevated cholesterol and anaemia were identified and characterized in this donor population.

Results Among 825 041 young first-time donors presenting between January 2009 and December 2018, with available measurements, 46·9% were either overweight or obese, 59·8% demonstrated high blood pressure (22·2% elevated blood pressure, 37·6% stage 1 or 2 hypertension), elevated cholesterol was identified among 6·3% of males and 8·8% of females, and anaemia was present in 3·5% of males and 5·2% of females. During the study period, all unfavourable health outcomes significantly increased in prevalence ($P < 0·0001$) when comparing 2009 vs. 2018 rates.

Conclusion Elevated weight and obesity are common in young first-time allogeneic United States blood donors, with fewer donors having elevated total cholesterol or anaemia. Such medical issues may have significant importance for future health and well-being as well as continued donor eligibility. Blood centres may be able to help support the identification and mitigation of important medical issues in donors and provide a public health benefit.

Key words: donor health, donors, donor motivation, blood collection, blood donation testing.

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Introduction

Blood centres rely upon healthy volunteer donors in order to support a safe and stable supply of blood. During donor qualification, a series of overlapping safeguards are utilized including a health history questionnaire, a limited physical examination and donor testing. Such donor eligibility criteria are intended to support a safe donation experience; however, it does not necessarily reflect an absence of underlying medical issues which may be of importance to long-term health.

Adolescence and young adulthood are often considered to be the healthiest period in an individual's life, falling between the peaks of early childhood mortality and the development of chronic disease conditions in later adulthood. During adolescence and early adulthood, individuals establish behavioural foundations that define health trajectories into later life. Therefore, implementation of

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healthy lifestyle interventions during this formative period can have significant impact on reducing later disease states and improving long-term well-being. While adolescents and young adults are generally considered to be healthy, it has increasingly been recognized that modifiable chronic health risks may exist in this group. Early obesity has significant public health implications given a strong association with other health complications, premature mortality, reduced quality of life in adulthood and increased healthcare expenditures [1].

While there has been heightened recognition of the types of medical conditions that may exist in adolescence and young adulthood in the general population, the impact and prevalence of this has not been fully characterized in this donor cohort. Such information may be useful not only to help support donor safety and availability during individual blood donation encounters but also to help support longitudinal public health surveillance and community health improvement initiatives. Using blood donor and donation data from a large US blood system, we sought to characterize medical issues that may be present in young first-time blood donors.

Materials and methods

Vitalant provides blood and special services to patients in more than 1000 hospitals across 40 states in the United States with approximately 1·8 million donations per year. Out of the 26 regional centres based in 19 states from coast-to-coast, our data set included data on donations from 19 regional centres across 14 states from collections using the same blood establishment computer system during the analysis period. We included de-identified data obtained from all first-time allogeneic donors who presented over a ten-year period between January 2009 and December 2018 with a focus on young first-time donors (YFTD) age 16–22 years. Only the first visit data were included for donors who presented or gave more than one donation during the analysis period. Donor race/ethnicity, weight and height were self-reported by donors, while blood pressure (BP) and haemoglobin (Hgb) were measured and recorded by the staff during routine donor qualification.

Blood pressure was evaluated using either a validated automated vital sign instrument or a manual sphygmomanometer. Donor BP was classified as normal with systolic blood pressure (sBP) <120 mmHg and diastolic blood pressure (dBP) <80 mmHg; elevated BP was sBP 120-129 mmHg and dBP <80 mmHg; stage 1 hypertension (HTN) was sBP 130–139 mmHg or dBP 80–89 mmHg; and stage 2 HTN was sBP ≥140 or dBP ≥90 mmHg [2]. Point-of-care quantitative Hgb using a Hgb analyser (HemoCue 301, HemoCue, Inc., Lakeforest, CA) was used for donor qualification using a pre-donation capillary fingerstick sample. Donor anaemia was defined as Hgb <13·5 g/dL in males and <12·0 g/dL in females [3]. Donor body mass index (BMI) was calculated using self-reported height and weight in kg/m^2. BMI was calculated separately for 16- to 18-year-old donors using the paediatric calculations and considering CDC growth chart references [4]. Overweight BMI was defined as 25·0–29·9, obesity as BMI ≥ 30·0, and severe obesity as a BMI ≥ 40·0 [5]. Donor blood pressure, height, weight and haemoglobin were available for most presenting donors. Non-fasting total cholesterol (mg/dL), on the other hand, was obtained only with a successful donation. Cholesterol < 200 mg/dL was classified as being desirable and ≥200 mg/dL as borderline high/high [6]. The distribution of donors, donation and medical screening/health characteristics were summarized for males and females separately and overall. Multivariate analyses were performed to assess factors associated with each of the YFTD health outcomes. Health outcomes between 2009 and 2018 for the various health outcomes (2010 vs. 2018 for Hgb) were compared using chi-square tests with $P < 0·05$ classified as statistically significant. Data management and analyses were performed using STATA/MP 15.1 (StataCorp LP, College Station, TX, USA) and Microsoft Excel 2010 (Microsoft, Inc. Redmond, WA, USA).

Results

Study inclusion criteria were met by 825 041 YFTD over a 10-year period from January 2009 to December 2018 (Fig. 1). First-time donors represented 65% of total unique donors, and 50% of first-time donors were between the ages of 16 and 22. Over 9 million total allogeneic donation visits occurred over the study period, and YFTD represented 33% of total unique donors. Blood donor and donation characteristics for this group are presented in Table 1. The majority of YFTD were females (51·8%), 16–17 years of age (57·1% YFTD), and white (50·3%) or Hispanic (35·0%). Twenty-one per cent of presenting YFTD were ineligible to donate and no collection procedure was performed. Complete characterization of deferrals for this group was not performed; however, for this age group, deferrals are predominantly due to an unacceptable haemoglobin, vital signs outside of range or low estimated total blood volume. Over the ten-year study period, there was an increase proportion of YFTD until 2014 (53·6% of first-time donors), after which there was a steady decline with overall less young first-time donors in 2018 (45·4% of first-time donors) compared to 2009 (47·4% of first-time donors).

Donor health characteristics evaluated are presented in Table 2 and include characterization of donor BMI, BP,

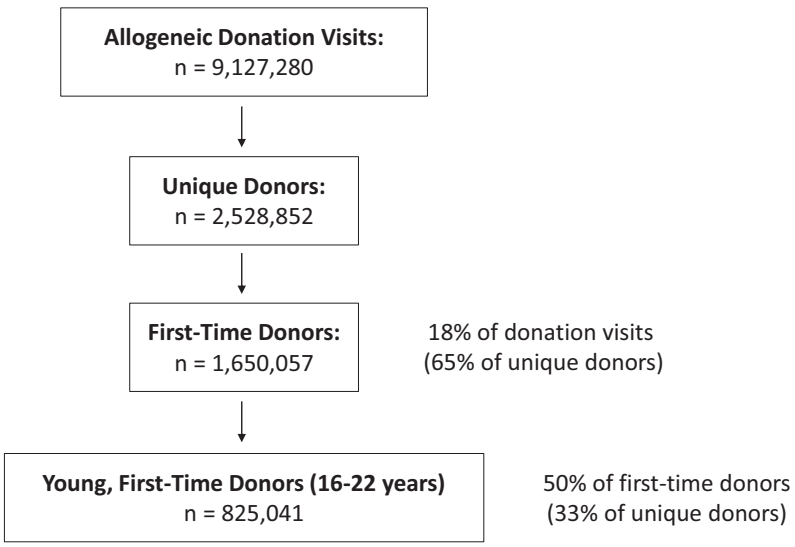


Fig. 1 2009–2018 blood donations.

Table 1 Donor and donation characteristics, young first-time donors 2009–2018

		Young first-time donors		
Donor/donation characteristics		**Total 825 041**	**Male 397 994 (48·2%)**	**Female 427 047 (51·8%)**
Age Group (years)	16–17	57·1%	53·7%	60·2%
	18–19	27·3%	29·8%	25·0%
	20–22	15·7%	16·5%	14·9%
Race/Ethnicity	Black, non-Hispanic	7·5%	6·9%	8·1%
	Hispanic	35·0%	35·2%	34·8%
	Native American/Alaskan, non-Hispanic	2·0%	1·8%	2·2%
	Asian or Pacific Islands	2·7%	3·0%	2·4%
	White, non-Hispanic	50·3%	50·5%	50·0%
	Other	2·4%	2·5%	2·4%
Intended Collection	Whole Blood	83·3%	71·3%	94·6%
	2RBC apheresis	14·4%	27·0%	2·6%
	Plasma, platelet, or multicomponent apheresis (+/– RBC)	1·1%	1·1%	0·9%
	Undefined	1·3%	0·7%	1·8%
Procedure Outcome	No Phlebotomy	21·2%	13·2%	28·7%
	Successful Phlebotomy	74·8%	83·2%	67·0%
	Unsuccessful Phlebotomy	4·0%	3·6%	4·3%
Collection Site	Fixed site	5·3%	5·0%	5·6%
	Mobile bus	27·2%	27··5%	26·9%
	Mobile set-up	67··5%	67·5%	67·5%

cholesterol and Hgb. Forty-seven per cent of young first-time donors were found to be either overweight (28·3%) or obese (18·6%). Sixty per cent of YFTD had a BP reading at the time of donor qualification which would be considered elevated (22·2%) or either stage 1 (24·9%) or stage 2 (12·7%) hypertension. During the study period, all health outcomes significantly increased in prevalence ($P < 0·0001$) when comparing 2009 vs. 2018 rates for HTN (32·8% vs. 38·5%), overweight/obesity (44·5% vs. 52·1%) and elevated cholesterol (6·5% vs. 8·5%) and between 2010 vs. 2018 for low haemoglobin (3·5% vs. 4·3%). Elevated donor weight/obesity, HTN and elevated

cholesterol were found to have positive associations in multivariate analyses (Fig. 2). Males (compared to females), 20- to 22-year-old donors (compared to 16- to 17-year-old donors), overweight/obesity and donors with cholesterol ≥200 mg/dL had higher odds ratios (OR) for HTN. Non-white donors, higher BP and cholesterol ≥200 mg/dL had higher OR for elevated donor weight/obesity. Finally, 18- to 22-year-old donors (compared to 16- to 17-year-old donors), overweight/obesity and donors with higher BP had higher OR for elevated cholesterol. Statistically significant variation in donor health outcomes was noted in multivariate analysis among the 19 regional blood centres evaluated (data not shown). Compared to first-time donors of other age groups, the proportion of donors with overweight/obesity, hypercholesterolaemia, HTN and anaemia increased with age (Fig. 3).

Discussion

Using a large blood donor and donation data set from nineteen US blood centres in our organization, we characterized the prevalence of important health conditions in donors generally considered to be among the healthiest in the population. We identified a variety of underlying medical issues that may have significant impact on future donor health, quality of life and continued donor eligibility. Unfortunately over the 10-year study period, an upward trend is observed in every unfavourable health outcome.

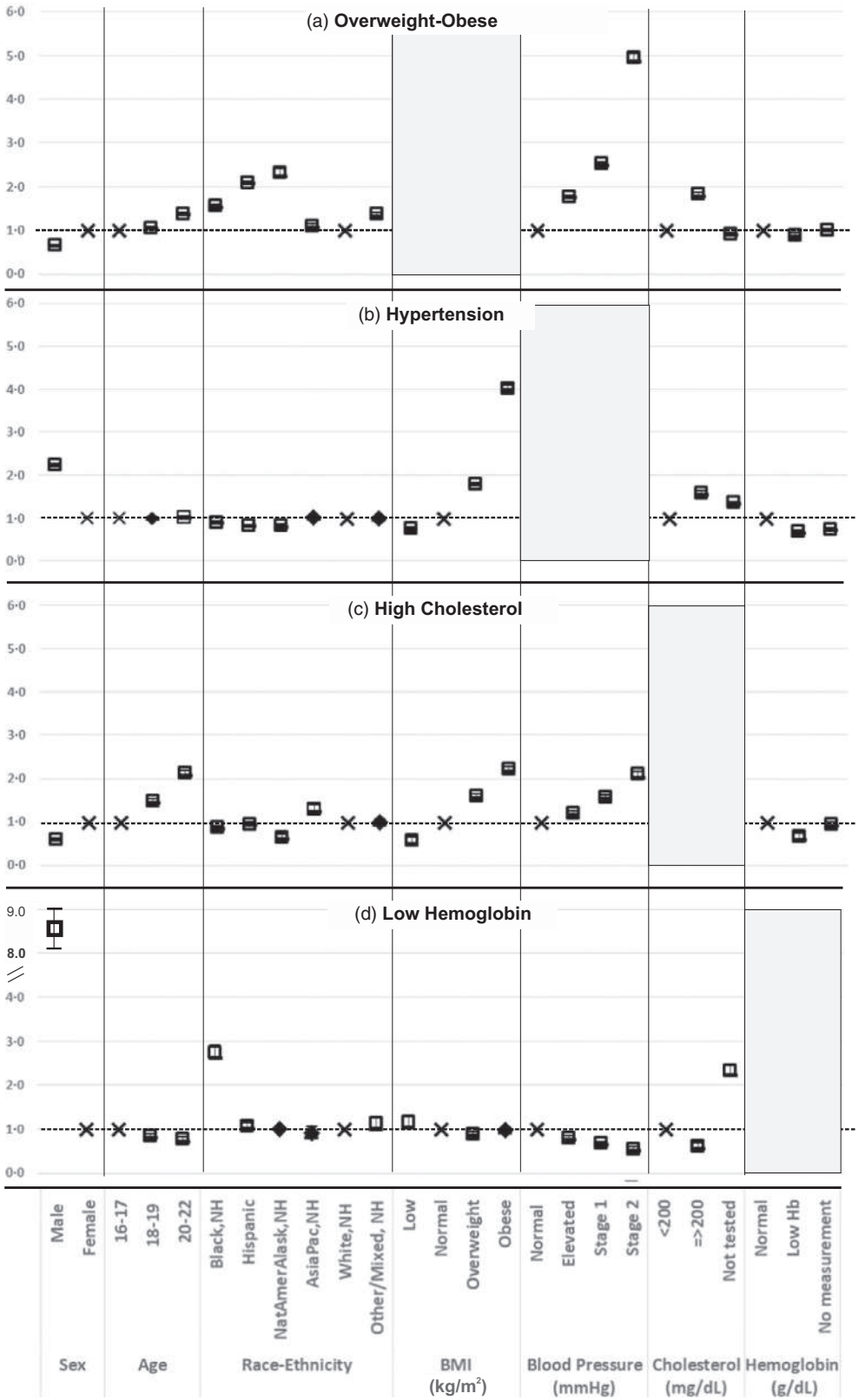
We found a YFTD obesity rate of 18·6%, similar to the reported prevalence of 20·6% in the general US adolescent population age 12–19 years [7], yet still higher than the public health target of 14·5% for children and adolescents [8]. Elevated donor total cholesterol was found in 7·5% of our YTFD and is modestly lower than the reported prevalence of 8·9% in the general US adolescent population age 16–19 years [9]. Lower rates of obesity and elevated cholesterol in donors are likely due to a selection bias in which blood centres select for healthy individuals to donate and individuals with a higher baseline level of health self-select for initiating interest in blood donation. Additionally, cholesterol data were limited to only successful donations rather than all presenting donors.

In contrast to the rates of obesity and elevated total cholesterol, we found a higher rate of elevated BP and HTN in our YFTD compared to the general population.

Table 2 Donor health characteristics, young first-time donors 2009–2018

		Young first-time donors		
Health characteristics		**Total 825 041**	**Male 397 994**	**Female 427 047**
Blood Pressure (ACC-AHA Classification)	Total with BP reading	737 390 (89·4%)	380 337 (95·6%)	357 053 (83·6%)
	Normal	40·3%	29·2%	52·2%
	Elevated	22·2%	26·0%	18·1%
	Stage 1 hypertension	24·9%	27·2%	22·4%
	Stage 2 hypertension	12·7%	17·7%	7·3%
BMI (kg/m^2)	Total with BMI measurement	761 565 (92·3%)	378 540 (95·1%)	383 025 (89·7%)
	Underweight	1·6%	2·1%	1·1%
	Normal	51·6%	52·3%	50·9%
	Overweight	28·3%	27·4%	29·1%
	Obese	18·6%	18·3%	18·9%
Cholesterol (mg/dl)	*Total with cholesterol measurement	614 004 (74·4%)	329 615 (82·8%)	284 389 (66·6%)
	<200	92·5%	93·7%	91·2%
	≥200	7·5%	6·3%	8·8%
Haemoglobin (g/dl)	Total with Hgb measurement	705 789 (85·5%)	344 540 (86·6%)	361 249 (85·5%)
	<12·0	2·7%	0·1%	5·2%
	12·0–12·4	2·9%	0·2%	5·5%
	12·5–12·9	7·7%	0·9%	14·2%
	13·0–13·4	9·8%	2·3%	16·9%
	13·5–14·4	22·2%	10·6%	33·3%
	14·5–15·4	21·5%	24·3%	18·8%
	>15·5	33·2%	61·7%	6·1%

*Cholesterol result available only with successful donation.



X Reference Category; ◫ OR (95% CI) statistically significant difference from **X**; ◆ OR (95% CI) no significant difference from **X**

Fig. 2 Multivariate analysis of factors associated with young first-time donor health outcomes.

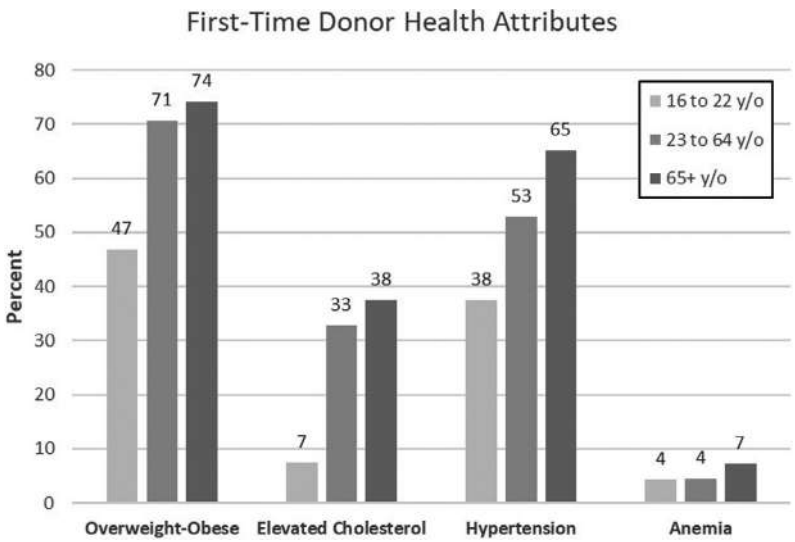


Fig. 3 Health attributes in first-time donors, across age group.

Thirty-eight per cent of our YFTD had a stage 1 or stage 2 HTN blood pressure reading at the time of presentation compared to a 1–5% reported prevalence of HTN in US children and adolescents [10]. Of note, however, the definitional criteria for HTN have changed in recent years complicating comparative analysis. Additionally, the diagnosis of HTN requires an elevated BP on at least three separate readings in order to establish a normalized baseline evaluation and we only had a single BP reading to evaluate. Therefore, while some of our YFTD may truly have essential HTN, others may have had a high BP reading due to donor anxiety during their first-time donation experience. Multimorbidity, the coexistence of two or more chronic conditions, has become prevalent among older adults as mortality rates have declined and the population has aged. Not surprisingly we also found multimorbidity in our YFTD cohort as noted in multivariate analysis.

Adolescent and young adulthood obesity, elevated cholesterol and hypertension are important public health issues as these are predictive of continued abnormalities into adulthood as well as the development of future health complications, lower quality of life and increased mortality [1,10–12]. Given the relative frequency of the donor encounter, the breadth of medical information gathered, functional blood centre core competencies and a 'lifesaving' mission, a potential expanded role of blood centres as a community health resource has been proposed [13–14]. The New York Blood Center has explored an expanded community health role in hypertension detection, counselling and referral [15] as well a comprehensive cardiovascular disease risk screening programme [16]. The latter involved point-of-donor care testing for cholesterol, HDL and Haemoglobin A1c (HbA1c) as well as measuring donor body mass index, waist circumference and BP. As a community health service, Oklahoma Blood Institute provides a fasting lipid panel as well as prostate specific antigen (PSA) screening for purchase with or without an associated blood donation [17]. Finally, Carter BloodCare has described their experience in implementing a regional HbA1c screening programme in a large adolescent blood donor population as a means to support public health [18].

Addressing chronic medical issues often requires long-term lifestyle and dietary changes which are best addressed through a comprehensive systems approach. The more an environment consistently promotes healthy behaviour, the greater likelihood such behaviour will be implemented and successful [19]. Blood centres should, therefore, consider the supportive role they may play in addressing donor health. Given resource and scope of practice limitations, it is unlikely that blood centres will function as a primary responsible provider in preventative health care. However, blood centres do have access to important donor health data and can reinforce and support healthy lifestyle choices through regular engagement with donors and utilization of online donor profiles containing donor health data (e.g. Hgb, BP, weight, calculated BMI, cholesterol) that can help track progress. Online donor portals currently exist within many blood

centres and may be expanded to provide a greater focus on donor health, educational materials and referral to, integration with, available public health resources. A blood centre role in supporting donor health serves the dual purpose of fostering donor engagement while additionally helping to support continued donor health and eligibility. Blood centre activities in this area should be evaluated to ensure all ethical, regulatory and privacy considerations are addressed.

Strengths of this study include the large number of donors and the evaluation of medical issues in a first-time young donor population that has not been fully characterized to date. Study limitations include the fact that only a snapshot of donor health status was obtained. Only a single BP was measured at the time of donor presentation, and therefore, this may be influenced by first-time donor anxiety and may not be reflective of true donor hypertension. Additionally, donors self-reported height and weight and therefore donor BMI classification may have been influenced by inaccurate donor estimates. As our YFTD cohort ranged from 16 to 22 years of age, for ease of reporting and consistency of definitions we utilized adult, rather than adolescent/paediatric definitions of hypertension and elevated total cholesterol. This study was limited to the characterization of YFTD health, and we do not have follow-up data related to any health issues identified and whether donors sought additional medical attention.

First-time adolescent and young adult donors represented 33% of total unique donors in our study and are an important donor cohort for the continued provision of a safe and stable blood supply for patients. It is in our interest, as well as the interest of donors, to help address chronic medical issues and help maintain donor health. Because adolescent health issues like obesity strongly predict continued obesity and the development of comorbidities in adulthood, adolescence and young adulthood is a particularly useful age group for initiating effective health interventions. Further research and review are required to evaluate the efficacy of any blood centre interventions in addressing chronic donor medical issues.

Conflict of interest

No author conflicts identified.

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ORIGINAL PAPER

Research initiatives of blood services worldwide in response to the covid-19 pandemic

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Background and Objectives While coronavirus (COVID-19) is not transfusion-transmitted, the impact of the global pandemic on blood services worldwide is complex. Convalescent plasma may offer treatment, but efficacy and safety are not established. Measuring seroprevalence in donors would inform public health policy. Here, we survey blood services around the world to assess the different research programmes related to COVID-19 planned or in progress.

Materials and Methods Blood collection services were surveyed in June 2020 to determine whether they were participating in serosurveys or convalescent plasma collection and clinical trials.

Results A total of 48 countries (77% of those contacted) responded. Seroprevalence studies are planned or in progress in 73% of countries surveyed and in all continents, including low- and middle-income countries. Most aimed to inform public health policy. Convalescent plasma programmes have been initiated around the globe (79% of surveyed), about three quarters as clinical trials in high-, middle- and low-income countries.

Conclusion Blood services around the world have drawn upon their operational capacity to provide much-needed seroprevalence data to inform public health. They have rapidly implemented preparation of potential treatment when few treatments are available and mostly as clinical trials. At the same time, they must continue to provide blood products for recipients despite challenges of working in a state of emergency. It is important to track and coordinate research efforts across jurisdictions to gain a composite evidence-based view that will influence future practice and preparative strategies.

Key words: convalescent plasma, COVID-19, research, seroprevalence.

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Introduction

The emergence of coronavirus disease (COVID-19) in late 2019 has strained healthcare services, in some cases beyond their capacity. Worldwide, there have been more than 10 million diagnosed cases and over 500 000 deaths as of 30 June 2020 [1]. Public health policies to address risk have included cancellations of elective surgeries and

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recommendations that people self-isolate. While COVID-19 has not been reported to be transfusion-transmissible, blood services around the world have been impacted in a variety of ways [2]. Surgery cancellations prompted rapid adjustment to blood collections, and aligning supply of components with demand for those components has been challenging. Some donors stopped donating to avoid social contact, but for others the sudden crisis motivated them to donate. Supply chains were threatened including availability of consumables for collections. Staff availability was reduced. Concomitant with these operational challenges has been a need to gear up for research specific to COVID-19.

Given the lack of proven effective treatment options, the potential for convalescent plasma to treat COVID-19 became a very high-priority research topic. The benefit was unclear from early reports with adverse events apparently rare [3–5]. However, neither the efficacy nor the safety has been conclusively shown. The dose criteria have not been established, and assays for qualifying plasma have been in various stages of rapid development [6]. As it is *sensu stricto* a new therapy, regulatory bodies in some countries have been unwilling to license blood establishments to collect and distribute convalescent plasma [7]. Rapid mobilization of clinical trials enabled this treatment to be available and studied.

Management of public safety during the pandemic relies on quality data. In the early phase of the pandemic, infection rates were monitored through nucleic acid testing of symptomatic individuals and counting the number of deaths attributable to COVID-19 infection [8]. These measurements are prone to certain biases. For example, the number of individuals testing positive depends on the criteria for being tested and the availability of tests. The apparent death rate will be higher or lower depending on the testing strategy and the characteristics of the population and the availability and extent of medical care. Population-based studies on the proportion of people with COVID-19-specific antibodies will provide a clearer estimate of the number of individuals who have been infected with COVID-19. These will allow evaluation of the efficacy of risk mitigation strategies and will aid in the mathematical modelling of the future course of the pandemic [9,10]. The World Health Organization has recommended that countries conduct seroprevalence studies and has indicated that blood donors are a suitable study population [11].

There have been early reports describing convalescent plasma research [4,12] and seroprevalence studies in blood donors [10,13,14]. The breadth of such research in blood centres has not yet been reported, but the scope of initiatives is important to describe in order to encourage collaboration and knowledge sharing. We aimed to canvas blood services in as many countries as possible to understand the types of research different organizations are engaging in relative to COVID-19.

Methods

The survey instrument was distributed as an Excel spreadsheet and participants were asked about the region they were reporting for, whether donor seroprevalence studies were planned or in progress, and if so, the types of study design. The survey also collected information on whether the services had programmes to collect from donors who have recovered from COVID-19 infections including both convalescent plasma programmes and programmes to collect plasma for hyper-immune immunoglobulin.

A list of contacts was compiled from the membership of the International Society of Blood Transfusion (ISBT), Transfusion Transmitted Infectious Diseases Working Party and individuals who volunteered when contacted by a representative of the European Blood Alliance – Emerging Infectious Disease Monitoring Working Group. Additional participants were identified by the investigators. In June 2020, all potential participants were invited by email to complete the questionnaire on behalf of their country, or else for their region, or blood service. A data set of responses was compiled and sorted by geographic region to prepare summary tables.

Results

Overall, 79 contacts from 62 countries were invited, and 65 blood centres (82% of those contacted) from 48 countries (77% of countries with at least one contact) completed the questionnaire. These included responses from all continents (see Fig. 1). Many of the respondents reported on research being conducted in some or all areas of their country. For some countries, we received reports for one or more regions, or services within that country, which we have reported for the country although it is possible other research is being conducted in some other parts of the country. Many were from a large city or region such as Guatemala City, Mexico City, Ankara, in Turkey and Khartoum state in Sudan. Others provided diverse patches from their country. For example, from India there were blood centres in Udupi District, Manipal (south-west India), Raipur (central India), Saurashtra Region of Gujarat state (north-west India) and Chandigarh (North India). In China, questionnaires reporting activities in Hong Kong, Guangzhou, Macao, Wuhan, Chengdu, Shenzhen and Shanghai were received.

As shown in Table 1, 32 of 48 (73%) countries have a seroprevalence study planned or in progress. Most Western countries are carrying out seroprevalence studies,

Fig. 1 Participation in the survey: (■) – participation, (▬) – invited but no participation, (□) – not contacted.

and most have serial cross-sectional designs to be able to track the infection rates in donors over time. Many centres in Asia, Africa, the Middle East and Latin America including some in low- and middle-income countries are also conducting seroprevalence studies, but more have single cross-sectional designs. Only a few countries have longitudinal cohort studies (tracking antibodies in the same donors over time). The majority of seroprevalence studies are intended to inform public health policy.

Table 2 shows the responses related to convalescent plasma programmes. Overall 38 of 48 countries (79%) have a convalescent plasma programme, 29 (76%) of these as a clinical trial. All European countries who responded to the survey, as well as respondents from the United States and Canada, have convalescent plasma programmes, and most are involved in clinical trials. Many centres in Africa, Asia and the Middle East also have convalescent plasma programmes, and about half are involved in clinical trials. The United States and some countries in Europe and Korea, Egypt and Turkey have programmes for hyper-immune immunoglobulin either planned or in progress.

We also asked respondents whether they were engaged in any other research activities; in response, some provided additional information. For example, blood services have a role in vaccine-related research (the Netherlands, Kenya) and studies in patient groups (the Netherlands, Spain, Brazil), as well as research on donor health, behaviour and awareness (the Netherlands, India, Cameroon).

Discussion

This survey provides a snapshot of COVID-19 research in progress in blood services around the globe as of June 2020, approximately 6 months since the first case reports from Wuhan [15] and three months since the World Health Organization declared COVID-19 a pandemic [16]. The pandemic has progressed through its first wave in Europe, Canada, Australia and New Zealand, whereas cases continue to increase in other areas [1]. The two most salient observations are that blood services worldwide have engaged in seroprevalence studies primarily to inform public health policy, and they have initiated convalescent plasma programmes, many within the framework of clinical trials.

Due to the rapid pace of activity during the pandemic, much of this research has been developed within country rather than as large internationally coordinated studies. There has been interaction and sharing of information. For example, the European Blood Alliance facilitated knowledge exchange on convalescent plasma via online meetings and an online site where protocols could be uploaded to share. Starting a little later in the course of the pandemic, six francophone African countries are carrying out seroprevalence under the umbrella of AfraCoV-

Table 1 Seroprevalence studies, International COVID-19-Related Research

Region	Country	Seroprevalence	Single cross-sectional	Serial cross-sectional	Longitudinal cohort	Informing public health policy	Informing convalescent plasma programme
United States/Canada	Canada	Seroprevalence studies		✓		✓	✓
	United States			✓	✓	✓	✓
Latin America	Argentina	Seroprevalence studies			✓		✓
	Brazil			✓		✓	✓
	Mexico		✓			✓	
	Guatemala	No Seroprevalence studies					
Europe	Belgium	Seroprevalence studies		✓		✓	
	Denmark			✓	✓	✓	✓
	France			✓		✓	
	Germany		✓		✓	✓	✓
	Ireland			✓		✓	✓
	Italy		✓			✓	✓
	Malta		✓			✓	
	the Netherlands			✓	✓	✓	✓
	Norway						✓
	Slovenia			✓		✓	✓
	Spain			✓	✓	✓	
	Sweden		✓			✓	
	Switzerland			✓	✓	✓	✓
	United Kingdom			✓		✓	✓
	Portugal	No seroprevalence studies					
	Romania						
	Poland						
Asia	China	Seroprevalence studies		✓	✓	✓	✓
	India			✓		✓	✓
	Japan		✓				
	Kazakhstan			✓			✓
	Russia			✓			✓
	Korea	No seroprevalence studies					
	Malaysia						
	Singapore						
Africa	Burkina Faso	Seroprevalence studies	✓			✓	
	Cameroon		✓			✓	
	Ghana		✓				✓
	Kenya					✓	
	Mali		✓			✓	
	South Africa			✓		✓	✓

Table 1 (Continued)

Region	Country	Seroprevalence	Single cross-sectional	Serial cross-sectional	Longitudinal cohort	Informing public health policy	Informing convalescent plasma programme
	Algeria	No seroprevalence studies					
	Ethiopia						
	Malawi						
	Sudan						
	Uganda						
Middle East	Iran	Seroprevalence studies	✓			✓	✓
	Oman		✓				✓
	Turkey						✓
	Egypt	No seroprevalence studies					
	Pakistan						
Oceania	Australia	Seroprevalence studies				✓	✓
	New Zealand			✓			

19 coordinated by the French Institute for Public Health (INVS). In the United States, as a result of the widespread distribution of SARS-CoV-2 infection, donor and recipient studies are being conducted both locally and as part of large national initiatives. Individual blood centres have implemented programmes to monitor infection in donors, including offering SARS-CoV-2 antibody testing as part of health screening to all donors. In parallel, blood centres have implemented recruitment efforts to encourage recovered COVID-19 patients to donate convalescent plasma. Eligibility for convalescent plasma donation has evolved along with testing of the units to determine neutralizing antibody levels that are appropriate for transfusion to patients to increase the odds of efficacious clinical impact. Data from these local initiatives are pooled together to understand the pandemic in the country. These efforts draw on and expand initiatives such as the Transfusion-Transmissible Infections Monitoring System (TTIMS) in ways in which donor testing is considered fundamental to understanding broader infection trends in the general population.

Estimating the seroprevalence of COVID-19 has clear relevance to public health policy and could have some relevance to convalescent plasma programmes as well. The true progression of the pandemic is not fully understood by testing for active infections or by related death rates; both of these statistics are likely underestimates [8]. Actual morbidity and mortality attributable to COVID-19 may be under-reported because of incomplete ascertainment and will also vary depending on the age distribution of the populations and availability of medical care, which has been reduced in some areas due to overwhelming numbers of symptomatic cases. The identification of active infections depends on test availability, the recognition of suspected cases and accessibility, which varies by jurisdiction. About 80% of infections are mild or asymptomatic and thus are less likely to be identified [17]. Seroprevalence studies can therefore provide a better estimate of the proportion of people that have been infected since COVID-19 outbreaks have occurred in a given population. Although the availability of sensitive and specific assays was initially a limitation, they have improved since then. There are now several commercially available assays that appear to have excellent sensitivity and specificity. However, access to the better performing tests is not universal meaning data reported by jurisdiction may be of variable quality. Perhaps a greater concern is the availability of samples from a representative population. Community population-based studies such as random household surveys are not practical because they cannot be conducted quickly to immediately inform public health decision-making. Samples leftover from unrelated patient testing are a possibility, but the extent to which such samples

Table 2 Convalescent plasma programme, International COVID-19-Related Research

Region	Country	Convalescent plasma	Part of a clinical trial	Hyper-immune immunoglobulin
United States/Canada	Canada	Convalescent plasma programme	✓	
	United States		✓	✓
Latin America	Argentina	Convalescent plasma programme	✓	✓
	Brazil		✓	✓
	Guatemala		✓	
	Mexico	No Convalescent plasma programme		
Europe	Belgium	Convalescent plasma programme	✓	
	Denmark		✓	
	France		✓	✓
	Germany		✓	
	Ireland		✓	
	Italy		✓	✓
	Malta			
	the Netherlands		✓	✓
	Norway		✓	
	Poland		✓	✓
	Portugal			
	Romania			
	Slovenia		✓	
	Spain		✓	✓
	Sweden		✓	
	Switzerland		✓	✓
	United Kingdom		✓	
Asia	China	Convalescent plasma programme	✓	✓
	India		✓	
	Kazakhstan			
	Malaysia			
	Russia		✓	
	Singapore			
	Japan	No convalescent plasma programme		
	Korea			✓
Africa	Burkina Faso	Convalescent plasma programme	✓	
	Ethiopia			
	South Africa		✓	
	Sudan			
	Uganda		✓	
	Algeria	No convalescent plasma programme		
	Cameroon			
	Ghana			
	Kenya			
	Malawi			
	Mali			
Middle East	Egypt	Convalescent plasma programme	✓	✓
	Iran		✓	
	Oman		✓	
	Turkey			✓
	Pakistan	No convalescent plasma programme		
Oceania	Australia	Convalescent plasma programme	✓	
	New Zealand			

are representative of the general population is questionable, and the numbers of samples at particular time periods may be insufficient. Blood donors can provide convenient samples and are reasonably representative of the healthy adult population, although older people and those living in rural areas may be under-represented. Importantly, many donations provide leftover samples that could be used for COVID-19 antibody testing and large numbers of donations are collected on a daily basis, allowing monitoring of seroprevalence over time. Several seroprevalence studies currently underway capitalize on these strengths and leverage to maximum benefit the serial cross-sectional study design.

There is a clear rationale for so many countries to turn to blood services for seroprevalence estimates. Of particular note, this observation represents a marked departure from the traditional role of blood services. Instances of blood donors participating in non-transfusion-related research are limited. For example, the Danish Blood Donor Study has examined questions not related to transfusion medicine [18]. In Sweden and Denmark, a large database of blood donor and recipient records (SCANDAT) has been used to analyse aspects of donor health, but has largely focused on research to support blood donor/transfusion policy [19]. A few countries have biobanks of blood donor samples [20,21], but these are mainly intended for blood service-related work such as in the investigation of potential transfusion-transmitted infections. Of note, most emerging infectious disease research has focused on infections that may have posed a risk to blood recipients. For example, in the United States and Canada studies of *Babesia Microti* infection and in the Netherlands studies of Q fever and Usutu virus have measured the frequency of infections in large samples [22–24]. Calls from the World Health Organization to consider blood donors for COVID-19 seroprevalence studies no doubt influenced decisions to do so [11]. The concept of conducting blood donor studies to inform public health policy is not exactly new. It has been discussed in various forums over many years. It did not gain traction at the time, but it might have laid the foundation by which the urgency for seroprevalence data saw quick uptake by blood services in response to COVID-19.

Convalescent plasma programmes also have been quickly implemented in most centres worldwide. Convalescent plasma is not a new therapy *per se*. Examples of past applications include treatment of SARS, MERS, H1N1 influenza and Ebola virus, although evidence was largely observational. It is generally considered a stopgap ahead of more targeted therapies such as antivirals or hyper-immune immunoglobulins, but in low- and middle-income countries it could be a longer-term therapy due to resource limitations [7] or as a therapy requiring limited manufacturing capacity and short time span to be available to treat patients. In spite of the great urgency to treat patients, the transfusion community and its regulators have acknowledged that the efficacy of this therapy is unknown: Is it effective at all, if so which patients will benefit, when in the course of infection should it be given, and importantly will some patients be harmed by the treatment? It is encouraging that most have opted to test the procedure in a clinical trial, even though it adds an extra layer of complexity to strained healthcare systems and carries the burden of some patients not receiving the treatment. Such studies may be particularly challenging in low- and middle-income countries due to funding limitations, limited testing to confirm cases and reliance on replacement donors which may compound the difficulty of recruiting volunteers with resolved infections. In addition, concerns have been raised regarding the safety of plasma transfusion in low- and middle-income countries where product safety standards may not be as high as in high-income countries [25].

Much will be learned from blood donor studies as the pandemic progresses. As results are generated, it will be important to bring together the learnings from different countries to gain an evidence-based composite view. The World Health Organization has plans to bring together data in general, including blood donor studies. The ISBT Transfusion Infectious Diseases Working Party plans to facilitate collaboration between different blood services to compare data and to examine related topics. The data will in turn influence future practice and preparative strategies. Our survey already shows that the impact of the COVID-19 pandemic on blood donor research is evident. The necessity of clinical trials for novel therapies even in a state of emergency is established. The previously untapped resource of blood donors to quickly mobilize large numbers of samples from the healthy adult population has been recognized. This may prove to be a turning point in the relationship between blood establishments and public health entities.

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Conflict of Interests

The authors have no conflicts of interest to declare.

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ORIGINAL PAPER

Effectiveness of the post-donation instruction sheet in conveying information to repeat blood donors

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Vox Sanguinis

Background and objectives Written materials are commonly used for blood donor education. While pre-donation materials are largely standardized across US blood collectors, the post-donation instruction sheet (PDIS) is variable and few have been evaluated to assess their effectiveness in conveying information as reflected by donors' attention, understanding and recall.

Methods An online survey was sent to two independent randomly selected samples of repeat donors, before and after implementation of the enhanced PDIS.

Results A total of 12 935 blood donors responded (33·4% response rate). Most donors did not read the entire PDIS - 34·3% less than half and 18·1% none. Of the 10 593 donors who reported reading any of the PDIS, 97·8% recalled instructions about immediate post-donation care (e.g. extra fluids/no exercise) and 88·0% to call with questions/problems. However, only 50·1% remembered reading about what to do if you felt dizzy/faint and 32·4% about care for bruises. Recall rates in every area were similar before and after revision; except after revision, more donors remembered seeing information about maintaining iron and fewer that you should call the centre back with additional health information ($P < 0{\cdot}0001$).

Discussion Blood collectors rely heavily on written materials to convey instructions to donors. Most repeat donors do not read the entire PDIS, and many do not recall important information. More donors recalled seeing how to maintain iron with the enhanced PDIS, but recall deficits remained on how to care for adverse reactions. Written materials alone appear to be insufficient to educate some donors about new or updated topics.

Key words: blood donors, donor education, donor health, intervention, repeat donors.

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Background

Every year in the United States (US), millions of individuals donate their blood to help others. Blood donation is not without risk though and blood collectors often rely on written educational materials as an expedient way to convey information to their donors about these risks and how to mitigate them. Using written materials, such as brochures or information sheets, is an established method for communicating standardized health information to large groups of people; however, the success of using written materials for delivery of health information varies considerably based on the content of the messages and the population to which they are being delivered. The US Food and Drug Administration (FDA) recognizes the AABB's pre-donation written educational materials that are given to US blood donors as part of the Uniform Donor History Questionnaire [1] and updated by the AABB Donor History Task Force. While AABB-accredited blood establishments must comply with the AABB Standards to provide donors with written instructions, the content of these post-donation instructions is left to the

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discretion of the individual blood centres [2]. In 1990, Davis, et al. suggested educational documents used were at a reading level higher than that of the general population [3]. Previous studies examining donor reading and comprehension of donor educational materials have largely focused on the pre-donation educational materials. More recent studies have shown that first-time donors are more likely than repeat donors to read provided materials and to read the materials carefully [4, 5]. It is not known if this holds true for the post-donation materials.

In September 2012, the AABB Interorganizational Task Force on Donor Hemoglobin Deferrals issued *Association Bulletin #12-03 – Strategies to Monitor, Limit, or Prevent Iron Deficiency in Blood Donors,* which addressed the need for blood collection organizations to monitor, limit and/or prevent iron deficiency in their blood donor population [6]. Specific recommendations included that all donors be provided with information regarding the risks of iron deficiency after blood donation and that all organizations take action to address iron deficiency in their donors or in at-risk sub-populations [6]. After the issuance of the Association Bulletin, the American Red Cross implemented the recommendations regarding informing donors about the risks of iron deficiency after blood donation by adding information and advice on maintaining iron after blood donation to the content of the post-donation instruction sheet (PDIS) given to all donors after every donation. In addition, a dedicated iron webpage, www.redcrossblood.org/iron, was added to the Red Cross website with additional detailed educational content on maintaining iron balance.

Because of the importance of the PDIS in the overall iron education strategy and the role the PDIS plays in educating donors about care after donation, we conducted an online survey with two cross-sectional samples of frequent/active red blood cell donors prior to and after the implementation of the new PDIS. The survey targeted these repeat red cell donors because much of the new iron information was tailored towards them. Questions focused on both attention to and recall of the PDIS itself and recall of the specific content on the PDIS. To specifically assess the effectiveness of the changes to the PDIS in educating the donors about maintaining iron after donation and getting them to take iron supplements or talk to their doctor about blood donation, the survey also had a large section of questions on these topics.

Methods

Modifications to post-donation instruction sheet – information for blood donors

The PDIS is a 2-sided, single sheet of written instructions, with the header 'Information for Blood Donors'. These instructions are provided to every donor immediately following each blood donation or deferral. Affixed to the PDIS is the donor's Donation/Deferral Identification Number, for use when donors call the centre back with post-donation information. A contact number for the Red Cross is in several locations on the PDIS with the statement that donors should call if they have any problems or questions after their donation or to report additional health information. A Spanish language version of the PDIS is also available.

The changes made to the PDIS in early 2013 were largely to the back of the sheet, to provide instructions about iron balance and clarify instructions about donation-related adverse events. Previously, the PDIS contained only a single sentence that blood donation could cause iron depletion or make it worse and contained a densely worded paragraph about the possible complications after blood donation (e.g. fainting, bruises). The changes in the revised PDIS included:

- A new highlighted box entitled 'Maintaining Your Iron Level After Blood Donation'. In this section, donors were told that donating a unit of whole blood or double red cells removes iron from the body, that iron is needed for new red blood cells and that low iron levels may cause anaemia or make it worse.
- Clear and directive instructions advising donors to eat a balanced, healthy diet containing iron-rich foods (with examples), take an iron supplement (specifically for certain donors) and talk to their doctor. Donors were asked to discuss with their doctor their iron level, how much they donate and if they need to take an iron supplement. Specific groups of frequent blood donors were advised to take an iron supplement or a multi-vitamin with iron to replace the iron lost with blood donation.
- Instructions to visit a dedicated website to learn more about iron balance after blood donation at www.redcrossblood.org/iron.
- Delineation under a new header, 'Complications After Blood Donation' that introduced 2 clear sections: Bruises, and Dizziness and Fainting. Within each section, the language was simplified, clarified and put into a format that made it easier to read.
- More specific instructions about immediate post-donation care and directions to read the first aid instructions on the back of the sheet if they experience complications such as bruising or dizziness from their donation.

Survey development

The survey questionnaire was developed using previously validated questions from other surveys [4, 5, 7], and by

writing new questions to specifically address the objectives of this study. Experts in the areas of blood donor research and patient educational material evaluation were consulted and provided revisions to the questions. The survey questionnaire was pre-tested with 10 current and former blood donors to the Red Cross and revised based on their feedback. Minor modifications and additions were made to the survey questionnaire used after the revised PDIS was implemented to specifically address comprehension of the material that had been changed in the post-donation instruction sheet and to assess use of the iron education webpage. In addition, minor modifications were made to the how the questions were presented, and the skip patterns based on preliminary analysis of the data in the first survey.

Questions for the survey were developed to measure donors' attention to and understanding of the PDIS. On both surveys, an image of the front of the PDIS in use at the time preceded the questions about the PDIS. This was intended to help donors recall what it looked like and to delineate it from the pre-donation booklet materials. Because many of the following questions on the survey dealt with recall of the material on the back of the PDIS, that page was not shown. The survey also included a question on the pre-donation written materials, which did not change between the time of the first and second surveys. The remaining questions focused on iron-related questions including questions to determine whether the donors were taking supplemental iron. Finally, donors were asked to self-report their number of donations in the previous 12 months as well as their standard demographic information. In addition to questions about reading and recalling the educational materials, the survey contained additional questions about actions that the donor might take that was described in the PDIS. These questions were asked of all donors whether they reported reading the PDIS or not, to get a baseline about what the donor population was doing. Text in the PDIS encourages donors to talk to their primary health providers about their blood donation history and, if they receive notification of low haemoglobin, their iron status.

Sampling

A sample of 40 000 whole blood or double red cell donors who had a successful donation in February 2013 (first survey – before the revised PDIS) or December 2013 (second survey – after the revised PDIS) were randomly selected for the survey if they had a previous donation with the organization, a valid email address and had agreed to receive email communications from the Red Cross. For the second sample in December 2013, donors who had been previously sampled for the survey were excluded. In 2013, approximately 30% of all active donors in the database had email addresses and had consented to contact. Surveys were cross-sectional and the donor samples independent of each other. From the list of 40 000 emails, 20 000 donors were chosen at random to receive a survey.

Survey administration

We used SurveyMonkey™ to administer the survey and collect responses. For both surveys, donors were emailed an invitation letter and a link to an online survey within 1 month of their donation; donors who did not respond received up to two email reminders spaced in 2-week increments. The surveys and procedures used in this study were reviewed and approved by the American Red Cross Institutional Review Board.

Data analysis

Descriptive analyses on each survey were conducted. Frequencies, chi-square test and Fisher's exact calculations, when appropriate, were used to evaluate whether responses were different between the first and second surveys were performed using SAS v9.4. A P-value < 0·05 is considered significant for this analysis. Change or lack of change was assessed overall and by subgroups of interest. A multivariable logistic regression model was used to look at differences in iron supplement intake controlling for demographic variables such as age, sex, race/ethnicity and education and donation intensity.

Results

A study invitation letter and link to the survey was distributed via email to a total of 38 714 donors (excluding donors' email addresses that were undeliverable or for those donors who had previously opted to not be contacted by SurveyMonkey), and complete responses were received from 12 935 donors, a 33·4% response rate for both surveys combined. The first survey had 6330 evaluable donor responses (response rate 30·7%), and the second survey had 6605 (response rate 36·5%). The respondents to both surveys were very similar, with more than 90% self-reporting Caucasian race and 94% non-Hispanic ethnicity (Table 1). Significantly more females than males answered both surveys. They were highly educated with more than 90% reporting an education level greater than high school. There was a higher percentage of donors aged 50 and older compared to younger donors, but on the first survey there were slightly more donors 18–29 years old (15·8% vs. 11·6%) and on the second more donors older than 60 (28·8% vs 23·4%). The

first survey also had significantly more donors self-reporting higher blood donation activity in the previous 12 months than the second survey ($P < 0{\cdot}0001$). In general, if there were no significant differences between the first survey answers (before the revisions to the PDIS) and the second (after the revisions to the PDIS) they are combined in the rest of the results. The general Red Cross repeat donor population in 2013 had a higher percentage of male donors (48·8%), tended to be younger (ages 18–29, 24·4%) and had fewer Caucasians (84·4%) than the survey respondents.

As a measure of control, the survey included an information recall question about the pre-donation written materials (Table 2). Recall of both survey groups was essentially the same for all the items, except for two items with significant differences. For these items, the actual percentages were less than 4% different. Most respondents in both surveys recalled reading about the potential for physical consequences such as bruising and/or a sore arm (96%), dizziness (93%), fatigue (86%) and fainting and injuries from falls (73·6% vs. 70·9%, $P = 0{\cdot}0007$). Fewer participants recalled less immediate issues such as finding out about having an infectious disease (61%) or being deferred if you are risk of an infectious disease (57%). Two items were recalled less than 40% of the time in both survey groups: recall that donors could be deferred from blood donation even if an infectious disease test is falsely positive (39%) and that blood donation could cause iron deficiency anaemia or make it worse (24% vs. 27·6%, $P < 0{\cdot}0001$).

Because the rest of the survey was focused on the PDIS, donors first were asked how much of the PDIS they had read (Table 3). Greater than 80% of respondents read at least some of the PDIS; however, slightly more respondents in the second survey group read any of it compared to the first survey (82·7% vs. 81·1%, $P = 0{\cdot}0007$). More than 50% reported reading 'all of it' or 'most of it', and these donors were not asked further questions about reading the PDIS. Of the approximately 27% of donors who said they read about half or less than half of the PDIS, more than 96% gave 'I am a repeat donor and have read it before' as the reason. This was the same reason given by the majority (>85%) of those who reported reading none of the PDIS; however, 10%–12% of those reading none of it reported not receiving the sheet at all.

For those who indicated on the first or second survey that they read any of the PDIS, $n = 5133$ and $n = 5460$, respectively, questions were asked about their thoughts on the instruction sheet as well as a recall question asking what the they remembered reading on the PDIS. Over 94% of respondents from both surveys reported reading the PDIS sometime during the day of their donation with the majority (55·2%) reading the sheet at the donation site, 38·7% on the same day as their donation and only 5·6% sometime after the day of donation (Table 4). After the revisions were made to the PDIS, more respondents thought the length of the sheet was 'about right' (72·3% vs. 67·6%, $P < 0{\cdot}0001$). Over 98% of respondents on both surveys felt the information was easy or very easy to understand, with more respondents on the second survey expressing that it was 'very easy to understand' compared to those who responded to the first survey (39·4% vs. 36·3%).

For the question regarding what they remembered reading on the instruction sheet, there were eight areas of recall and five were not significantly different between the first and second survey despite the increased amount

Table 1 Cohort characteristics for first and second survey respondents

	First Survey (n = 6330)		Second Survey (n = 6605)		
	n	**%**	***n***	**%**	**Significance**
Age, years					
18–29	1002	15·8	767	11·6	$P < 0{\cdot}0001$
30–39	727	11·5	692	10·5	
40–49	1160	18·3	1255	19·0	
50–59	1954	30·9	1990	30·1	
60–69	1212	19·1	1519	23·0	
70+	275	4·3	382	5·8	
Sex					
Female	3554	56·1	3558	53·9	$P = 0{\cdot}0094$
Male	2776	43·9	3047	46·1	
Race					
Caucasian	5720	90·4	5948	90·1	NS
African American	143	2·3	146	2·2	
Other	170	2·7	186	2·8	
Multiple	63	1·0	96	1·5	
Missing	234	3·7	229	3·5	
Ethnicity					
Hispanic/Latino	145	2·3	219	3·3	$P = 0{\cdot}0045$
Not Hispanic/Latino	5976	94·4	6185	93·6	
Missing	209	3·3	201	3·0	
# Donations in previous 12 months					
One	496	7·8	736	11·1	$p < 0{\cdot}0001$
Two	1295	20·5	1627	24·6	
Three	1912	30·2	1972	29·9	
Four+	2380	37·6	1942	29·4	
Missing	247	3·9	328	5·0	
Highest education level					
Some/All High School	536	8·5	561	8·5	NS
Some College	1575	24·9	1639	24·8	
College Graduate	2154	34·0	2169	32·8	
Some/All Graduate School	1963	31·0	2135	32·3	
Missing	102	1·6	101	1·5	

Table 2 Recall question about educational materials that are reviewed **prior** to donation

	First Survey (*n* = 6330)		Second Survey (*n* = 6605)		
	n	**%**	***n***	**%**	**Significance**
'What are some of the things that could happen after blood donation that were described in the written material you were given at the blood drive? (Check ALL that COULD happen after donation, even if none has happened to you.)'					
Bruising and/or a sore arm	6164	97·4	6374	96·5	$P = 0·0043$
Fatigue	5460	86·3	5686	86·1	NS
Having your name placed on the blood centre's deferral list if you have or are at risk of having an infectious disease	3614	57·1	3834	58·1	NS
Dizziness	5931	93·7	6157	93·2	NS
Fainting and injury from falls	4656	73·6	4682	70·9	$P = 0·0007$
Finding out you have an infectious disease like HIV or Hepatitis	3921	61·9	4076	61·7	NS
Being deferred from blood donation even if an infectious disease test is falsely positive	2488	39·3	2568	38·9	NS
Causing iron deficiency anaemia or making it worse	1521	24	1825	27·6	$P < 0·0001$

Table 3 Questions about how much of the post-donation instruction sheet donors read

	First survey (*n* = 6330)		Second survey (*n* = 6605)		
	n	**%**	***n***	**%**	**Significance**
How much did you read?					
All of it	1641	25·9	1667	25·2	$p = 0·0007$
Most of it	1739	27·5	2037	30·8	
About half of it	701	11·1	710	10·7	
Less than half of it	1052	16·6	1046	15·8	
None of it	1197	18·9	1145	17·3	
If 'less than half of it' or 'about half of it' why not all?	$n = 1762$		$n = 1755$		
I am a repeat donor and have read it before	1704	96·7	1696	96·6	NS
It was too long and/or difficult to understand	21	1·2	29	1·7	
I lost it/threw it away before I finished reading it	16	0·9	17	1·0	
None of the information applied to me	10	0·5	8	0·5	
I don't remember getting this instruction sheet	11	0·6	5	0·3	
If 'none of it' why didn't you read any of the instruction sheet?	$n = 1197$		$n = 1145$		
I am a repeat donor and have read it before	1042	86·9	981	85·7	NS
It was too long and/or difficult to understand	21	1·8	13	1·1	
I lost it/threw it away before I finished reading it	10	0·8	8	0·7	
None of the information applied to me	8	0·7	6	0·5	
I don't remember getting this instruction sheet	118	9·8	137	12·0	

and improved content and formatting of the information (Table 4). Over 97% of donors remembered reading that they should drink extra liquids/avoid heavy exercise/keep the bandage on. More respondents to the first survey remembered reading about calling the Red Cross if they had additional health information to share (82·5% vs. 78·7%, $P < 0·0001$) and how to care for bruises (33·5% vs. 31·4%, $P = 0·0277$). However, there were significantly more respondents to the second survey who remembered reading about how they could maintain their iron after donation (34·0% vs. 28·0%, $P < 0·0001$). There were no other significant differences between the first and second survey groups on recall of information read on the instruction sheet.

The donors responding to both surveys did not exhibit high adherence to the suggestion in the PDIS to talk to

Table 4 Questions about the post-donation instruction sheet

	First survey (n = 5133)		Second survey (n = 5460)		
	n	%	*n*	%	Significance
When did you read it?					
At the donation site before I left	2754	53·7	3091	56·6	$P = 0.0024$
The same day as my donation	2064	40·2	2039	37·3	
Sometime after the day of my donation	295	5·7	297	5·4	
Did you think the length of this instruction sheet was					
Too short	6	0·1	14	0·2	$p<0.0011$
About right	3469	67·6	3946	72·3	
A little too long	1445	28·2	1300	23·8	
Much too long	197	3·8	171	3·1	
Did you think the information was					
Very easy to understand	1861	36·3	2150	39·4	$P = 0.0004$
Easy to understand	3211	62·6	3237	59·3	
Hard to understand	35	0·7	33	0·6	
Very hard to understand	5	0·1	0	0·0	
What do you remember reading on the instruction sheet?					
That you should drink extra liquids/avoid heavy exercise/keep bandage on after you give blood	5010	97·6	5354	98·1	NS
That you should call the Red Cross if you have additional health information to tell them	4236	82·5	4299	78·7	$P < 0.0001$
That you should call the Red Cross if you have questions or problems after donation	4542	88·5	4778	87·5	NS
What reactions you may have after donating	3872	75·4	4110	75·3	NS
How to care for bruises	1717	33·5	1716	31·4	$P = 0.0277$
What to do if you feel dizzy or faint	2599	50·6	2709	49·6	NS
How you can maintain your iron after donation	1436	28·0	1858	34·0	$P < 0.0001$
What you should do if you are injured after fainting	593	11·6	665	12·2	NS

their primary health provider about iron status if they receive notification of low haemoglobin. Approximately half (48·1% first survey, 51·4% second survey) of donors reported discussing their haemoglobin or haematocrit values and approximately one-third (34·6% first survey, 32·5% second survey) discussing anaemia/low iron with their doctor; however, all other topics probed for showed a less than 20% rate of discussion between donor and doctor. For most topics, fewer donors on the second survey after the materials were changed reported discussing with their doctors than those on the first survey. Prior to the PDIS being changed, 38% of donors reported taking some form of iron (29·1% multi-vitamin with iron, 5·3% separate iron supplement, 3·8% both). After the PDIS was revised, 34% of donors reported taking some form of iron (28·5% multi-vitamin with iron, 8·7% separate iron supplement, 3·3% both). The difference between the first survey and the second was significant ($P < 0.0001$). Significantly, more donors prior to the PDIS being changed reported taking iron than after ($P < 0.0001$).

Discussion

As research identifies additional possible adverse effects of blood donation on donor health, it is important to continue to educate and inform donors of these risks as well as to assess the effectiveness of new and existing delivery methods [2]. For US blood establishments using the standardized DHQ, the pre-donation informational material is included as a component of the DHQ materials (http://www.aabb.org/tm/questionnaires/Pages/dhqaabb.aspx). In contrast, blood centres have full discretion over the content and completeness of any other educational materials they distribute. In late 2013, the Red Cross updated their PDIS highlighting donation risks and care for post-donation adverse events, additional information for donors for recovery, reporting of post-donation information as well as a new section emphasizing how to replace iron that is lost during donation. To assess repeat donors' attention to an original and redesigned PDIS and the effectiveness of these changes in conveying this information, a survey

was conducted with two cross-sectional samples of Red Cross donors.

When respondents to this survey answered the questions related to the pre-donation educational materials, over 80% of all donors indicated that they were aware of the most common complications after blood donation, that blood donation could cause bruising and/or a sore arm, dizziness and fatigue. However, the pre-donation materials did not effectively convey everything contained in them. At the time, the pre-donation document contained an explicit statement about iron depletion, to which less than a quarter of respondents recalled reading. Similar low recall of pre-donation educational material has been previously reported [4] and should alert blood organizations that different approaches, with different types of communication and media, may be needed to improve the informed consent process.

One of the major limitations of using written materials such as the PDIS to educate repeat donors is the lack of attention these donors pay to materials that they have received before. While frequent donors often receive the same instruction sheet at every donation, when important updates such as the ones included in this changed document occur, it is important that all donors read it, regardless of their donor status (first-time vs. repeat donor). Staff should be engaged to ensure that repeat donors are alerted and encouraged to read the new information with any revision of the PDIS. Blood centres should also consider additional ways to educate donors, whether it be through email or text messages updates, websites, social media platforms or other means.

There were some positive outcomes from the revisions to the PDIS. After the revisions were made, more respondents thought the length of the sheet was 'about right' and that it was 'very easy to understand' compared to those who responded to the first survey. The revised instruction sheet added a large section at the top of the second page with information about maintaining iron levels after blood donation. This information had not been included on previous versions of the instruction sheet and was associated with a significant increase in donor recall. Though the increase was statistically significant, both groups' participants' recall of this information shows that including language about iron in the PDIS may not be enough to combat the risk of iron deficiency in frequent blood donors. This mirrors the findings of a multi-centre study of regular blood donors which showed a strategy of only informing donors about the risk of iron depletion does little, if anything, to change their donation or iron supplementation behaviour [8,9]. And while the AABB bulletin on iron at that time stated that centres could just give donor-specific instructions about taking over-the-counter iron dietary supplements, this may not be enough to get them to take action [6].

Given the space limitations in the PDIS, adding new information to the sheet usually requires removing, reformatting or abbreviating some of the other information on the sheet. These changes may account for some of the changes observed in the recall rates on the second survey.

One of the primary limitations of any research using surveys is a low-response rate. Because of budget limitations, we were only able to distribute the survey online. However, blood donors tend to be very responsive to research requests and we had a good response rate for an online survey. Another limitation is using independent cross-sectional studies to evaluate the effectiveness of a new education material or intervention. Using this methodology, you cannot conclude with certainty that the item in question caused the change in knowledge or behaviour [10].

We also limited this survey to repeat donors because the goal of the survey was to see how the PDIS reached repeat donors with the messages about iron supplementation. Therefore, many of these results may not be applicable to first-time donors who may read the educational materials both pre- and post-donation more carefully. As well, the age distribution was roughly equivalent to what would be seen in the overall repeat donor population with a higher percentage of 50- to 59-year old and 60- to 69-year-old donors compared to younger donors and may not reflect how these materials would do with younger donors.

Our results indicate that using the written PDIS to distribute health information to donors has a more limited benefit than previously assumed, and changes to improve PDIS content were associated with only minimal effect especially in this population of repeat donors. Notably, the level of awareness about the possibility of iron depletion or false-positive infectious disease test results was low in both cohorts, as well as the recall rates for what to do after reactions or how to maintain iron levels after blood donation. A major limitation with written post-donation instructions is the extent to which repeat donors read the information citing previous familiarity with the material as the reason for not reading it. As blood organizations need to convey new important information and instructions to donors, it is important to assess if this information is reaching all donors. If the PDIS is used to convey information, it will be essential to assess donor attention, recall and comprehension of the material, and to explore ways to more effectively deliver post-donation instructions, especially to repeat blood donors.

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Conflicts of interest

The authors have no relevant conflicts of interest.

Author contributions

AFE contributed to this work when with the American Red Cross but has since joined the FDA, Center for Biologics Evaluation and Research. The article reflects the views of the authors and should not be construed to represent FDA's views or policies.

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ORIGINAL PAPER

Putting the spotlight on donation-related risks and donor safety – are we succeeding in protecting donors?

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Abstract

Background and objective The European consortium project TRANSPOSE (TRANSfusion and transplantation: PrOtection and SElection of donors) aimed to assess and evaluate the risks to donors of Substances of Human Origin (SoHO), and to identify gaps between current donor vigilance systems and perceived risks.

Materials and methods National and local data from participating organizations on serious and non-serious adverse reactions in donors were collected from 2014 to 2017. Following this, a survey was performed among participants to identify risks not included in the data sets. Finally, participants rated the risks according to severity, level of evidence and prevalence.

Results Significant discrepancies between anticipated donor risks and the collected data were found. Furthermore, many participants reported that national

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data on adverse reactions in donors of stem cells, gametes, embryos and tissues were not routinely collected and/or available.

Conclusions These findings indicate that there is a need to further develop and standardize donor vigilance in Europe and to include long-term risks to donors, which are currently underreported, ensuring donor health and securing the future supply of SoHO.

Key words: blood safety, donors, donor health, hemovigilance.

Introduction

Since the spread of human immunodeficiency virus (HIV) and hepatitis C virus through transfusions and transplantations in the 1980s, both blood and tissue establishments have successfully reduced the risk of transmission of infections [1,2] resulting in very low numbers of transmissions being reported [3–5]. After the introduction of nucleic acid testing (NAT), the risk of transmitting viruses in the transfusion and transplantation chain has further declined, but the concern of transmission to recipients remains [6]. As a consequence, the precautionary principle has been widely applied when establishing eligibility criteria for donors of substances of human origin (SoHO) [7].

Recently, there has been increasing scientific focus on the safety and the well-being of donors. This includes possible adverse reactions in repeat donors, for example long-term effects of frequent donations such as iron deficiency in whole blood donors [8,9] and possible citrate-related osteoporosis in plasma donors [10,11]. Frequent plasma donation, in combination with poor knowledge of nutrition, has now been shown to result in low IgG levels within 3 weeks after beginning plasma donation [12–15] as well as reducing product yield [16].

Donor management in haematopoietic stem cell (HSC) donation poses different issues as donors can be both unrelated (UD) and related (RD). Focus has been on donor management and awareness of the risks to donor health has increased in general, and improving the care of RDs is an area of specific interest. Research in this field has shown that changing accreditation standards may also improve donor safety [17].

In gamete donors, there has been increasing focus on the ethical aspects of donor care. This includes careful information regarding donation-related risks, improving communication and follow-up [18–20] as well as paying attention to the psychosocial aspects of donation [21,22]. For oocyte donors specifically, the long-term risk of cancer following hormone treatment is of concern [23–25].

Post-mortem tissue donation poses other challenges; not only must donation be respectful to the donor but equally to the relatives, who must approve donation. Research in donor care within this field of donation is therefore centred around understanding the ethical dilemmas and supporting the families in their decision-making [26].

In European Union (EU), member states must comply with the relevant Directives concerning blood and tissues. The specific requirements for blood donation are contained in the various annexes in Directive 2004/33/EC and in Directives 2005/62/EC and the associated Good Practice Guidelines contained in Directive 2016/1214. The relevant requirements are also identified in The European Directorate for the Quality of Medicines and Healthcare (EDQM) Guide to the preparation, use and quality of blood components products along with other non-mandatory recommendations.

In 2002, the surveillance of adverse reactions in transfusion recipients (haemovigilance) was first introduced in the Directive 2002/98/EC. Biovigilance (including adverse reactions to cell and tissue transplants) was later incorporated into legislation in Directive 2004/23/EC. Since then, many European countries have implemented donor vigilance systems, although reporting of donor complications is currently only voluntary.

Complications in haemo- and biovigilance are traditionally divided into adverse reactions and adverse events as defined in Directive 2002/98/EC. The first is an unintended response in the donor or recipient related to the donation or transfusion/transplantation. The latter includes accidents and errors related to the collection, testing, processing, storage and distribution of the products, and complications observed during or after donation. Adverse reactions are predominantly described by severity and imputability. Imputability describes the likelihood of a complication being a result of the donation/transplantation/transfusion, as defined in Directive 2005/61/EC. This is rated on a scale from zero (excluded/unlikely) to three (certain). In 2010 the NOTIFY project (https://www.notifylibrary.org/) developed a database which compiles scientific references of complications in haemo- and biovigilance and also vigilance and surveillance reports.

TRANSPOSE aimed to critically evaluate donation-related risks and to identify risks currently not (or insufficiently) included in donor vigilance as well as discrepancies between reported and anticipated donation-related risks.

Methods

TRANSPOSE was initiated in September 2017 and involved 25 associated partners from 15 European countries (https://www.transposeproject.eu) who were directly part of the project and 14 collaborating stakeholders, who could be consulted for external reviews of the project outputs. The participants and stakeholders covered the following domains; blood, plasma, haematopoietic stem cells, gametes, embryos and tissues in the field of donor management. As part of the project, an investigation of current donation-related risks was launched for all SoHO (i.e. whole blood [WB], plasma for fractionation [PFF], HSC and Bone marrow [BM], medically assisted reproduction [MAR, including gametes and embryos] and tissues) excluding solid organs.

Participants working in one of these fields were invited. Relevant disciplines were represented at an academic level, such as transfusion medicine, laboratory testing, public health, epidemiology, risk assessment, behavioural sciences, marketing, economics and project management. Furthermore, the project was built on existing relationships, for example the DOMAINE project and the Erasmus Lifelong Learning Programme 'Donor Health Care'. In addition, stakeholders from both European and global bodies and organizations within the field of transfusion, transplantation and donor health were also invited.

Reported risks to donors

The data collection is illustrated in Fig. 1 and took place in the spring of 2018. All TRANSPOSE participants were asked to provide donor vigilance data and to include data on both serious and non-serious adverse reactions, regardless of severity. Data provided for tissue donors included both living (bone) and deceased donors (ligaments, tendon, ocular tissue, heart valves and other). Furthermore, participants were asked to send data from the previous 3 years and, if data for 2017 were not accessible at the time, then to provide data for 2014–2016.

Data from the European Commission (EC) annual reporting on serious adverse reactions for blood, blood products, cells and tissue were not included, since they neither include non-serious adverse reactions nor the total number of donations. Furthermore, reporting donor adverse reactions is not mandatory and many countries are currently not providing data. The EC reports of serious adverse reactions (SAR) could therefore not be used for statistical purposes. Also, including these data, which are largely anonymized by state, would give the risk of including the same data twice, when pooling them with the provided national data. We therefore chose to exclude the reports from this analysis.

From the data received, reported adverse reactions were included regardless of level of imputability. Furthermore, only data that stated the denominators were included. For whole blood and plasmapheresis, the data were compiled according to the International Society of Blood Transfusion's (ISBT)/International Haemovigilance Network (IHN) 2014 definitions of categories of adverse reactions in donors [27]. The analysis of complications rates and most common risks were subsequently performed on the compiled data.

Anticipated risks to donors

First, a database of risks to donors was compiled using the original risk categories from the donor vigilance reports.

Then, methodological triangulation was used to complete the list of known and anticipated donor risks. We took advantage of expert knowledge within the TRANSPOSE collaboration to identify donor risks currently not included in donor vigilance. This included risks described in literature and theoretical risks. The process is shown in Fig. 2. Based on this work, the final list of risks to donors was compiled. A method for classification was then developed that would allow participants to rate each risk. It was agreed that this should include an estimate of prevalence, available scientific evidence and an assessment of the impact of the risk to the donor.

Statistics

For each SoHO, all donor vigilance data were pooled and the numbers presented are total numbers from the combined reports. Proportions were calculated using the combined data. Confidence intervals were calculated using the Wilson procedure without correction for continuity.

Results

Donor vigilance data

The overall results of the data collection are presented in Table 1. Three stakeholders provided national reports where the data on adverse reactions in whole blood donation and plasmapheresis had been combined. These results have been presented separately in Table 1, as it was not possible to access raw data and further subcategorize according to type of donation.

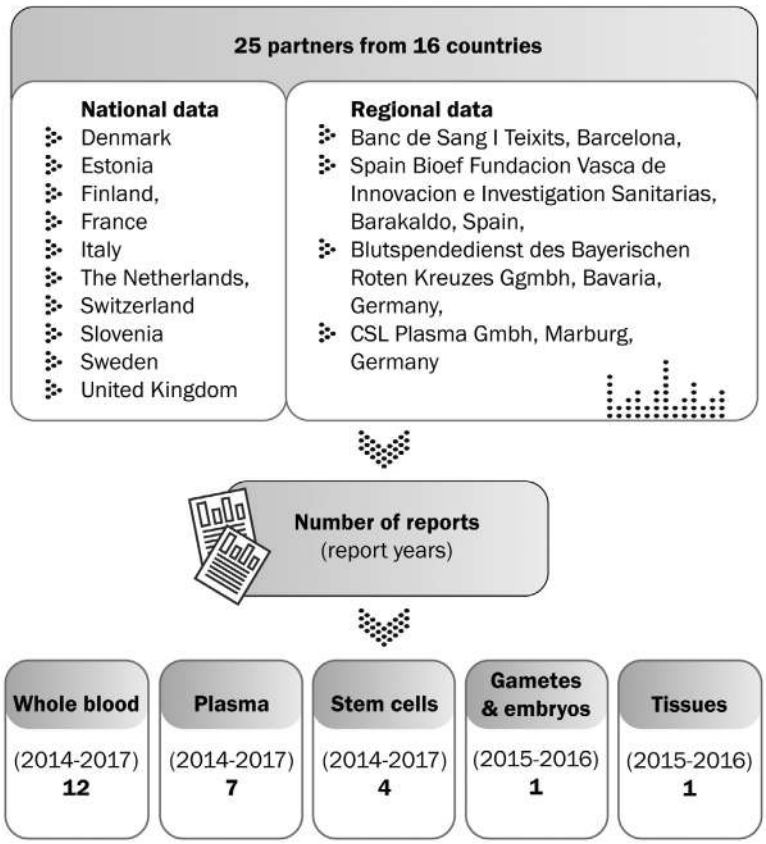

Fig. 1 TRANSPOSE collection of donor vigilance data.

Whole blood (WB) and plasma for fractionation (PfF)

Characteristics of the data collection are shown in Table 2. Two organizations adhered completely to ISBT definitions of adverse reactions in donors and three organizations included the total number of complications divided by gender and first-time vs. repeat donor, with one organization also stratifying by age and donation site. The results of the data collection according to ISBT definitions are shown in Table 3, and the data from the three organizations that had combined their data for whole blood and plasmapheresis are presented in a separate column. The plasmapheresis results were dominated by one organization where the adverse reactions were defined by severity and not by categories of complications, and therefore these have all been labelled as 'other'. Overall, most organizations subdivided vasovagal reactions by timing of reaction (on-site/off-site) and did not include details on loss of consciousness (LOC). Only one organizations had subcategorized LOC into duration of < or >60 s. There were a total of 33 and 27 categories describing donor adverse reactions across all the received data, for WB and PFF respectively.

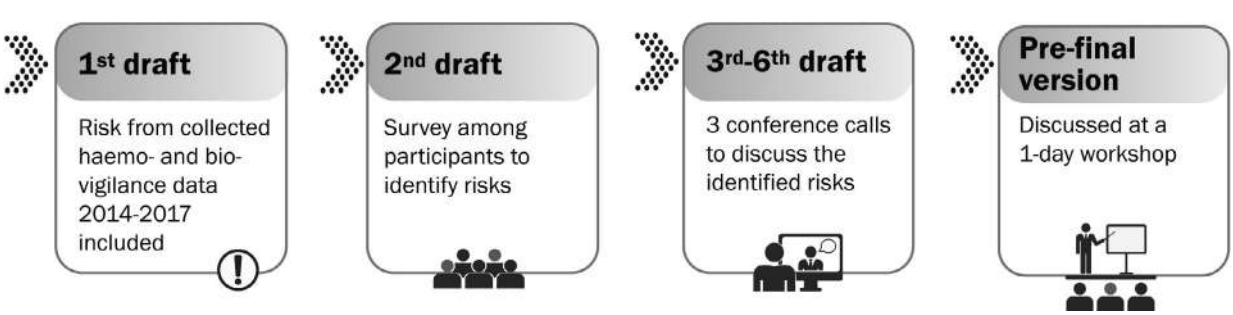

Fig. 2 The TRANSPOSE work process to identify risk to donors of SoHO.

Table 1 Complications in the donation of SoHO reported by TRANSPOSE participants

Donors	Report years	Total number of donations	Total number of complications	Complication rate
Whole blood	2014–2017	19 721 150	95 871	0·0049 (0·0049–0·0049)
Plasma	2014–2017	1 979 972	12 577	0·0064 (0·0063–0·0065)
Unspecified type of blood donation	2014–2017	15 848 803	37 012	0·0023 (0·0023–0·0023)
Haematopoietic stem cells	2014–2017	10 744	135	0·0126 (0·0107–0·0149)
Medically assisted reproduction	2015–2016	378 078	17	0·00004 (0·0–0·0)
Tissues	2015–2016	42 405	0	0

The complication rates are presented as proportions (95% CI) of the total number of complications. Three countries provided the combined data for whole blood and plasmapheresis. These are presented in the third row as 'unspecified type of blood donation'.

Haematopoietic stem cells (HSC), medically assisted reproduction (MAR) and tissues

Characteristics of the data collection for these categories are shown in Table 4. Table 5 details the results for HSC and tissues; only few of the participating organizations could provide data for these SoHO. For MAR, it was noted that the vast majority of donations were sperm donations without any registered adverse events/reactions.

Anticipated risks to donors

The assessment of anticipated risks is presented in Table 6. Each risk was rated according to the level of evidence, severity and prevalence. Prevalence was defined as the participant's personal estimate of the prevalence among all the donors who were available for donation. For comparison of the ratings by the different participants, a total score based on each individual rating was calculated for each risk. This score was the product of the severity, level of evidence and prevalence ratings. To rank the risks from unlikely to highly likely, the individual total scores for each risk was compiled and a mean total score was calculated. The highest rated risks were then compared to the risks reported in the vigilance data to identify discrepancies.

TRANSPOSE participants identified 40 risks in total across all types of SoHO that they believed should be part of donor vigilance. Thirty-three of these risks were commonly known risks directly related to the donation procedure. Seven risks concerned long-term health issues as a result of donation, some that are currently not part of the reported donor vigilance. They included induced cancer, autoimmune disease, osteoporosis, cytopaenia(s), psychosocial complications, and low levels of iron, protein and immunoglobulin. Due to the different nature of the SoHOs, some risks were not equally relevant to all donors.

For WB, the long-term risk of iron deficiency was the highest rated anticipated risk to donors followed by adverse reactions directly associated with the donation procedure: vasovagal reactions, haematomas and nerve damage. The highest rated risk to plasma donors was vasovagal reaction. This was directly linked to the concern of volume overdraws in plasma donors when the donation volume is solely estimated based on body weight especially in those donors who have an uneven balance in body weight and plasma volume, for instance, due to obesity. The highest rated long-term risks for plasma donors was iron deficiency (rated fourth) and low protein and/or Immunoglobulin levels which was the seventh highest rated risk to plasma donors.

For haematopoietic stem cell donation, the highest rated risks were directly associated with the donation procedure. However, a potential long-term risk of autoimmune disease and cytopenia was a concern despite being rated as having a low level of evidence and prevalence. For all SoHOs, the risk of psychosocial complications to donation, for example anxiety, donation stress and the loss of working capacity following donation, was mentioned as risks that should be included in future donor vigilance.

Discussion

Data from 12 countries over 4 years and for four types of SoHO showed that reported donor complications rates are low even when including non-serious reactions. However, as reporting is not mandatory a significant degree of underreporting is likely. Even so, the total number of complications in blood, plasma and stem cells were substantially higher than the combined numbers of the 2015–2017 EC reports (19 177 SAR on blood donors and 163 SAR in HSC donors.

There is already international consensus on the need for a standardized donor vigilance system [28] and work has been done to harmonize current systems [29]. However, our results for WB and PFF show that despite consensus there is still variation in the categories included in donor vigilance. Furthermore, there is a significant variation in how these adverse events/reactions are recorded

Table 2 Characteristics of whole blood and apheresis data collection in the participating organizations

Organization	Taxonomy used for adverse reactions	Severity criteria used	Minimum severity in the data	Imputability criteria used	Minimum level of imputability in the data
1	Local definition	Grade 1–3	None	No	None
2	ISBT/IHN 2014 definitions with additional categories	Grade 1–3	≥2	Yes	≥2
3	ISBT/IHN 2014 definitions	Mild/Moderate/Severe	None	Yes	≥1
4	Local definition	Non-severe/Severe	Only for citrate reactions (min. severe)	No	None
5	Local definition	Mild/Moderate/Severe (SHOT* definition for severe)	None	No	None
6	ISBT/IHN 2014 definitions with additional categories	Grade 1–4	None	Yes	≥1 and including NE**
7	None	No	None	No	None
8	ISBT/IHN 2014 definitions with additional categories	Mild/Moderate/Severe	None	No	None
9	ISBT/IHN 2014 definitions	Grade 1–3	≥1	Yes	≥1
10	ISBT/IHN 2014 definitions	IHN*** criteria	≥2	Yes	None
11	ISBT/IHN 2014 definitions	Mild/Moderate/Severe (SHOT definition for severe)	Severe	Yes	≥1
12	Common Approach for SARE reporting to the European Commission	Grade 1–4	≥2	Yes	None
13	Local definition	Mild/Moderate/Severe	None	No	None
14	Local definition	Mild/Moderate/Severe	None	No information	No information

*Serious Hazards of Transfusion. **Not able to evaluate.

according to imputability and/or severity as well as donor demographics. This continues to make international comparison complicated and affects the overall collective quality of data being collected.

TRANSPOSE participants agreed that adverse reactions which transform healthy donors to patients should be reported. This also includes reactions that have a negative influence on quality of life. The majority of the potential long-term effects of donation are risks that can be mitigated through clinical tests including routine monitoring of ferritin, immunoglobulin, protein levels and a bone density scan. Psychosocial complications can be addressed through validated donor questionnaires including the 12-item Short Form Survey. Assessment of the risk of cancer and autoimmune disease in donors relies on a valid clinical monitoring of the general population in order to identify an increased risk among donors. Within the field of HSC, long-term adverse reactions such as iatrogenic malignancy, is already part of donor vigilance. Collaboration and exchange of experience across SoHOs could improve follow-up in all types of donors.

Importantly, the risk of iron deficiency in WB donors, deemed the most important risk by the participating stakeholders, was only included in one haemovigilance report. This despite current literature supporting that iron deficiency in WB donors is considered a relevant risk that should be addressed to improve both donor care and donor health [30,31]. However, this would require both ferritin monitoring by the blood collecting facilities and consensus on how non-anaemic iron deficiency should be defined and mitigated.

Only limited data for HSC, MAR and tissue donation were received. The participants commented that this was probably due to the fact that collecting donor complication data is not mandatory on a European level. However, the WMDA do collect mandatory data from registered member countries, predominantly European, on SARs in HSC donors. In their 2018 report, 62% of SARs in donors occurred >30 days after donation and 52% were non-haematological malignancy and autoimmune disease, which are to be reported by Worldwide Network for Blood and Marrow Transplantation standards regardless if causal connection to donation is established [32]. Our data for HSC donors suffered from being both very heterogenic in terms of adverse reaction categories and also included non-

Table 3 Adverse reactions to whole blood and plasma donation

	Whole blood		Plasmapheresis		Unspecified type of blood donation	
	Total number	Proportion of total adverse reactions (95% CI)	Total number	Proportion of total adverse reactions (95% CI)	Total number	Proportion of total adverse reactions (95% CI)
A. Complications mainly with local symptoms						
A 1. Complications mainly characterized by the occurrence of blood outside the vessels.						
A1.1 Haematoma	17 064	0·178 (0·1756–0·1804)	3155	0·2509 (0·2434–0·2586)	5797	0·1566 (0·1529–0·1604)
A1.2 Arterial puncture	599	0·0062 (0·0057–0·0067)	32	0·0025 (0·0017–0·0036)	102	0·0028 (0·0023–0·0034)
A1.3 Delayed bleeding	215	0·0022 (0·0019–0·0025)	11	0·0009 (0·0005–0·0016)	0	0·00 (0·00–0·00)
Complications mainly characterized by pain						
A2.1 Nerve injury/irritation	396	0.0041 (0·0037–0·0045)	38	0·003 (0·0022–0·0042)	193	0·0052 (0·0045–0·006)
A2.2 Other Painful arm	568	0·0059 (0·0054–0·0064)	88	0·007 (0·0057–0·0087)	147	0·004 (0·0034–0·0047)
A3. Local inflammation/infection	68	0·009 (0·0005–0·0009)	13	0·001 (0·0006–0·0018)	82	0·0022 (0·0018–0·0027)
A 4. Other major blood vessel injury						
A4.1 Deep Venous Thrombosis	7	0·0001 (0·0001–0·0002)	1	0·0001 (0·00–0·0005)	0	0·00 (0·00–0·00)
A4.2 AV fistula	0	0·00(0·00–0·00)	0	0·00(0·00–0·00)	4	0·0001 (0–0·003)
A4.3 Compartment syndrome	0	0·00(0·00–0·00)	0	0·00(0·00–0·00)	0	0·00 (0·00–0·00)
A4.5 Brachial pseudoaneurysm	0	0·00(0·00–0·00)	0	0·00(0·00–0·00)	0	0·00 (0·00–0·00)
B. Complications mainly with generalized symptoms: vasovagal reactions						
B1.1 Vasovagal reaction with loss of consciousness	0	0·00(0·00–0·00)	0	0·00(0·00–0·00)	747	0·0202 (0·0188–0·0217)
B1.2 with injury	99	0·001 (0·0008–0·00012)	1	0·0001 (0–0·0005)	69	0·0019 (0·0015–0·0024)
B1.3. without injury	531	0·0055 (0·005–0·006)	20	0·0016 (0·001–0·0025)	0	0·00 (0·00–0·00)
B2.1 Vasovagal reaction without loss of consciousness	3229	0·0337 (0·0326–0·0349)	120	0·0095 (0·0079–0·0114)	7648	0·2066 (0·2025–0·2108)
B2.2 with injury	0	0·00(0·00–0·00)	0	0·00(0·00–0·00)	0	0·00 (0·00–0·00)
B2.3 without injury	0	0·00(0·00–0·00)	0	0·00(0·00–0·00)	0	0·00 (0·00–0·00)
C. Complications related to apheresis						
C.1 Citrate reactions	-	-	1404	0·1116 (0·1062–0·1173)	833	0·0225 (0·021–0·0241)
C.2 Haemolysis	-	-	0	0·00(0·00–0·00)	0	0·00 (0·00–0·00)

Table 3 (Continued)

	Whole blood		Plasmapheresis		Unspecified type of blood donation	
	Total number	Proportion of total adverse reactions (95% CI)	Total number	Proportion of total adverse reactions (95% CI)	Total number	Proportion of total adverse reactions (95% CI)
C.3 Air embolism	-	-	0	0·00(0·00–0·00)	0	0·00 (0·00–0·00)
C.4 Infiltration	-	-	45	0·0036 (0·0027–0·0049)	0	0·00 (0·00–0·00)
D. Allergic reactions						
D.1 Allergy (local)	51	0·0005 (0·0004–0·0007)	8	0·0006 (0·0003–0·0013)	13	0·0004 (0·0002–0·0007)
D.2 Generalized allergic reaction (anaphylactic reaction)	1	0·00(0·00–0·00)	8	0·0006 (0·0003–0·0013)	13	0·0004 (0·0002–0·0007)
E. Other serious complications related to blood donation						
E.1 Major cardiovascular event	25	0·0003 (0·0002–0·0004)	10	0·0008 (0·0004–0·0015)	13	0·0004 (0·0002–0·0007)
F. Other complications						
F.1 Other	27 891	0·2909 (0·288–0·2938)	4715	0·3749 (0·3664–0·3834)	923	0·0249 (0·0233–0·0266)
Other vasovagal reactions categories						
VVR unspecified	9229	0·0963 (0·0944–0·0982)	147	0·0117 (0·0099–0·0138)	0	0·00 (0·00–0·00)
VVR onsite	32 793	0·3421 (0·3391–0·3451)	2561	0·2036 (0·1966–0.2108)	17 447	0.4714 (0.4663–0·4765)
	143	0·0015 (0·0013–0·0018)	13	0·001 (0.0006–0·0018)	0	0·00 (0·00–0·00)
-with injury						
	0	0·00(0·00–0·00)	0	0.00(0·00–0·00)	0	0·00 (0·00–0·00)
-without injury						
VVR off site	2870	0·0299 (0·0288–0·031)	187	0·0149 (0·0129–0·0172)	2981	0·0805 (0·0778–0·0833)
	105	0·0011 (0·0009–0·0013)	0	0·00(0·00–0·00)	0	0·00 (0·00–0·00)
-with injury						
	56	0·0006 (0·0005–0·0008)	0	0·00(0·00–0·00)	0	0·00 (0·00–0·00)
-without injury						
Total	95 871	1	12 577	1	37 012	1

Three countries provided the combined numbers for whole blood and plasma donations, and these are presented in the last column as 'unspecified type of blood donation'.

Table 4 Characteristics of haematopoietic stem cells, medically assisted reproduction and tissues data collection in the participating organizations

Organization	Taxonomy used for adverse reactions	Follow-up time after donation	Severity criteria used	Minimum severity in the data	Imputability criteria used	Minimum level of imputability in the data
Haematopoietic stem cells						
1	Common Approach for SARE reporting to the European Commission	Related: No standardized requirements but up to 1 year Unrelated: 5 years	Grade 1–4	≥2	Yes	None
2	Vigilance and Surveillance of Substances of Human Origin (SOHO VℰtS) Guidance for Competent Authorities	Unrelated: 10 years recommended	Vigilance and Surveillance of Substances of Human Origin (SOHO VℰtS) Guidance for Competent Authorities	≥2	Yes	≥1
3	WMDA S(P)EAR*	Unrelated: 10 years	WMDA S(P)EAR	None	Yes	None
4	Unspecified	1 year	Non-severe/severe	Severe	No	None
5	NOTIFY	Minimum 6 months	Grade 1–4	None	Yes	≥1
Medically assisted reproduction and tissues						
1	Common Approach for SARE reporting to the EC	-	Grade 1–4	≥2	Yes	None
2	Vigilance and Surveillance of Substances of Human Origin (SOHO VℰtS) Guidance f or Competent Authorities	-	Vigilance and Surveillance of Substances of Human Origin (SOHO VℰtS) Guidance for Competent Authorities	≥2	Yes	≥1

*World Marrow Donor Association Serious (Product) Events and Adverse Reactions.

Table 5 Most frequent adverse reactions in stem cell and gamete donors reported by TRANSPOSE participants

	Total number of complications	Proportion of the total number of complications
Haematopoietic stem cells		
Citrate reactions	58	0·4296 (0·3449–0·5139)
Adverse reactions to granulocyte-colony stimulating factor	8	0·0593 (0·0304–0·1126)
Medically Assisted reproduction		
Ovarian hyperstimulation syndrome	8	0·4706 (0·2617–0·6904)
Pelvic inflammatory disease	3	0·1765 (0·0619–0·4103)
Bladder lesion	3	0·1765 (0·0619–0·4103)

The complication rates are presented as proportions (95% CI) of the total number of complications.

Table 6 Classification of donor risks; all risks and categories were rated according to descriptions

Score	Estimated level of evidence	Estimated severity	Estimated prevalence
1	Not accessible	Minor injuries or discomfort. No medical treatment or measureable physical effects.	<0·001%
2	Theoretical: no cases described	Injuries or illness requiring medical treatment. Temporary impairment	0·001%–0·01%
3	Possible: few cases described not confirmed	Injuries or illness requiring hospitalization	0·01%–1%
4	Likely: few cases described and confirmed	Injury or illness resulting in permanent impairment	1%–10%
5	Definite: frequently described and confirmed	Fatal	>10%

serious adverse reactions. This may account for the differences between our data and the WMDA report. However, a general concern for both data collections was the underreporting of adverse reactions in related allogenic donors in comparison with unrelated donors [33].

Conclusion

In Europe, donor complications are rare but probably underreported. The reporting is very heterogenic and non-standardized despite international consensus. In order to ensure the health of donors, we should first collaborate to implement a standardized donor vigilance system. An international focus on donor vigilance is strongly needed and should be a key priority for all stakeholders including regulatory bodies and national competent authorities.

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Conflicts of interest

The authors declare no conflicts of interest.

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ORIGINAL PAPER

Determinants of intention to return to donate blood among first-time blood donors in Ghana

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Objective This study seeks to identify factors that are predictive of intention to return to donate blood among first-time blood donors.

Methods A cross-sectional survey of 505 first-time blood donors, selected from blood donation sessions across three regions in Ghana. Data were obtained on their intention to donate blood in the next four months, factors that would influence this decision. Logistic regression models were used to test factors that were predictive of intention to return.

Results First-time donors were young with 87·4% below 35 years of age, male (72·5%), single (73·3%), Christian (93·7%), employed (58·8%), with at least a basic education (98%). Factors that positively predicted intention to return included: motivational incentives (OR = 1·67, 95%CI: 1·01–2·78; $P = 0·045$); ease of access to the donation site (OR = 2·65, 95%CI: 1·48–4·73; $P = 0·001$); SMS and email reminders (OR = 2·84, 95%CI: 1·60–5·06; $P < 0·001$); and television, radio or newspaper advertisements (OR = 2·97, 95%CI: 1·66–5·31; $P < 0·001$). Factors that negatively predicted intention included preferential access to transfusions (i.e. 'blood credits') (OR = 0·43, 95%CI: 0·23–0·83; $P = 0·012$); getting to know test results (OR = 0·40, 95%CI: 0·20–0·80; $P = 0·010$); and not knowing and/or trusting what happens to the blood after donating (OR = 0·50, 95%CI: 0·28–0·88; $P = 0·016$).

Conclusion Motivational incentives, convenient access to donation sessions, reminders and mass media advertisements appear to positively influence intention to return to donate. Conversely not knowing what happens to the blood after donation negatively influenced intention to return. Interventions to promote repeat blood donation should consider the identified factors.

Key words: blood donation, first-time donors, intention to return, sub-Saharan Africa.

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Introduction

Maintaining adequate levels of blood for transfusion is a global challenge, and a critical public health problem in sub-Saharan Africa (SSA). The World Health Organization recommends a minimum blood collection index of 10 units of blood per 1000 population. However, all 66 countries reporting a blood collection index of less than 10 to the WHO were low- and middle-income countries, with 33 of these, including Ghana, located in SSA [1].

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Voluntary non-remunerated blood donors are defined as blood donors who donate blood by their own free will without receiving any payment in cash or 'in kind'. WHO recommends donation by voluntary non-remunerated blood donors because, compared to other types of donors, they have lower levels of markers for transfusion transmissible infections (TTI) especially if they donate repeatedly. Voluntary non-remunerated blood donors are uncommon in low- and middle-income countries. Low- and middle-income countries constitute 50 of the 58 countries worldwide that collect more than 50% of blood from family replacement blood donors who donate blood only in response to need by a patient who is known to them, usually a family member, friend or an acquaintance [1]. Family replacement blood donors are the main source of blood in several African countries, with less than 25% of blood in countries such as Cameroon and Democratic Republic of Congo being provided by voluntary non-remunerated blood donors [2]. Blood from family replacement blood donors in SSA serves as either an alternative for, or a supplement to insufficient donations from voluntary non-remunerated blood donors.

Blood shortages in SSA are predominantly attributed to insufficient numbers of reliable, regular donors. The decision to donate blood is influenced by both the factors that motivate and those that deter blood donation. These factors have been used to predict actual blood donor return in a South African study [3].

The Theory of Planned Behaviour expounds that human behaviour is guided by beliefs about outcomes of the behaviour (behavioural beliefs), normative expectations of others (normative beliefs) and the presence of factors that may affect the performance and the perceived power of these factors (control beliefs) [4]. According to the Theory of Planned Behaviour, intention is a strong predictor of behaviour, and attitude, subjective norm and perceived behavioural control, predict intention [5]. In the context of blood donation, the Theory of Planned Behaviour has been applied in a number of studies, mostly in high-income countries. In SSA, a study in Ethiopia [6] tested the Theory of Planned Behaviour and found that knowledge, subjective norm and attitude explained 12·7% of the variance of the intention to donate blood, although this did not hold for SSA migrant communities in Australia [7].

In Ghana, a nation in SSA with a population of 30 million, the National Blood Service Ghana coordinates blood collections through one stand-alone blood centre (the Southern Area Blood Centre), two hospital-based blood centres (the Central and Northern Area Blood Centres) and 147 hospital blood banks. National Blood Service Ghana's records show that the annual blood collection has been relatively static for the last five years and is about 60% of the estimated annual requirement of 300 000 donations, blood donation is predominantly by family replacement blood donors, with only about 33% from voluntary non-remunerated blood donors, and first-time donor return rate in six months is 15·2%.

A better understanding of the motivators for, and barriers to, blood donation is needed in order to make a significant impact on increasing blood donations in Ghana. There has been very little research from Ghana, or from SSA, on the factors that affect first-time blood donors' decisions to become regular donors. The aim of this study was therefore to identify factors that predict intention to return to donate among first-time blood donors in Ghana. This information could then inform interventions that the National Blood Service and other organizations across SSA could introduce to increase the number of returning donors and consequently increase the blood supply.

Methods

Study design and methods

A prospective, cross-sectional survey of first-time blood donors was conducted at the Southern Area Blood Centre from June to October 2015. The Southern Area Blood Centre serves a population of about 5 million and covers the Greater Accra Region, and parts of the Eastern and Central Regions of Ghana. Donors were recruited from 75 blood donation sessions of fixed blood donation clinics located in six hospitals in Greater Accra Region, and mobile blood donation sessions in settings such as secondary and tertiary schools, religious organizations (churches and other religious groups), a social youth group, a soccer academy, shopping malls and workplaces.

To detect a return rate of 15·2% (National Blood Service Ghana records) with 80% power at a confidence level of 95% and 5% margin of error, the required study sample size was 505 (250 voluntary non-remunerated blood donors and 255 family replacement blood donors) with a stratified design for voluntary non-remunerated blood donors and family replacement blood donors, and 10% non-response rate. The 15·2% donor return rate was used to calculate the sample size because the study initially aimed at predicting first-time donor return rates. However, due to logistic challenges at the study site, the return rate was very low (3·1%), therefore the study looked at predictors of intention, which is antecedent to donor return [4]. For each session within the selected area for the period of the study, all first-time donors were approached and recruited, until the end of the particular session, for the questionnaire survey. All first-time donors at each session were recruited based on the stratification for voluntary non-remunerated blood donors and family

replacement blood donors until the required number of respondents was achieved.

Questionnaire design and administration

The contents of the questionnaire were based on findings from a qualitative study on determinants of blood donation [8], and the constructs of the standard Theory of Planned Behaviour. The constructs of the theory of planned behaviour measures including intention to donate blood were based on published measures [9]. The questionnaire, which has been presented as supplementary file 1, assessed several indicators including socio-demographic characteristics and motivators (30 items) and deterrents (33 items) to blood donation among first-time donors, as well as predictors of donors' intention to return to donate, using the Theory of Planned Behaviour model. The questionnaire contained different formats of items, which were multiple-choice with one or multiple answers, five-point Likert-type ranging from strongly disagree (1) to strongly agree (5), dichotomous and open-ended questions. The United States Census and Survey Processing System (CSPro) software [10] was used as a platform for the questionnaire administration and data entry. The English version of the developed questionnaire was captured into the software by a database developer.

Six data collectors were trained to administer the questionnaire and collect data alongside the lead investigator. The questionnaire was piloted with 10 respondents, who were then excluded from the main study.

Measures

The Theory of Planned Behaviour constructs measured was intention (one item), attitude (six items), subjective norm (two items), perceived behavioural control (two items) and altruism (five items) (See Appendix A).

Data analysis

Descriptive summaries were generated for socio-demographic characteristics such as age, sex, marital status, education, ethnic background and employment, as well as for motivators and deterrents to blood donation. Deterrent and motivational factors were categorized into binary variable with significantly disagree to neutral being coded as 0 (disagree) and agree to strongly agree being coded as 1 (agree). Univariate test was done after which significant variables were included in a binomial logistic regression analysis to test for independent significant predictors of intention to return to donate blood, using intention to return to donate blood as the dependent variable and the demographic characteristics, motivators for, and deterrents to blood donation, as well as the attitude, subjective norm, behavioural control and altruism, as independent or explanatory variables. Significant level was set at alpha equal at 0·05 ($\alpha = 0{\cdot}05$; thus $P < 0{\cdot}05$).

Ethical considerations

This study was approved by the Ethics Committees the Ghana Health Service (GHS-ERC: 10/09/13) and the Liverpool School of Tropical Medicine (Research Protocol: 13·27). In conducting the study, voluntary participation, confidentiality and anonymity of respondents were ensured. Written informed consent was also obtained from all respondents.

Results

Demographic characteristics of respondents

The age of respondents ranged from 18 years to 58 years (Table 1), with highest proportion being those in the age group 18–24, and most being male (72·5%), employed (58·8%), Christian (93·7%) and receiving at least basic

Table 1 Demographic characteristics of respondents in the study

Characteristics	Categories	Number (total = 505)	Percentage %
Age in years	18–24	239	47·3
	25–34	189	37·4
	35–44	63	12·5
	45–60	14	2·8
Sex	Male	366	72·5
	Female	139	27·5
Marital status	Single	370	73·3
	Married	119	23·6
	Other	16	3·2
Level of education	No formal education	10	2·0
	Basic	157	31·1
	Secondary	185	36·6
	Tertiary	153	30·3
Ethnic background	Akan	199	39·4
	Ewe	122	24·2
	Ga/Dangbe	130	25·7
	Hausa/Dagbani	27	5·3
	Other	27	5·3
Religion	Christian	473	93·7
	Muslim	32	6·3
Employment	Student	165	32·7
	Unemployed/Homemaker	38·	7·5
	Employed/formal/self	297	58·8
	Other	5	1·0

education (98·0%). Respondents below 35 years of age formed 84·7% of the study population.

First-time donor return

One item was used to measure actual return behaviour after six months of follow up. 83% of donors were reached, one donor (0·2%) declined to respond. Of 418 donors who responded, 3·1% had returned to donate blood. About 91% (n = 385) of participants who did not return gave reasons for not returning to donate. Sixty-eight per cent did not return because they had not received information on need, where and when to donate to donate from the Blood Centre, or the blood collection teams had not returned. Nineteen per cent had not returned due inconvenience of distance to the donation site, or busy schedule.

Factors relating to the respondents' decision to donate blood

Most respondents were family replacement blood donors (50·5%) who donated specifically for someone (sick friends, acquaintances, colleagues and family members); while those donating for no-one specifically comprised of 49·5%. However, based on their own understanding of volunteering, most respondents (82·6%) perceived themselves as having donated voluntarily, with only 17·4% either not knowing or perceiving themselves as non-voluntary donors. Of all the respondents, 67·9% reported receiving incentives for donating, and of those, 96·2% received incentives in the form of motivational items such as branded pens, exercise books, and carrier bags; as well as refreshments. Of those who reported receiving incentives, 84·8% received them from the Blood Centre or Blood Bank, 14% from other sources such as churches or sponsors, and 1·2% from the blood recipients. The factor that mostly influenced respondents' perceptions about blood was formal education (59%), although religion and culture also influenced perceptions. Of the 398 respondents who responded to seeing or hearing National Blood Service Ghana/Blood Bank advertisements, 374 (93·7%), heard or saw the adverts via radio or television. Receiving reminders by phone or SMS was preferred (84·5%) to mail or email (12·5%). Moreover, 68·7% of respondents planned to return to donate in four months' time, and 87·7% planned to continue donating for as long as their health allowed.

Association between respondents' demographic characteristics and intention to return to donate

Six items were used to assess the demographic predictors of intention to return to donate blood, and three were significant. These were: (1) Marital status (P = 0·036), with those who were married being two times as likely to intend to return to donate compared to those who were single (OR = 1·953, 95% CI: 1·059–3·600; P = 0·032): (2) Education; those with basic education (OR = 2·341, 95% CI: 1·401–3·912; P = 0·001) and secondary education (OR = 2·194, 95% CI: 1·332–3·613; P = 0·002) were twice as likely to intend to return compared to those with tertiary education: (3) Ethnic background; the Ga/Dangbe ethnicity being about half as likely to intend to return compared to the Akan ethnicity (OR = 0·565, 95% CI: 0·346–0.924; P = 0·023). The Nagelkerke R-square value for the final logistic regression model was 0·085.

Association between factors related to the respondents' decision to donate blood and respondents' intention to return to donate blood.

Of the six items reflecting other characteristics of respondents, two were statistically significant (Table 2). There was no significant association between 'type of donor' and intention to return. However, respondents (either voluntary non-remunerated blood donors or family replacement donors, according to the definition of the National Blood Service Ghana, and based on who the respondent donated blood for) who did not consider themselves as voluntary donors (OR = 0·295, 95% CI: 0·134–0.649; P = 0·002) or who did not know whether they considered themselves as voluntary donors (OR = 0·356, 95% CI: 0·148–0·853; P = 0·021) were significantly less likely to intend to return to donate as compared to those who considered themselves to be voluntary donors. The Nagelkerke R-square value for the final logistic regression model was 0·124.

Association between motivating factors for blood donation and intention to return to donate blood in Ghana

Of the 30 items that were entered into the model to determine motivators for blood donation that predict intention to return to donate blood, seven were significantly associated with intention to return (Table 3). Five factors ('if it is easy to get to the blood donation site', 'if Ghana needs blood', 'because it would make me feel good about myself', 'if I am notified through SMS/email reminders', and 'by radio, TV or newspaper advertisement on blood donation') were positively associated, and two ('for blood credits for me and my family', and 'if I will get to know my transfusion transmissible infection test results') were negatively associated with intention to return. The Nagelkerke R-square value for the final logistic regression model was 0·362.

Table 2 Association between factors related to the respondents' decision to donate blood and intention to return to donate

Predictor Variable	Categories	*P*-value	OR	95% CI for OR	
				Lower	Upper
Type of donor (Ref – Voluntary)	Replacement	0·066	0·420	0·166	1·060
Who the donor donated for (Ref -Friend/acquaintance/colleague)	Relative	0·056	2·061	0·982	4·324
	Blood bank/Blood service	0·943	1·030	0·459	2·311
	Community	0·218	2·399	0·596	9·664
Whether a donor considers self as voluntary donor (Ref - Yes)	No	**0·002**	0·295	0·134	0·649
	Don't know	**0·021**	0·356	0·148	0·853
Whether donor received incentive/refreshment for donating (Ref – No)	Yes	**0·033**	1·710	1·043	2·804
Factor that mostly influence donor's perceptions of blood (Ref - Culture)	Education	0·184	0·542	0·219	1·338
	Religion	0·188	0·511	0·188	1·389
	Other	0·727	0·745	0·143	3·883
Ever seen/heard advertisement from NBSG/Blood Bank (Ref – Radio)	Television	0·606	1·141	0·692	1·880
	Newspaper/Other	0·335	0·250	0·015	4·193

NBSG, National Blood Service Ghana; Ref, reference categor.

Association between deterrents to blood donation and intention to return to donate blood

Thirty factors were included in the model to determine deterrents to blood donation that are associated with intention to return to donate blood (Table 4). Of these, four deterrents ('because, the motivational items that are given to blood donors are not good enough', 'if I do not know where the nearest blood donation site is', 'that, I think blood mostly goes to people who are rich', and 'that, it is against my culture') were positively associated, and one ('that, I do not know what happens to the blood after donation') was negatively associated with intention to return. The Nagelkerke R-square value for the logistic regression model was 0.167.

Association between attitude, subjective norm, behavioural control and altruism, and intention to return to donate blood

Of the four items that were used to determine the association between attitude, subjective norm, behavioural control and altruism on one hand, and intention to return to donate on the other hand, three were significantly associated with intention to return. Only attitude was not significantly associated with intention to return (OR = 2·093, 95% CI: 0·889–4·929; $P = 0·091$). Behavioural control score (OR = 1·905, 95% CI: 1·267–2·865; $P = 0··002$); altruism score (OR = 2·309, 95% CI: 1·125–4·740; $P = 0·023$); and subjective norm score (OR = 1·909, 95% CI: 1·249–2·919; $P = 0·003$) were positively associated with intention to return. The Nagelkerke *R*-square value for the logistic regression model was 0·088.

Determinants of intention to return to donate blood among first-time voluntary non-remunerated blood donors and family replacement blood donors

When 20 variables that were identified as significant predictors of intention from all the group analyses were entered into a single multivariable logistic model, half were statistically significant (Table 5).

Being given refreshment, a motivational item or an incentive to donate blood; ease of access to the blood donation site; donating to help country; feeling good about self; SMS/email reminders and notification and television, radio or newspaper advertisement on blood donation were all positively associated with intention to return to donate. Blood credits (a form of a contract with the blood centre, where blood donors receive preferential access to blood transfusion for family and oneself), getting to know their test results for transfusion transmissible infections, and not knowing what happens to the blood after donating were negatively associated with intention to return to donate. The Nagelkerke *R*-square value for the final logistic regression model was 0.404.

Discussion

This study has identified the demographic and other factors that predict the intention of first-time blood donors to return to donate blood. To the best of our knowledge, this is the first study in Ghana to comprehensively explore the predictive values of determinants of intention to return to donate blood among of first-time donors, and

Table 3 Association between motivation for blood donation and intention to return to donate

Motivators (Ref – Disagree)	*P*-value	OR	95% CI for OR	
			Lower	Upper
… if it is easy to get to the blood donation site	**0·006**	2·306	1·277	4·163
… to help save lives	0·358	2·370	0·376	14·923
… if my friends or relatives needed blood	0·267	0·386	0·072	2·071
…to help my community	0·547	0·729	0·261	2·037
… if it meant that there will be blood available in future when my family or friends need it	0·819	0·867	0·257	2·931
… if it meant that there will be blood available in future when I need it	0·506	1·398	0·520	3·760
… because my religion encourages me to donate blood	0·851	0·947	0·540	1·663
… to help the Blood Bank	0·732	0·837	0·303	2·313
… if Ghana needs blood	**0·010**	3·572	1·349	9·459
… for blood credits for me and my family	**0·013**	0·440	0·231	0·839
… because it would make me feel good about myself	**0·002**	2·639	1·431	4·867
… to know how it feels like	0·052	0·560	·0312	1·006
… if I am notified through SMS/email reminders	**0·004**	2·354	1·310	4·229
… by educational talks on blood	0·214	1·610	0·760	3·412
… if I was asked by my peers who are blood donors	0·554	1·192	0·666	2·136
… by radio, TV or newspaper advertisement on blood donation	**0·006**	2·467	1·296	4·694
… by a blood drive at my school or workplace	0·904	1·046	0·506	2·162
… if I will get to know my blood group	0·146	1·779	0·818	3·870
… if I will get to know my other (TTI) test results	**0·023**	0·389	0·173	0·877
… if I will get a free medical check-up	0·641	0·837	0·396	1·767
… if I will get cash payment	0·735	0·884	0·433	1·804
… if I will get cash gifts	0·662	1·169	0·580	2·356
… because it is good for my health	0·736	1·111	0·601	2·056
… if I will get incentives such as milk, milo, T-shirts, blood tonic etc.	0·424	0·738	0·350	1·555
… to get the motivational items given to donors such as pens, exercise books etc.	0·490	1·300	0·617	2·741
… by the awards/prizes given on blood donor day	0·165	0·641	0·342	1·201
… because it is a way to make a difference	0·965	1·015	0·534	1·926
… because many of my friends/family are blood donors	0·245	1·400	0·794	2·468
… by an appeal for blood donation on radio or TV	0·052	1·968	0·995	3·891
… if my friends, relatives or co-workers asked me to donate blood)	0·574	0·838	0·453	1·551

Ref, reference category; SMS, Short Message Service; TTI, transfusion transmissible infection; TV, television.

among first-time voluntary non-remunerated blood donors and family replacement blood donors in Africa.

Based on the bivariate logistic regression models performed at group levels, motivators explained the greatest variance in intention to return to donate blood (36·2%;), followed by deterrents (16·7%) and three constructs of the Theory of Planned Behaviour (attitude, behavioural control and subjective norm) and altruism score (8·8%). The final logistic regression model with all 20 significant variables explained 40·4% of the variance in predicting intention to return to donate blood. These findings suggest that interventions to aid the intention to return to donate blood among all first-time donors should focus more on motivational factors. The low explanatory power of the Theory of Planned Behaviour in predicting the intention to donate blood suggests that scholars should not only explore these theoretical constructs in related future studies among the study population but should include other factors including deterrents, motivators and demographic factors.

In Ghana attitude as a construct of the Theory of Planned Behaviour was not found to be a significant predictor of intention to return to donate blood. This supports the findings of a study of African migrant communities in Australia [7], but not those of studies in Ethiopian adults [11], and in some high-income countries [12,13] where attitude is a significant contributor to intention to donate blood. Those who perceived themselves to have control over behaviour relating to blood donation and who had family and friends who supported blood donation were more likely to return as compared to those who did not in the group analysis. This is in agreement with the study by Kassie *et al.* (2020). Also, those who agreed to being altruistic were more likely to return,

Table 4 Association between deterrents to blood donation and intention to return

Deterrents (Ref – Disagree)	*P*-value	OR	95% CI for OR	
			Lower	Upper
... that, I do not have time to donate blood	0·491	0·846	0·526	1·361
... that, I think do not have enough blood	0·799	1·065	0·658	1·723
... that, I think blood donation is for other people	0·381	1·410	0·653	3·044
... that, the blood collection times are not convenient to me	0·096	0·663	0·408	1·076
... that, I do not like to complete the blood donor questionnaire	0·916	1·038	0·519	2·074
... if, the queues are too long	0·079	0·649	0·400	1·052
... if I am not called or asked to give	0·083	0·646	0·394	1·059
... because, the TV/Radio advertisements do not convince me to donate blood	0·256	0·735	0·433	1·249
... because, the motivational items that are given to blood donors are not good enough	**0·002**	3·505	1·558	7·885
... because I do not receive money for donating blood	0·175	0·529	0·211	1·327
... if I do not know there is a need for blood	0·141	0·695	0·428	1·128
... if I do not know where the nearest blood donation site is	**0·019**	1·798	1·101	2·937
... that, I do not know what happens to the blood after donation	**0·023**	0·541	0·318	0·918
... if I am not treated well by the Blood Bank staff	0·628	0·883	0·534	1·460
... if, the blood donation clinic setting is poor	0·955	0·986	0·603	1·614
... that, I am scared of the needle or pain/discomfort	0·947	1·020	0·563	1·850
... that, I am afraid of bruising/having a sore arm	0·527	1·278	0·597	2·736
... that, it can make me sick	0·092	0·561	0·286	1·099
... that, it can make me weak spiritually	0·563	1·290	0·545	3·052
... that, I am afraid of catching HIV if I donate blood	0·450	0·741	0·340	1·615
... because I had a bad reaction or fainted when I gave blood	0·671	1·188	0·536	2·632
... because I heard that others had a bad reaction or fainted after donating	0·121	0·599	0·314	1·144
... that, I am afraid of the sight of blood	0·088	2·129	0·895	5·064
... that, I am afraid of finding out about my HIV status	0·791	1·102	0·539	2·253
... that, I think the blood bank sells the blood that is donated for free	0·087	0·585	0·316	1·082
... that, I think blood mostly goes to people who are rich	**0·008**	2·709	1·301	5·640
... that, I am afraid the blood bank gives away donated blood to occultists/'sakawa' practitioners	0·927	0·968	0·478	1·957
... that, it is against my personal beliefs	0·390	0·676	0·277	1·652
... that, it is against my culture	**0·040**	3·515	1·059	11·664
... that, it is against my religion	0·478	0·689	0·246	1·928

HIV, Human Immunodeficiency Virus; Ref, reference category; TV, television.

supporting the proposition that blood donation is an altruistic behaviour. However, as with Polonsky *et al.* (2013), these Theory of Planned Behaviour constructs did not predict intention to return in the final logistic analysis.

Overall, the age of respondents in the current study was skewed towards younger donors and followed a similar pattern to the age distribution of blood donors who donate at the Southern Area Blood Centre. Gender representation of respondents was 72·5% males and 27·5% females. Data on age distribution of 30 140 blood donors at the Southern Area Blood Centre of National Blood Service Ghana, from March 2017 to February 2018 (National Blood Service Ghana records), showed that 74·4% of donors were below 35 years, and 76·8% were males. Although marital status, education and ethnicity were significantly associated with intention to return to donate blood in the sub-group analysis, they were insignificant in the final logistic model. The major ethnic groups in Ghana are Akan 47·5%, Hausa/Dagbani 16·6%, Ewe 13·9%, Ga-Dangme 7·4% of the population (Ghana Statistical Services records). The study covered three regions in southern Ghana, therefore it is not surprising that the Ga/Dangbe and Ewe were more than the Hausa/Dabgani, predominant in northern Ghana, in this study. The non-significant finding regarding education resonates with those studies conducted in high-income countries including Australia [12] and Ireland [13]. The significant associations found at the sub-group analysis level mirrors other studies conducted elsewhere. For example, in our study, marital status was a significant determinant of intention to return to donate blood with the married people being twice as likely to return as the unmarried. A study in Saudi Arabia [14] showed that married individuals had

Table 5 Determinants of intention to return

Predictor Variable	Categories	*P*-value	OR	95% CI for OR	
				Lower	Upper
Demographic characteristics					
Marital status (Ref - Single)	Married	0·629	0·868	0·489	1·541
	Other	0·142	4·444	0·607	32·538
Education (Ref - No formal education)	Basic	0·470	0·445	0·049	4·003
	Secondary	0·669	0·617	0·067	5·665
	Tertiary	0·289	0·302	0·033	2·764
Ethnic background (Ref - Akan)	Ewe	0·755	0·905	0·484	1·691
	Ga/Dangbe	0·156	0·649	0·357	1·180
	Hausa/Dagbani	0·179	0·491	0·174	1·386
	Other	0·360	0·612	0·214	1·751
Factors related to the respondents' decision to donate blood					
Whether a donor considers self as voluntary donor (Ref - Yes)	No	0·211	0·610	0·281	1·324
	Don't know	0·884	1·074	0·413	2·791
Whether donor received incentive/refreshment for donating (Ref - No)	Yes	**0·045**	1·678	1·011	2·785
Motivators					
… if it is easy to get to the blood donation site (Ref - Disagree)	Agree	**0·001**	2·650	1·485	4·731
… if Ghana needs blood (Ref - Disagree)	Agree	**0·034**	2·572	1·075	6·155
… for blood credits for me and my family (Ref - Disagree)	Agree	**0·012**	0·434	0·226	0·834
… because it would make me feel good about myself (Ref - Disagree)	Agree	**0·049**	1·792	1·004	3·201
… if I am notified through SMS/email reminders (Ref - Disagree)	Agree	**<0·001**	2·843	1·596	5·064
… by radio, TV or newspaper advertisement on blood donation (Ref - Disagree)	Agree	**<0·001**	2·972	1·662	5·315
… if I will get to know my other (TTI) test results (Ref - Disagree)	Agree	**0·010**	0·397	0·196	0·804
Deterrents					
… because, the motivational items that are given to blood donors are not good enough (Ref - Disagree)	Agree	**0·046**	2·363	1·017	5·490
… if I do not know where the nearest blood donation site is (Ref - Disagree)	Agree	0·967	0·989	0·587	1·668
… that, I do not know what happens to the blood after donation (Ref - Disagree)	Agree	**0·016**	0·499	0·283	0·877
… that, I think blood mostly goes to people who are rich (Ref - Disagree)	Agree	0·107	1·800	0·881	3·675
… that, it is against my culture (Ref - Disagree)	Agree	0·204	1·911	0·703	5·191
TPB constructs and altruism					
Subjective Norms (Ref - Negative)	Positive	0·089	1·561	0·935	2·606
Behavioural control (Ref - Negative)	Positive	0·120	1·507	0·899	2·525
Altruism (Ref - Negative)	Positive	0·228	1·768	0·700	4·463

Ref, reference category; SMS, Short Message Service; TPB, Theory of planned behaviour; TTI, transfusion transmissible infection; TV, television.

higher blood donation knowledge level compared to unmarried (mean rank was 182·3 vs. 158·9), and higher blood donation attitude score compared to unmarried (mean rank was 184·6 v.s 153·8). However, contrary to the findings of the study by Alfouzan (2014), which showed that married individuals had higher rate of blood donation compared to unmarried individuals (53·3% vs. 29·4%), our study of first-time donors showed lower blood donation rates among married people compared to unmarried individuals, possibly due to the younger age of most respondents.

Similarly, secondary and tertiary education were identified as a significant positive predictors of intention to return to donate compared to those with tertiary education. This is similar to findings by a study in Botswana [15]. Secondary schools are a convenient organized group that are targeted, educated and mobilized for blood donation in Ghana. Blood collection in schools increases the convenience of access to donation sites for donors and eliminates barriers relating to time, lack of opportunity and difficult access. Having a convenient place to donate has been identified as a motivator for frequent repeat donations [16].

In the final logistic regression model, factors that positively predicted intention to donate blood included: motivational incentives for donating; ease of access to the blood donation site; donating blood because Ghana needs blood; donating because it makes one feel good about

oneself; SMS and email reminders; and television, radio or newspaper advertisement on blood donation. Other studies have also identified the use of mobile phones, television, radio or newspaper advertisements for promoting repeat blood donation in SSA [3,17] and elsewhere [18,19]. Thus, interventions for encouraging first-time blood donors to return to donate should include those that focus on television and radio advertisement and educational information; telephone calls and mobile phones messages with reminders to donors on when and where to donate. The potential impact of reminders to blood donors with information on when blood is needed, when and how to donate is supported by the finding that 68% of reasons for donors not returning were due the Blood Centre's failure or inability to send such reminders.

In Ghana, 'blood credits' have been used as incentive for blood donation, but is in the process of being phased out due to poor implementation and abuse. First-time donors were less likely to have the intention to return if they were motivated by 'blood credits'. They are also less likely to have intention to return if they would donate blood with the motive of getting to know their results for transfusion transmissible infection tests. These findings are contrary to the findings of previous qualitative studies which identified these factors as motivators for blood donation [8,20]. 'Blood credit' as a negative predictor of intention to return is mirrored by the findings of a study in South Africa which showed that donors were more likely to return if they were not motivated to donate because blood would be available for themselves [3]. The fear of knowing one's transfusion transmissible infection, especially HIV test results, and associated stigmatization has been identified as a strong deterrent by numerous studies in SSA [20–23], and especially among young donors in Ghana [8]. It is, therefore, not surprising that getting to know the results of transfusion transmissible infection tests negatively predicted intention to return to donate among respondents in this study who are mostly young. Interventions for helping first-time blood donors in the study population to become repeat blood donors should, therefore, include education on the importance of infectious disease screening of donated blood, and avoid any focus on providing 'blood credits'.

Similarly, group analysis indicated that those who received refreshment/incentives were twice as likely to return as compared to those who did not receive refreshment/incentives. The understanding of what constitutes an acceptable motivational item for donation compared to an item that has a value high enough to be considered as remuneration, or even paid donation, varies widely [8,24]. In our study, respondents' description of incentives referred to refreshments, token motivational items (e.g. pens) and items received by both voluntary non-remunerated blood donors and family replacement blood donors from patients or their families. Another surprising finding was that those who considered inadequate motivational items for blood donors as a deterrent to blood donation were more likely to have the intention to return to donate. This could also be attributed to the lack of clarity on what items are considered as motivational items by blood donors. It is also possible that the respondents, who were all first-time blood donors, considered what they received as motivational items for donating blood to be adequate. Unfortunately, this study does not have enough data to determine whether the respondents considered the current motivational items as being adequate. In Ghana, incentives are not clearly defined and could vary between donation centres. An important step for the Blood Service is to discuss with stakeholders to define which incentives are acceptable for non-remunerated donations, and which constitute remuneration for donations; and develop a policy document and donor education materials based on the outcome of such discussions. It is also important to have a dialogue with all stakeholders and standardisz incentives. This will facilitate a controlled implementation and evaluation of the effect of incentives on repeat blood donations, thus providing evidence on how to effectively apply incentives without compromising the autonomy of the donor and the safety of the blood supply. The issue of what constitutes an incentive and remuneration for blood donation has received some attention in the in SSA [17] and non-SSA countries [25]. Thus, it was not surprising that motivational incentives significantly increased the intention of respondents to return to donate blood.

Although 'not knowing where the nearest blood donation site is', 'thinking that blood mostly goes to people who are rich', and cultural connotations to blood donation were not significantly associated with the intention to return in the final logistic regression model, these were significantly associated with intention to return in the in the sub-group analysis. The lack of awareness of blood donation site as a deterrent [20] to returning to donate is mirrored by ease of access to the blood donation site as a motivator [20]. Therefore, improvement of access to donation site should be a critical focus of interventions to promote blood donation. Negative influence of cultural beliefs and practices have been identified by a previous study as a deterrent to blood donation [26].

Respondents who would be deterred from donating blood by not knowing what happens to the blood after donation and if they thought that blood mostly goes to the rich were less likely to have the intention to return to donate blood. Rumours, mistrust and misconceptions related to blood and blood donation have been identified [8,20,27] that could make donors worry about what

happens to the blood. Common misperceptions include the belief that blood has spiritual significance; that it is used for rituals and sacrifices to deities and for covenants between persons, including covenants between the blood donor and the blood recipient [8]; and that donated blood is sold [21,22,26]. Spiritual connotations relating to blood were identified as a key perception about blood and blood donation, possibly influenced by certain traditional practices, in a qualitative study in Ghana [8], and it is therefore not surprising that this deters intention to return to donate in the study population. Interventions aimed at promoting blood donation in Ghana need to focus on demystifying myths and misperceptions through education.

Limitations of the study

The current study involved three regions of Southern Ghana, Greater Accra, Eastern and Central regions, and thus the findings may not reflect the population of first-time blood donors in whole of Ghana. The current study did not assess the determinants of actual return to donate blood but used intention to return as a predictor of donor return. Although intention is a predictor of actual behaviour, intention to return to donate blood may not necessarily translate into actual blood donation behaviour.

Conclusion

Factors that positively influence blood donor return include motivational items, convenient access to blood donation session, if the donors know that Ghana needs blood, and if it makes people feel good about themselves, SMS and email reminders, and advertisements on blood donation through television, radio or newspapers Factors that negatively influence repeat blood donation include, donating to get 'blood credits', getting to know one's TTI test, and not knowing what happens to the blood after donating. This study suggests that interventions that are likely to increase first-time donor return in Ghana include those aimed at providing information and education on blood donation, improving access to donation sites, reminders for blood donation and a more evidence-based incentive system. Incentives should receive priority attention, as they could potentially motivate or demotivate blood donors. There is the need for the Ghana NBS to work with academic institutions and implementation researchers to develop and implement interventions in an empirical manner to facilitate quality evaluations and scale-up studies.

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Conflicts of interest

The authors declare no conflict of interests.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:
Appendix S1. Survey Questionnaire.

AAppendix

Measures

Intention

Intention to return to donate blood was measured by using one questionnaire item 'I plan to return to donate blood in 4 months when I will be due for donation'. Responses ranged from 'strongly disagree' (1) to 'strongly agree' (5). Intention to donate blood was categorized into binary outcome as intend to return (1) or not (0).

Attitude

Attitude towards blood donation was assessed using six items, 'I find giving blood negative/positive, good/bad, meaningless/worthwhile, pleasant/unpleasant, annoying/enjoyable, unappealing/appealing' on five-point Likert scale. The negative items were reverse scored. A mean score of attitude was computed and categorized into a binary variable using a cut-off point of </=3.4 as 0 'disagree', and>/=3.5 as 1 'agree'.

Subjective norm

Subjective norm was assessed using two questionnaire items, "My family/friends think I should continue giving blood as long as my health allows it; and 'I normally do what my family and friends want me to do' on five-point Likert scale. A mean score of subjective norm was computed and categorized into a binary variable using a cut-off point of </=3.4 as 0 'disagree', and>/=3.5 as 1 'agree'.

Perceived behavioural control

Direct perceived behavioural control was assessed by two items, 'If I wanted to, I would be able to continue giving

blood as long as my health allows it; and I find it hard to give blood time after time' on five-point Likert scale. The negative items were reverse scored. A mean score for perceived behavioural control was computed and categorized into a binary variable using a cut-off point of </=3.4 as 0 'disagree', and>/=3.5 as 1 'agree'.

Altruism

Altruism was assessed using five items, 'I prefer working towards my own well-being', 'I try to work towards the well-being of society', 'I am not very interested in helping others', 'It is important to me that I help others', and 'It is important to help the poor and the needy'. Respondents were to select only one item that most applied to them. The negative items were coded as '0' and positive items as '1'.

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ORIGINAL PAPER

Endoscopies, blood-borne viruses and blood donors: time to move on from precaution

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Vox Sanguinis

Background and objectives Based on the Council of Europe directive which dictates regulatory requirements in Australia, blood donors are currently deferred from donating for 4 months after an endoscopic procedure if either polyps were removed or a biopsy sample was taken. We aimed to assess the incidence of blood-borne viruses (BBVs) (HIV, hepatitis B and C) in blood donors who donated after an endoscopic procedure and evaluate the risk to blood safety through risk modelling.

Materials and methods Donors from 1/1/2013 to 31/12/2017 with an endoscopy deferral on their blood donor file with pre- and post-BBV testing were analysed to determine an incidence of BBVs using standard methods. The standard blood donor cohort was used as a comparator group. Using the incidence of endoscopies and BBV risk, the total residual risk estimate of allowing donors to return postendoscopy without restriction was calculated.

Results The incidence of a BBV postendoscopy in this large cohort of 16,283 where testing has been confirmed postendoscopy was zero (95% CI 0–0·000105). The upper confidence interval of the zero events is 10·5 per 100 000 donations. Total positive donations from 2017 repeat donors were 1·87 per 100 000 (95% CI 0·0000117–0·0000277). Sensitivity analysis demonstrated that the residual risk remained negligible under realistic worst-case scenarios.

Conclusion A BBV endoscopy deferral is not required for blood safety in Australia. The presented data has enabled us to submit a request for an exemption to our regulator, which has been approved and the policy change subsequently implemented by Lifeblood on 4/4/2020.

Key words: endoscopy, blood safety risk, infection.

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Introduction

As per regulatory requirements in Australia, a donor who has undergone an endoscopy in which polyps were removed or a sample is taken was ineligible to donate for 4 months, irrespective of whether the procedure was undertaken inside or outside the country. This requirement is due to the theoretical risk of exposure to a blood-borne virus (BBV), defined as human immunodeficiency virus (HIV), hepatitis B virus (HBV) or hepatitis C virus (HCV), from the procedure [1]. Prior to 2005, based on Australian infection control practices, the lack of reports of transmission in Australia and the considered negligible risk, there was no BBV deferral for endoscopic procedures. However, in 2004, the updated Council of Europe Guideline version 11 required a deferral period of 4 months for blood donors who underwent an endoscopic examination using flexible instruments [2], the version to which Australian Red Cross Lifeblood (Lifeblood) was regulated to at the time, and thus, Lifeblood closed this gap by implementing this deferral.

As endoscopic equipment is reusable, a failure of sterilization could occur and collection of biopsy samples results in an increased risk of blood contact, potentially

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transmitting a BBV such as transfusion-transmissible infections (namely HBV and HCV). Of convincing reports, a single case of HBV transmission via endoscopy has been reported in 1983 [3], and two cases of HCV transmission were reported in 1997 [4]. Since these reports, endoscope design and reprocessing methods have been improved and standardized. To date, there has never been a case reported of HIV transmission via endoscopic procedures. Bacterial infections have been transmitted by endoscopes with a recent review cited 18 outbreaks of bacterial infection [5]; however, 16 of these were associated with duodenoscopes, nearly all the described patients had underlying disease necessitating deferral, and the transmission events changed colonic flora rather than caused bloodstream infection, and so there would be no risk contaminating a blood donation from bacteria.

Endoscopic procedures are increasing in Australia. In 2016–2017, there were 916 360 endoscopies and colonoscopies with biopsy performed [6], which increased to 956 936 in 2017–2018 [6]. The expansion of the National Bowel Cancer Screening programme to all Australians aged 50–74 is expected to double the number of colonoscopy procedures in the future [7]. Data from blood donors with approximately 1·3 million donations a year document approximately 4400 deferrals a year in blood donors who have had an endoscopy with biopsy, although the data are incomplete, as the procedure is not documented if the deferral period has already elapsed through self-deferral. Therefore, there is a potential sufficiency gain in reducing the deferral period.

A recent systematic review and meta-analysis graded the quality of evidence for a BBV risk and endoscopy as 'very low' [8]. However, the authors concluded there was an association. For HBV, the pooled odds ratio (OR) for 9 case–control studies was 2·21 (95% CI 1·26–3·86 p = 0·0005). However, this association was weakened when sub-group analyses was performed such as using the adjusted OR when known confounders were adjusted for (OR 1·76, 95% CI 1·28–2·43), low prevalence regions (OR 1·34, 95%CI 1·01–1·79) and there was no association in case–control studies published after 2004 (OR 1·47, 95% CI 0·95–2·29). For HCV, 17 case–control studies showed a pooled OR of 1·76 (95% CI 1·45–2·14, p < 0·00001). For HCV, the sub-group analysis did not appreciably change the result. The authors concluded that further high-quality studies are required to formulate stronger evidence-based recommendations on endoscopic deferral and blood donation.

Our study aimed to determine if there was sufficient evidence to remove the endoscopy deferral by estimating the incidence of BBVs among Australian donors returning to donate after an endoscopy with biopsy and integrated these data into a model to estimate the recipient BBV infection risk of removing the existing deferral.

Materials and methods

The endoscopy cohort consisted of all blood donors with a record of endoscopy with biopsy deferrals from 1 January 2013 to 31 December 2017 and followed up until June 2018, providing between 6 and 58 months to return, depending on when the endoscopy with biopsy deferral was applied. The comparator group was all repeat donors who donated in 2017 (1 232 537) [9] minus those donations who donated postendoscopy deferral in 2017 (n = 3701).

All donations are screened for HIV-1 RNA, HCV RNA and HBV DNA using either one of two assays (the Procleix Ultrio, until July 2013; or Ultrio Plus, from July 2013 onwards, Grifols Diagnostic Solutions, Inc., Emeryville, CA) on a fully automated nucleic acid testing (NAT) platform for blood screening (Procleix Tigris system; Grifols Diagnostic Solutions Inc., Emeryville, CA). Samples reactive on the Ultrio assay are 'discriminated' to identify the specific virus using the Procleix HIV-1, HCV and HBV discriminatory assay. Donations are also screened by serological screening tests including anti-HIV-1/2 and p24 Ag, anti-HCV and hepatitis B surface antigen using a sequential immunoassay strategy [10]. All positive results are referred externally for confirmatory testing. Positivity was determined by a confirmed discriminated NAT result and/or positive serology on sequential immunoassays and confirmed by immunoblot for HIV and HCV. All donations with confirmed positive results for HIV, HBV and HCV were included in the results.

Initial descriptive analysis was done in Microsoft Excel. Confidence intervals (CIs) for rates were calculated using standard methods.

Lifeblood uses the Weusten model internally [11] to calculate the window period residual risk estimates for BBVs. In brief, it derives the combined probability that the virus is not detected during the window period and that an infection develops in the recipient of the contaminated blood product. Input data for the 2017–2018 modelled estimates can be found in the Appendix S1. Given zero BBV infections were found in the endoscopy cohort, a sensitivity analysis was performed using the 2017–2018 calculated residual risk. Various theoretical rates of infection from endoscopy (1 in 500 000, 1 in 10 000 and 1 in 76) based on current or double endoscopy deferrals were then added to the number of donors with an identified incident infection based on 2017–2018 data to provide the total additive risk expected from allowing endoscopy donors to donate without restriction.

Results

Blood donor deferrals and characteristics

In the 5-year study period, there were a total of 6 414 960 donations with females and males providing 43·4% and 56·6% of donations, respectively. There were 22 006 endoscopies with biopsy deferrals applied in the period from 1 January 2013 until 31 December 2017 and followed up until June 2018, of which 51·5% were in males. This approximates to 4401 registered endoscopy deferrals a year.

A total of 5723 donors (26%) did not return to donate after the endoscopy deferral, leaving 16 283 deferral instances where donors returned to donate. Of those, 704 (4·3%) were new donors with 15 579 (95·7%) deferral instances in repeat donors (see Fig. 1), with 14 587 unique repeat donors (given some donors had multiple deferrals in the study period), to total 15 291 unique donors.

BBV incidence

For the 15 579 instances postendoscopy with a documented negative test who returned to donate, no BBVs (HBV, HCV and HIV) were diagnosed in the cohort in the 5-year period with zero additional infections in the 704 new donors. The incidence of a BBV postendoscopy in this large cohort of 16 283 where testing has been confirmed postendoscopy is zero (95% CI 0–0·000105). The upper confidence interval of the zero events is 10·5 per 100 000 donations. Total positive donations from repeat donors not in the endoscopy cohort in 2017 were 23/1 228 836 or 1·87 per 100 000 donations (95% CI 1·186–2·809).

In donors with an endoscopy deferral, the numbers of deferrals peaked in the older age groups. The mean age of the deferral was 54 years, which is significantly higher than the mean age of non-endoscopy deferred donors of 44·6 years (2015–2018 data, per donation).

Residual risk calculation

Table 1 presents the sensitivity analysis performed using the residual risk calculations. It can be seen that even with a conservative rate of 1 in 500 000 endoscopies with biopsy procedures resulting in a transfusion-transmitted infection with HIV, HBV or HCV, and doubling the donor deferrals does not materially impact on the risk to recipients. The 1 in 10 000 approximates to the upper CI for the zero detections and remains under the negligible threshold of 1 in 1 000 000. Around 57 donors a year are required to be infected with HCV postendoscopy for the residual risk to approach 1 in 1 million or 1 in every 76 procedures resulting in a transmission. For HBV, because of the longer window period, the number of infections in donors per year is approximately 10·5 with a rate of infection following endoscopy of 1 in 419.

Discussion

We have demonstrated in our large cohort of blood donors, that there were zero HIV, HBV and HCV

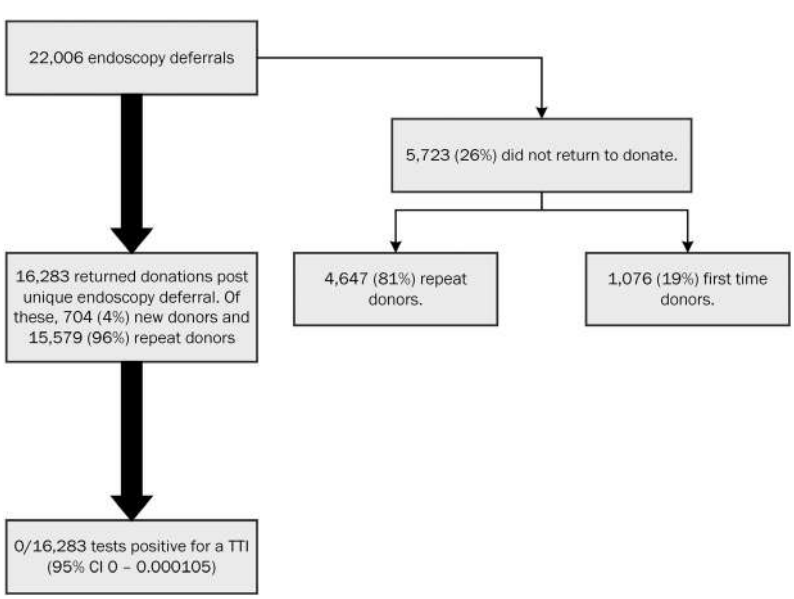

Fig. 1 Flow chart of endoscopy deferrals, 2013–2017.

Table 1 Residual risk calculations sensitivity analysis of allowing endoscopy donors to donate without restriction under various scenarios

Number of endoscopies per 2 years in donors	Rate of HBV[a] and HCV[b] infections postprocedure	Number of endoscopy donors with a TTI[c] in 2 years	Harmonic donation interval mean	Residual risk WP[d] calculation
8800 (found rate)	0	0	230 (HCV[b]) 84 (HBV[a])	1 in 96·6 million (HCV[b]) 1 in 42·8 million (HBV[a])
17 600 (double endoscopy rate)	1 in 500 000	0·035	230 (HCV[b]) 84 (HBV[a])	1 in 95·7 million (HCV[b]) 1 in 40·0 million (HBV[a])
17 600 (double endoscopy rate)	1 in 10 000	1·76	71 for HCV[b] (assume two additional positive donors have very conservative 30 day inter-donation period 45 for HBV[a] (two 30 day periods and two 60 day periods plus 84)	1 in 20·7 million (HCV[b]) 1 in 5·1 million (HBV[a])
8800 (found rate)	1 in 76	115	71	1 in 1 million (HCV[b]) 1 in 156 thousand (HBV[a])

[a]Hepatitis B Virus.
[b]Hepatitis C Virus.
[c]Transfusion-transmitted infection.
[d]Window Period.

infections detected postendoscopy. Whilst for the incidence comparison one year was chosen for ease of calculation, our internal published data demonstrate there has not been a change in incidence of BBVs over the study period. [9] Because of the upper bound of the confidence interval, it cannot be definitively concluded that there is not an elevated risk. Using the lower bound of the 2017 repeat cohort and upper bound of the endoscopy cohort, the upper limit of relative risk could be as high as almost nine. However, our sensitivity analysis using the residual risk demonstrates this is not a significant blood safety risk. The numbers shown in Table 1 are inconceivable in the current Australian context; given there has never been a published case of such a transmission, especially as there have been no known endoscopy outbreaks/transmissions in Australia and there are approximately 1 million endoscopies a year. It is clear that this upper confidence interval is likely attributable to the power of the cohort and transmission via endoscopy is documented as a negligible event (considerably less than 1 in 1 000 000). Therefore, transfusion-transmitted infection due to blood donation postendoscopy is also expected to be a negligible event, especially since donation immediately after endoscopy would not occur with the proposed 1-week deferral.

In the context of our findings, it is relevant to briefly consider the literature and the context of the endoscopy deferral with other risks and the impact a small increase in an odds ratio would have, whether real or due to confounding, on donor risk.

Case reports of endoscopic transmission of BBVs are exceptionally rare and in a time before standards of endoscopy reprocessing and monitoring were developed and implemented. Bronowicki *et al.* document transmission of HCV during a colonoscopy from a patient known to have HCV to two other patients [4]. Transmission was confirmed by sequencing the genomes of the HCV isolates of the patients. Through an investigation of the disinfection procedures used, it was noted that the disinfection recommendations made by the American Society for Gastrointestinal Endoscopy and the British Society of Gastroenterology were not followed. It was also noted that anaesthetic line contamination was also a potential mode of transmission. Another case report by Le Pogam et al. [12] regarding a transmission of HCV during a colonoscopy, hypothesized that the transmission of HCV during the procedure was potentially implicated due to improperly disinfected equipment but noted that it could have been used of a multidose anaesthetic vial. In addition, as there were two colonoscopes in use and the patients were directly after each other on the list, it was noted that it was unlikely the same colonoscope would have been used. Therefore, in this and other case reports [13, 14], the exact cause of transmission remains uncertain but multidose vials and/or drug diversion to an addicted healthcare worker are likely causes, given these routes have been repeatedly implicated as the cause of hepatitis outbreaks. [15–17]. This risk is not unique to the endoscopy procedure and has caused large outbreaks of other medical interventions not subject to blood donation deferral [18, 19]. Therefore, the endoscopy deferral should

be considered in the context of this larger but currently acceptable risk, given there is no donor deferral for procedures given with an anaesthetic.

No cohort studies have demonstrated an association between endoscopy and transfusion-transmitted infections [8, 20, 21]. It is acknowledged that two cohort studies are now decades old with a small sample size in the cohorts. The largest cohort included 9008 patients in the gastroscopy cohort. Our cohort is larger.

Meta-analysis [8] demonstrates a small odds increase as described in the introduction. However, there are several points when considering this: (1) the bias that is inherent in case–control studies. (2) Association and not causation. Similar associations have been demonstrated attributed to hospital exposure (e.g. multiuse vials, drug diversion) rather than the endoscopy procedure itself, but no deferral exists for other procedures. HBV and HCV symptoms are non-specific and include nausea, vomiting and abdominal pain. Gastrointestinal bleeding and GI symptoms are associated with hepatitis infections [22] and are also indications for endoscopic examination. Case–control studies cannot differentiate between people with HBV and HCV infections being more likely to undergo endoscopy. This potential source of confounding has not been explored or raised as a limitation. (3) Strength of the association and absolute risk versus relative risk. The American Society for Gastrointestinal Endoscopy [23] conclude that 'existing data suggest that the risk of viral transmission via endoscopy is extremely low to non-existent'.

Another way of considering the risk is considering the OR of HBV and HCV reported in the systematic review in the context of blood donors [8], whilst noting its limitations. The pooled OR of HBV in low prevalence areas was 1·34. It is assumed the endoscopy cohort is similar to the blood donor cohort in other characteristics (as is aimed for in a case–control study) and is expected given they are blood donors. There have been six acute HBV infections in blood donors in the period from 2015 to 2018 (Lifeblood internal data), although all except one were plasma for fractionation only donors and were therefore not a fresh component risk. A total of 5 294 789 donations occurred in that period giving a rate of 0·11 per 100 000 donations. With an increase of 1·34 times this would result of a rate of 0·15 per 100 000 donations in the endoscopy cohort, assuming the association is true. If the endoscopy cohort represents double the rate or 8800 endoscopy deferrals a year this would increase the risk by 0·01 of a positive donor in a year. Once the 0·01 extra donor is incorporated into the residual risk, this further dilutes the risk, which is based on the window period. This comparison shows that because the event is so rare, the attributable risk of this purported association and OR is not translated into a significant risk increase. Precautionary decision-making in the past seems not to have considered the context of total attributable risk of a rare event in a low prevalence population with a marginally elevated OR, whether the association is real or due to confounding. Therefore, even if the small increase in risk demonstrated in the case–control studies is accepted as a precautionary scenario, the attributable risk increase is negligible and does not approach Lifeblood's tolerability thresholds.

The numbers of donors and their donation ability affected by the deferral is likely an underestimate due to self-deferral, given the deferrals registered only include those where the donor advised Lifeblood of the procedure. If a donor returns to donate >120 days postendoscopy after a self-deferral, the deferral is not applied as the donor is allowed to donate. Allowing donors to donate without restriction is not expected to increase the risk of a transfusion-transmitted infection whilst having a positive impact on sufficiency, given it is regular older donors who are most impacted by this deferral.

A limitation of this study is that 26% of donors who had an endoscopy deferral did not return to donate. The return proportion is higher than found in a tattoo cohort, where 43·7% did not return [24] but lower than donors with an uneventful whole blood donation, where 16% did not return within 24 months [25]. However, non-return postendoscopy is unlikely to be related to self-perceived risk of a blood-borne virus and therefore this limitation is not expected to alter the risk profile.

Therefore, we conclude that reducing the BBV deferral for endoscopic procedures performed in Australia will not lead to an unacceptable BBV risk for blood recipients. To cover the risk of asymptomatic bacteraemia, we recommend a short-term deferral associated with recovery from the procedure.

Given the lack of evidence of a significant risk in the international literature of endoscopic procedures in regulated/licensed premises within Australia, as well as the conclusion of the analysis above, any increase in risk to recipients of HIV, HBV or HCV is theoretical in the Australian context. The current deferral is not justified, even using the precautionary principle, given the multiple evidence lines that demonstrate it is not a significant risk. We submitted a request to our regulator to remove the 4-month deferral requirement in cases where the procedure was undertaken in Australia, and this was approved on 7 January 2020. We implemented this change in April 2020. Due to uncertain infection prevention and control measures in some overseas countries, we did not apply for the exemption if the procedure was undertaken overseas. Other blood services may wish to consider if a BBV deferral for endoscopic procedures remains relevant in their context.

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Conflict of interest

All authors report no conflicts of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:
Appendix S1. Supporting Information.

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ORIGINAL PAPER

How donor selection criteria can be evaluated with limited scientific evidence: lessons learned from the TRANSPOSE project

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Abstract

Background and objective Donor selection criteria (DSC) are a vital link in the chain of supply of Substances of Human Origin (SoHO) but are also subject to controversy and differences of opinion. Traditionally, DSC have been based on application of the precautionary principle.

Materials and methods From 2017 to 2020, TRANSPOSE (TRANSfusion and transplantation PrOtection and SElection of donors), a European research project, aimed to identify discrepancies between current DSC by proposing a standardized risk assessment method for all SoHO (solid organs excluded) and all levels of evidence.

Results The current DSC were assessed using a modified risk assessment method based on the Alliance of Blood Operators' Risk-based decision-making framework for blood safety. It was found that with limited or diverging scientific evidence, it was difficult to reach consensus and an international standardized method for

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decision-making was lacking. Furthermore, participants found it hard to disregard their local guidelines when providing expert opinion, which resulted in substantial influence on the consensus-based decision-making process.

Conclusions While the field of donation-safety research is expanding rapidly, there is an urgent need to formalize the decision-making process regarding DSC. This includes the need for standardized methods to increase transparency in the international decision-making process and to ensure that this is performed consistently. Our framework provides an easy-to-implement approach for standardizing risk assessments, especially in the context of limited scientific evidence.

Key words: blood safety, donor health, donors, haemovigilance, donor vigilance, donor safety, donor selection.

Introduction

Over the last decades, there has been a strong focus on recipient safety with DSC often being based on the precautionary principle [1,2] in the face of lack of scientific evidence. There is a significant reluctance of revising DSC particularly for the categories concerning high-risk behaviour and the concomitant potential risk of transfusion- and transplantation-transmitted infections.

The European Directorate for the Quality of Medicines and Healthcare guides has provided the guidelines to change certain DSC if comprehensive risk assessments are carried out. The need for a definition of a tolerable risk level, with respect to both donor and recipient safety, and its impact on supply as well as costs has been suggested [3].

Numerous international collaborations have been initiated to improve these matters, among these the NOTIFY Library (https://www.notifylibrary.org), where published vigilance data as well as references of scientific papers on donor and recipient adverse reactions can be found.

Traditionally, DSC are assessed and re-evaluated applying validated risk assessment tools. However, despite numerous such assessment tools existing, there is currently no international agreement on the best method of carrying out such risk assessment.

For some DSC, where evidence is sparse or diverging, the guidance is often based on a combination of expert group decision-making and the precautionary principle. Group decision-making can be classified into three approaches [4]: majority-based, ranking-based and consensus-based approaches. The first includes a voting procedure where decision is based on majority votes. The second makes use of a numerical score to rank the overall performance of the DSC and the alternatives. The third and final define a certain level of agreement among participants.

To provide support for decision-making, a clinical decision support systems (DSS) may be implemented. These are computer-based programs that analyse data to provide prompts and reminders to assist healthcare providers in implementing evidence-based clinical guidelines at the point of care. Such systems have already been implemented or recommended as a standard part of transfusion service and patient blood management [5,6].

TRANSPOSE aimed to identify discrepancies between the available scientific evidence and the current DSC across Europe for blood, plasma, hematopoietic stem cells, gametes, embryos, and tissues and, furthermore, to propose new DSC that balances recipient and donor protection by either reducing the risk of adverse events and reactions or increasing sufficiency by relaxing precautionary deferrals that do not impact significantly on risk. Here, we present the results of our choice of methodology and address the limitations of the current methods used in donor risk assessment.

Methods

From 2017 until 2020, the following European stakeholders partnered in TRANSPOSE: Region Hovedstaden, Denmark, Sanquin Blood Supply, the Netherlands; Establissement Français du Sang, France; National Health Service Blood and Transplant, Scottish National Blood Transfusion Service; United Kingdom; CSL Plasma Gmbh, Germany; Aarhus Universitets Hospital, Denmark; Sihtasutus Pohja-Eesti Regionaalhaigla, Estonia; Banc de Sang I Teixits, Spain; Blutspendedienst des Bayerischen Roten Kreuzes Ggmbh, Germany; Bioef-Fundacion Vasca de Innovacion e Investigation Sanitarias-Osakidetza-Centro Vasco de Transfusión y Tejidos Humanos, Spain; Finnish Red Cross Blood Service, Finland; Ministry of Health, Malta; Zavod Republike Slovenije za Transfuzijsko Medicino, Slovenia; Universitätsklinikum Hamburg Eppendorf, Germany; Viesoji Istiaga Nacionalinis Kraujo Centras,

Lithuania; TRIP foundation, The Netherlands; Blood Transfusion Service SRC Berne Ltd, Switzerland; Associazione Voluntari Italiani Sangue, Centro Nazionale Sangue, Instituto Superiore di Sanità, Italy; Karolinska University Hospital, Sweden; Blood Center of University General Hospital of Alexandroupolis, Greece; Ïnstituto Português do Sangue e Transplantação, Portugal.

Of these, 38 partners, from here referred to as 'participants', participated in the work presented here; 28 worked within the field of blood and plasma donation; and 10 within the fields of cells and tissue donations. Of these, 81·6% were healthcare professionals, 2·6% worked in research and 15·7% in administration. Region Hovedstaden co-ordinated the study presented in this paper. All documents including risk assessments and the participants' details are available at https://www.transposeproject.eu/ and https://webgate.ec.europa.eu/chafea_pdb/health/projects/738145/summary.

Risk assessments

An inventory of available validated risk assessment tools within the field of transfusion and tissue/cellular transplantation was made based on a survey among all participants (Table 1). A subgroup of participants then evaluated the identified methods to assess if one method could be used to assess DSC across all types of SoHO. Some tools were designed to assess a particular transfusion risk (e.g. transfusion-transmitted infection) and others were found suitable to be used to assess broader issues in transfusion and transplantation practice. There were common themes to the assessment tools, in that they prompt gathering of all relevant information so that important considerations are not missed, and they provide a framework to assist in systematic assessment of risk, often using a matrix. Based on this, it was recommended to build on the principles of Alliance of Blood Operators' Risk-Based Decision-Making framework for blood safety (ABO RBDM) as this was found to be the most well-developed and extensive risk assessment tool applicable across SoHO. However, to allow the assessment of all DSC within the timeframe of the project this required the development of a shorter method. This was approved by all 38 participants. A comparison of the ABO RBDM and the TRANSPOSE risk assessment procedure is shown in Table 2. To assess local legislation or guidelines and the potential conflict with the conclusion of the individual risk assessment, participants were asked to state separately if the conclusion conflicted with the guidelines or legislation in their country.

To perform the risk assessments, the participants were split into three subgroups. One for assessing risks for whole blood (WB) donors (including platelet-apheresis

Table 1 Risk assessment tools for transfusion and transplantation of substances of human origin identified by TRANSPOSE

Tool name	Eustite (European System for Inspections in Tissue Establishments)	Eufrat (European up-front risk assessment tool)	Cost Utility Tool	GREAT (Geographical risk evaluation and assessment tool)	BRISK (blood risk tool)	Risk-based decision-making framework for blood safety (RBDM)
Organization	EU	EU	International Society Blood Transfusion	Food and Drug Administration (FDA)	Food and Drug Administration (FDA)	Alliance of Blood Operators
Short description	Used by SoHO EU projects for tissues and cells to assess the impact of serious adverse reactions and events	Quantification of risk of transmission of an emerging infectious agent by transfusion	Perform analysis of blood screening strategies for different test combinations	Generates geographic risk ranking maps (only available for FDA use)	Provides template for risk assessment models (only available for FDA use)	Provides framework for assessment of any risk to transfusion. May be used as rapid or more comprehensive tool

Table 2 A comparison of the Risk-Based Decision-Making framework (RBDM) for blood safety and the TRANSPOSE risk assessment for donors and recipients of substances of human origin (SoHO), excluding solid organs

Step	Alliance of Blood Operators' Risk-based decision-making framework for blood safety	TRANSPOSE risk assessment
Preparation	. Review the purpose of the tool . Review the risk management foundations . Understand the organization of the tool	. Understand the organization of the simplified tool
Problem formulation	. Characterize the risk . Identify the decision driver . Formulate the assessment question . List preliminary management options . Determine the needed assessments for 'assessments'	. Characterize the risk in general . List assessment questions
Participation strategy	. Review considerations for communication and stakeholder involvement . Define the need for stakeholder participation . Identify and assess stakeholder audience . Participation plan . Initiate the plan	. Invite all TRANSPOSE participants to the work . Invite collaboratoring stakeholders and advisory board members to review the output
Assessments	. Assessment principles . Screening assessment . Blood safety risk assessment . Health economic and outcomes assessment . Operational risk assessment . Contextual assessment . Summary of assessment	. List options to minimize the risk(s) including screening options . SoHO risk assessment, if not enough scientific evidence available then expert opinion . List potential considerations including impact on health economics, operational difficulties or costs or impact on donor behaviour or return.
Evaluation	. Use results to evaluate options to manage the risk . Involve stakeholders and include their comments . Evaluate impact of compromises for each option . Rank the risk management options	. Propose donor selection criteria . Invite stakeholders to comment
Decision	. Prepare a report . Make and present the recommendation . Share the recommendation . Create a plan for implementing the decision	

The RBDM description is based on the educational presentation in May 2018 (https://www.allianceofbloodoperators.org/media/164747/RBDM-Education-Presentation-01-May-2018.pdf).

and plasmapheresis for transfusion) and recipients of blood components, one assessing risks to donors of plasma for fractionation (PfF) and recipients of plasma-derived medicinal products (PDMP) and one group assessing risk to donors and recipients of hematopoietic stem cells (HSC), gametes, embryos (for medically assisted reproduction (MAR)), and tissues (C&T subgroup). Participants were allocated to the different subgroups based on their expertise and professional background. The work was commenced by the whole blood subgroup who proposed the initial DSC. These were then evaluated by the entire work package to establish whether they could be directly implemented in the DSC for all SoHO. If the PfF or C&T subgroups identified that this was not possible for their areas, then a separate assessment was made for the particular SoHO. Furthermore, the PfF and C&T subgroups were asked to perform risk assessments of the DSC, if these had not already been proposed by the whole blood subgroup.

Decision-making method

No standardized approach for evaluating DSC when scientific evidence is lacking or absent was identified. Instead, it was agreed within the group to approach the work with a majority-based decision-making. For the initial evaluation of the risk assessments and proposed DSC, an agreement of 75% or more was considered acceptable by the group. However, when the assessment of the risks that lacked or had diverging scientific evidence was attempted, it became apparent that a majority-based approach was not acceptable; individual participants and stakeholders strongly opposed some conclusions to such an extent that it became clear that a consensus-based approach would be more appropriate. All members were given equal votes regardless of professional background or number of participants per stakeholder to allow consensus to be reached.

The DSC were discussed and consensus sought at two face-to-face meetings in 2019 and in three tele-conferences. Furthermore, the reports were distributed to the whole group on three separate occasions to allow for full comments and clarifications.

Results

The quantitative results of the risk assessments and consensus debates are presented in Table 3. In total, 18 stakeholders participated in the first majority voting of the proposed DSC. Of these, 15 participated in the whole blood and plasma for fractionation subgroups and the remaining 3 in the tissues and cells subgroup. The different stakeholders represented 16 countries. In total, 54 general DSC were proposed by the whole blood subgroup; the discussions surrounding these are presented below. Of these, 3 were considered to be general DSC and included pre-donation assessment, disability and autoimmune disease, as the latter may impact multiple tissues and also have a genetic component, which requires assessment before all types of donation.

Proposed DSC that were not included in the final report or risk assessments

Four potential DSC (7·4% of the proposed DSC) were discussed but not included in the final DSC. These included the following: (1) assessment of mental health, (2) assessment of donor's fear of donation, (3) history of anaemia and symptoms of current anaemia (blood donors), (4) previous vasovagal reactions or fainting (blood and plasma donors). There was initial strong consensus (>80%) that the risk of vasovagal reactions, donor's mental health and fear of donation should be assessed; however, no consensus could be reached on how this should be done or how the risks should be assessed. It was also proposed to include assessments of previous or current iron deficiency or anaemia, but also here no consensus could be reached on how to carry this out. Participants, however, did agree that iron status should be monitored (but not how).

Included DSC where initial majority consensus could not be reached

Apart from the three areas where there was a lack of scientific evidence (presented below), no initial consensus could be reached for deferral periods for 28 (51·9%) of the proposed DSC. These included deferral after travel to West Nile virus and dengue virus endemic areas as some stakeholders initially supported longer deferral periods than the conclusion of the risk assessment. After discussion of the risk assessment, including information on the incubation periods [7–9], full consensus was reached. The same was the case for herpes simplex encephalitis [10], infectious mononucleosis [11,12] and periodontitis [13]. For autoimmune disease, there was initial disagreement on how the donors' health would be protected; however, full consensus was reached that included that there should be no organ impairment due to the autoimmune disease and the donor should otherwise be in general good health [14–17]. For donors with haemoglobin traits and histories of previous malignancies, safeguarding the donor's health was again the main concern that caused initial disagreement. After detailing the unacceptable traits and specifying the types of cancers that would lead to donor deferral, agreement was reached [18–21].

Table 3 Results of the risk assessments and consensus debate

Substances of Human Origin	Number of proposed donor selection criteria	Number of proposed criteria not included in the final criteria/risk assessment	Number of risk assessments pesrformed	Number of criteria with no initial consensus ≥ 75%	Number of criteria where consensus could not be reached
General criteria for all SoHO	54	4	3	0	0
Whole blood	-	-	46*	28	2
Plasma for Fractionation	-	-	8	1	1
Haemopoietic stem cells	-	-	6	0	0
Tissues	-	-	4	0	0
Medical Assisted Reproduction	-	-	11	0	0

*The proposed criteria for different types of medication and vaccination were combined into two overall risk assessment which accounts for the discrepancy between proposed number of criteria and the number of risk assessments performed.

For donors with a history of surgery, endoscopy, acupuncture and tattoos, the initial non-consensus was due to disagreement on the risk of hepatitis B or C virus or HIV when these procedures were performed in Europe in licensed establishments. After presentation of the risk assessment, full consensus of no deferral was reached [22,23]. For donors with a history of syphilis, the initial lack of majority consensus was due to no available definition on how to assess a donor with a previous infection. Consensus was reached after defining a negative test result as a negative non-specific antitreponemal test as this argues strongly against active and thus transmissible syphilis [24]. For medication and vaccination, the initial risk assessment was targeting specific vaccines and medications, with lack of consensus mainly caused by disagreement on which subtypes that should be assessed. When these DSC were made more general, so that different types of vaccines and groups of medication were considered, full consensus was reached.

In general, for all infectious diseases it was confirmed that consideration of the local epidemiology is always required and would surpass generic DSC for such conditions.

Included DSC where full consensus could not be achieved

Three areas (5·6%) with limited scientific evidence were identified: (1) high-risk sexual behaviour (all SoHO), (2) allergy (blood products) and (3) donation frequency (plasmapheresis). For high-risk sexual behaviour, there was strong evidence of the risk of transmission of hepatitis B and C virus or HIV [25,26], but no agreement could be reached on what the deferral period should be due to the potentially long incubation period of hepatitis B, whilst acknowledging that the UK, following an extensive risk assessment, reduced the deferral period to 3 months for donors with a history of potential exposure to HIV and hepatitis B and C virus [27]. For donors with a history of allergy, case reports were identified describing the passive transfer of IgE to recipients, and one study identifying a risk of passive sensitizing of mast cells and basophils in recipients of plasma with IgE antibodies [28–30]. However, this was not considered sufficient to recommend a general deferral for donors with a history of severe allergy, due to lack of evidence of clinical implications. When assessing donation frequency, the lack of randomized controlled trials of different donation frequencies for plasma donors and the effect on IgG and total protein was the reason for a lack of consensus as to what the upper limit for annual donations [31–34] should be. This lack of evidence is also true for the currently

quoted upper limit of 33 donations per year in the Council of Europe guide.

In addition to the above, there was also no consensus reached as regards iron supplementation in blood donors, despite strong scientific evidence. Although the risk assessment found strong evidence of the risk of iron deficiency in blood donors [35–38], there was no agreement on how this should be managed by the blood establishments (BE), due to the need for donor monitoring. A minority proposed that iron supplementation should be provided by BE, but the group collectively could only reach consensus on the need for iron supplementation not on whom should provide it.

Supplementary DSC for plasma for fractionation, tissues and cells

A total of 29 additional risk assessments were performed for T&C and PfF. This concerned five overall areas: differences in collection procedures to that of whole blood including frequency, potential surgical complications, post-donation preparation of the donated product for example the fractionation process for plasma-derived medical products, medical treatment of the donors prior to donation, for example granulocyte colony-stimulating factor treatment in stem cell donation, the issues concerning potential genetic disorders in gamete donors and finally uniquely to tissue donors: the aspect concerning whether the donor is living or deceased.

Furthermore, for all areas separate risk assessments were also made for the risk of transmission of infection, this was due to the large difference in donation procedures for these SoHO and post-donation preparation of the donated product.

Assessment of legislation in participating countries

It was decided not to include local guidelines or legislation in the assessment of the DSC to allow for the proposed DSC to be based only on scientific evidence as much as possible. However, many participants had difficulty with this and directly opposed some of the proposed DSC as these would violate local legislation, even if clinical evidence or clinical opinion supported the proposed DSC. Examples include assessment of high-risk behaviour with experts from one country opposing a recommendation of a 4-month deferral and experts from a different country opposing the differentiation between sexual orientation. For plasma donation frequency, experts from two different countries opposed increasing the current upper limit.

Discussion

The lessons learned from the TRANSPOSE project are important for the transplantation and transfusion field. We found that it was necessary to create a short non-validated version of the ABO RBDM to allow us to cover all current and proposed DSC within the restricted time frame of the project. Furthermore, when striving for consortium consensus, a broad representation of experts from different fields is needed. Unlike for blood and plasma, the consortium included only a small number of experts from other fields. This was of some concern, despite the high level of engagement of the participants.

For DSC, where the risk assessments were inconclusive due to lack of scientific evidence, it was decided that the recommendations would be based on full consensus among experts, as it was not possible to reach agreement on how a majority consensus should be defined. However, for none of these it was possible to reach full agreement and instead a precautionary disclaimer had to be made.

Interestingly, participants found it hard to disregard local legislation even in the presence of solid risk assessments supported by a large amount of scientific evidence. Instead, it was commented, that while the risk assessment may have proven no risk, this would still not be acceptable to implementing in their respective country due to the legal hurdles. It therefore seems that for some high-risk criteria with potential significant impact on donor and recipient health, assessments must be made on a formalized EU level with subsequent changes in the relevant guiding documents. Furthermore, this must be mandated by policymakers and competent authorities in the different countries as they are responsible for the legal framework in the respective member states.

The consensus-based decision-making process is well established and widely used within transfusion [39] and transplantation [40]. However, the definition of consensus and the process itself are rarely described. Frameworks supporting decision-making do exist, but reply on extensive mathematical models and while DSS has already been implemented in transfusion and solid organ transplantation [41,42], it has not previously been applied to DSC for other SoHO. A clearly defined international standardized risk assessment tool and DSS would increase transparency of how different DSC have been assessed as well as provide a systematic approach to risk assessments, ensuring consistency.

Important limitations were found to our choice of consensus-based decision-making. First, despite the general high level of engagement among participants, there was a group of non-responding participants. Second, all participants' comments were given equal weight, regardless of

the participant's expertise and whether a stakeholder was represented by one or many participants. Third, we were not able to neutralize the interference of local legislation and guidelines in this approach, with many participants commenting that this influenced their reply.

In the absence of conclusive scientific evidence, our results were instead based on consensus built on expert opinion which was considered the highest level of evidence available.

Conclusion

Our work shows that there is a critical need to evaluate and validate an appropriate and easy-to-use method for assessing DSC and to define an acceptable risk level. Furthermore, where lack of strong scientific evidence hinders a standardized risk assessment, we need to ensure that the precautionary principle is not excessively applied as a default solution to the detriment of the supply of safe SoHO. Research within these fields should be greatly promoted to produce the robust scientific evidence needed to serve both the health of donors and a sufficient supply of transfusion and transplantation products.

Conflicts of interest

The authors declare no conflicts of interest.

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INTERNATIONAL FORUM

Vox Sanguinis International Forum on Mitigation Strategies to Prevent Faint and Pre-faint Adverse Reactions in Whole Blood Donors: Summary

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Introduction

Blood donation is very safe for the vast majority of donors. However, approximately 2–5% of whole blood donors will experience a pre-faint reaction, including light headedness, dizziness, sweating, nausea and anxiety, while 1–3 in 1000 will go on to experience loss of consciousness. Even donors with mild reactions are less likely to return, while those with faint reactions are at risk of injury [1–3].

The underlying mechanisms for faint and pre-faint adverse reactions adverse are poorly understood. It is thought that both physiologic factors, such as hypovolaemia, and psychologic factors, such as neural-mediated reflexes, contribute. The risk factors for these adverse reactions have been well demonstrated in many studies and include first-time donation, younger age and small (below 3·5 litres) estimated blood volume (EBV) [1–4]. Fear of donation may increase the risk of adverse reaction [5]. However, the determination of reaction frequency and comparison of rates between blood centres have been hampered by variability in definitions and methods of ascertaining and reporting adverse events. In the last few years, standard donor complication definitions have been developed, endorsed and validated to attempt to improve donor vigilance [6–9].

Given their negative impact on the donor experience and the potential for donor injury, several studies have been performed to evaluate possible mitigation strategies. These include reducing fear and increasing feelings of self-sufficiency pre-donation, implementing more stringent EBV criteria in the youngest donors, encouraging donors to consume water or isotonic drinks before and/or after donation, encouraging salty snacks before and/or after donation, and movement of large muscle groups during and immediately after donation (applied muscle tension or AMT) [5,10–12]. Studies to assess efficacy of these measures are difficult to perform as many require active staff and donor participation, which is not easy to achieve and maintain. Additionally, the outcome of most interest, reactions with loss of consciousness, is relatively rare and not measured in many randomized controlled trials. Many of these strategies have shown mixed results in studies, and there is no universally implemented best practice [10].

The aim of this International Forum is to explore what mitigation strategies blood centres throughout the world have implemented to reduce faint and pre-faint complications. We hope that the exchange of information in this forum will help blood centres internationally refine their practices to enhance donation safety and encourage more research in this important area.

Participants

The International Forum was sent to 21 possible participants. We aimed to cover different geographic areas and include both large national blood suppliers and smaller blood centres who had published studies related to donor vigilance and mitigation strategies to prevent donor adverse reactions. Many centres are members of the ISBT Donors and Donations working party and/or the ISBT Haemovigilance working party. We received responses from 17 centres. This included four centres in North America (two large US centres and the two Canadian national centres), one regional centre in South America (Brazil), five European centres (national blood centres in the UK, France, the Netherlands and Finland, and regional centres in Norway, Denmark and Sweden) and three centres in the Asia-Pacific region (national blood centres in

Japan, Australia and the Hong Kong Red Cross). Finally, there were two centres in the Middle East (national centres in Israel and Iran). The list of participants is shown in Table 1.

Answers to questions

QI: Do you have national standards or regulations that specifically cover mitigation strategies to prevent faint or pre-faint complications? If so, what is the name of the organization(s) issuing the standards or regulations?

Most respondents indicated that blood collection establishments (BCEs) in their country answered either to national (governmental) regulations, accrediting agency standards or both, and all 17 participants indicated the name of their governing body(ies). However, only four provided specific requirements for mitigation. In the United States, two AABB Standards address mitigation: 5.2.1.5 (Donor Education) states, 'Donors are given education materials regarding the risks of post-donation iron deficiency and mitigation strategies', and 5.4.3.2 (Protection of the Donor) 'The collection facility shall have a process to reduce the risk of adverse reactions in young donors' [14]. That said, the Standards do not provide specific mitigation strategies. Of the remaining fifteen BCE, four indicated that their governing body had such requirements but provided no specifics, two did not answer the question regarding requirements for risk mitigation, and nine stated that while their internal procedures might require mitigation of vasovagal reactions, their regulatory agency did not have any stated requirements. Thus, generally speaking, regulatory and accrediting agencies have been silent regarding mitigation of reactions.

Q2: Do you record adverse donor reactions and follow reaction rates (donor vigilance system)? If so, indicate which of the following you record: reactions with injuries, faint reactions, pre-faint reactions, reactions report by donors post-donation, other reactions?

Donor vigilance appears to be alive and well in responding centres. All participants record and report reactions with injuries, faint reactions and reactions reported after donation. All participants also record pre-faint reactions, though one reports only prolonged pre-faint reactions, and another records only pre-faint reactions reported after leaving the donation site. In addition, all centres except one report other types of reactions consistent with ISBT 2014 definitions [7–9].

Q3: Do you routinely ask returning donors if they had a complication at their last donation?

Of 17 respondents, over half (9) do not specifically inquire about a previous reaction. An additional six

Table 1 Country, blood centre establishments (BCEs) and respondents (N = 17).

BCE Number	Country, Blood Centre Establishment	Respondent
North America		
1	US, Vitalant	Hany Kamel, Marjorie Bravo, Mary Townsend
2	US, American Red Cross	Kathleen Grima
3	Canada, Héma-Québec	Nancy Robitaille, Jessyka Deschênes
4	Canada, Canadian Blood Services	Mindy Goldman, Jennifer McKay
Europe		
5	England, National Health Service Blood and Transplant (NHSBT)	Emanuele Di Angelantonio, Amy McMahon, David Roberts
6	France, Etablissement français du sang (EFS)	Pierre Tiberghien, Généviève Woimant, Pascal Morel
7	Netherlands, Sanquin	Franke Quee, Katja van den Hurk, Jo Wiersum
8	Norway, Oslo University Hospital	Lise Sofie Haug Nissen-Meyer
9	Denmark, Odense University Hospital	Mie Topholm Bruun
10	Finland, Finnish Red Cross	Johanna Castrén
11	Sweden, Stockholm Blood Bank	Maria Kvist
Asia-Pacific		
12	Japan, Japanese Red Cross Society	Minoko Takanashi
13	Australia, Australian Red Cross Lifeblood	Joanna Speedy
14	Hong Kong, Red Cross Blood Transfusion Service	CK Lee, JNS Leung
Middle East, South America		
15	Brazil, Sirio Libanes Hospital, San Paulo	Silvano Wendel, Roberta Fachini
16	Israel, Magen David Adom National Blood Services	Eilat Shinar, V Gendelman, H Raz
17	Iran, Iranian Blood Transfusion Organisation, Tehran	Mahtab Maghsudlu

include a question on their donor health screening questionnaire asking about a reaction at the previous donation. One centre does not ask about a prior reaction but does call all first-time donors one week post-donation to inquire about how the donation went and if they are currently feeling well. The final respondent inquiries about a reaction on the previous donation only of 16- and 17-year-old donors.

Q4: Do you have general written information for donors provided before donation, focused on the donation process and mitigation measures? (Table 2).

In what form is the information provided (written pamphlet pre-donation, oral by staff, website line)?

Which of the following elements are included?

- *description of the donation process*
- *information about hydration*
- *information about salt intake*
- *information about Applied Muscle Tension (AMT)*

Answers to the question are shown in Table 2. All centres provide one or more written documents prior to donation, usually on the day of donation. A majority of BCE (10/17) also provide information orally, and 13 of 17 have one or more websites addressing pre-donation information and ways to prevent reactions. In addition, four centres provide other means of communicating this information including videos (2), an app, social media and an on-site banner. The majority of centres provide this information to all donors at each donation; however, two centres provide this information only to young donors and two provide it only to first-time donors and ad hoc thereafter. Content included a description of the donation and information about hydration in almost all cases. A majority (10/17) include information on AMT, while only three share information on salt intake.

Q5: What is the minimum age for whole blood donation? (Table 3).

Are any extra criteria in place for younger donors, or first-time donors, regardless of their age?

As younger donors are at higher risk of both vasovagal reactions and other adverse effects such as iron deficiency, BCEs were asked about the minimum age of donation, and if additional criteria are in place for younger donors or first-time donors, regardless of their age.

The minimum age limit ranges from 16 in Hong Kong, Brazil and the United States, to 17 in the UK, Denmark, Israel and part of Canada (Canadian Blood Services), and 18 in all other BCEs.

US state laws may preclude donation by 16-year-olds. In the United States, Brazil and Israel, signed consent

Table 2 Form and content of pre-donation information.

	Form of information					Content			
BCE Number	**Written**	**Oral**	**Website**	**Other**	**Every donation?**	**Description of process**	**Hydration**	**Salt intake**	**AMT**
North America									
1	✓	✓			Young donors	✓	✓	✓	✓
2	✓	✓	✓		Young donors	✓	✓		✓
3	✓		✓		✓	✓	✓	✓	
4	✓		✓		✓	✓	✓	✓	✓
Europe									
5	✓	✓			✓	✓	✓		✓
6	✓		✓		✓	✓	✓		✓
7	✓	✓	✓	Video	✓	✓	✓		✓
8	✓	✓	✓✓	Video	1st and ad hoc	✓	✓		
9	✓	✓			1st and ad hoc	✓	✓		
10	✓	✓	✓		✓	✓	✓		✓
11	✓	✓	✓		✓	✓	✓		
Asia-Pacific									
12	✓	✓			✓		✓		✓
13	✓		✓		✓	✓	✓		✓
14	✓		✓	App, FB	✓	✓	✓		✓
Middle East, South America									
15	✓	✓	✓		✓	✓	✓		
16	✓		✓		✓	✓	✓		
17	✓		✓	Banner	✓	✓	✓		

Table 3 Minimum and Maximum age of donation.

	Minimum age and extra requirements		Maximum age and extra requirements		
BCE region and number	**Minimum age**	**Extra requirements**	**First-time (FT) donor**	**Regular repeat donors**	**Extra requirements**
North America					
1	16[a]	EBV > 3·5 L for 16- to 18-year-olds, extra information provided	No	No	No
2	16[a]	EBV > 3·5 L 16-18	No[b]	No[b]	No
3	18	If EBV is between 3·2 and 3·5 L, 18- to 22-year-olds donate 450 ml rather than 485 ml	No	No	No
4	17	EBV > 3·5 L 17- to 22-year-olds, 5 min in donation chair	No	No	No
Europe					
5	17	EBV > 3·5 L for 17- to 19-year-old females	66	No	
6	18	No	70	70	Physician approval needed over 60 (FT) or 65 (repeat donor)
7	18	New and novice donors (up to 5 donations) encouraged to drink additional water pre-donation	65	80	Annual physician approval over 65
8	18	Additional 5 min in donation chair	65	No	Physician interview over 60 (FT), annual extra questionnaire (over 65)
9	17	No	65	70	Extra questionnaire (over 65)
10	18	Extra time on donation chair, extra information provided	59	70	over 65, must donate every 2 years
11	18	No	65	No	Physician approval needed for 61-64 (FT), annually over 65
Asia-Pacific					
12	16	16-year-olds donate 200 ml, 17-year-old males and 18-year-old females donate 400 ml	64	69	No
13	18	Extra information provided	75	No	Over 75, need to have donated in the last 2 years or have no history of reactions
14	16	No	65	75	Physician approval and annual health assessment over 65, need to have donated in last 2 years
Middle East, South America					
15	16[a]	No	60	69	Exceptions for some older donors with physician approval
16	17[a]	No	60	65	Treating physician approval needed over 60 (FT) or 65 (repeat donor), and donation at fixed site
17	18	No	60	65	May continue past 65 with physician approval

BCE = Blood Center Establishment, EBV = estimated blood volume, FT = first-time donor.

[a]16-year-olds, or for Israel, 17-year-olds require parental consent, and this may vary by state in the United States.

[b]75 for New York State.

from a parent or legal guardian may be necessary for the youngest donors (16 in the United States and Brazil, 17 in Israel). Australia has recently increased the minimum age of donation due to concerns over iron deficiency in the youngest donors.

More stringent criteria requiring a minimum EBV of 3·5 L are in place for donors in four BCEs; these vary in terms of the age group involved, inclusion of both males and females, and inclusion of only first-time or all donors in the given age group. Three of the four BCEs with a minimum EBV are in North America. Two other BCEs draw less volume from younger donors, either a slightly smaller donation based on EBV, or a donation of 200 ml instead of 400 ml based on age and sex.

Other changes for these donors include extra time on the donation chair (three BCEs), and more information, often with encouragement to hydrate more (three BCEs).

Q6: What is the maximum age for whole blood donors? (Table 3).

- *first-time donors*
- *repeat, regular donors*

Are any extra criteria in place for older donors?

Participants were asked about the upper limit for donation, as the risk of cardiovascular events and stroke increase with age.

The North American BCEs have no upper limit for donation for first-time or repeat donors (other than New York state, which has an upper limit of 75) and do not require extra medical approval for older donors. All other BCEs distinguish between first-time and repeat donors. Regular repeat donors (donors who have successfully donated in the last 2 years) often can continue to donate longer, compared with first-time donors or lapsed donors who have not donated for several years. Upper age limits for first-time donors range from 59 (60th birthday) to 75, while limits for regular repeat donors range from 65 to 80; there is no upper age limit for regular repeat blood donors in Sweden, Norway, Australia and the UK. Nine BCEs require either an extra questionnaire about medical conditions, and/or physician approval for donors over a certain age, starting either at age 60 or at age 65. Note that two BCEs had recently increased the upper age limit either for first-time donors (Denmark, from 60 to 65) or for repeat donors (Sanquin, from 69 to 79).

Q7: What are your policies around fluids (water, isotonic drinks)? (Table 4).

Are all donors or a subset of donors (such as first-time donors) routinely offered water or isotonic fluids pre-donation and/or post-donation on the donation site?

- *if so, which drinks and what volume?*
- *are the drinks simply available, or strongly encouraged?*

Q8: What are your policies around snacks?

- *are all donors or a subset of donors offered snacks pre-donation and/or post-donation on the donation site?*
- *if so, what types?*
- *have the snacks been specifically chosen for their salt content?*
- *are snacks simply available or strongly encouraged?*

All BCEs routinely offer water pre-donation to all donors, except for ARC in the United States (water provided to younger donors or if requested). Some BCEs (Japan and Hong Kong) also provide isotonic drinks, while Denmark provides a variety of drinks. Drink volumes are generally 200 to 500 ml, and hydration is strongly encouraged. Most BCEs also offer a variety of snacks pre-donation. Four BCEs encourage pre-donation snacks, chosen for their salt content, for all donors. An additional seven BCEs provide pre-donation snacks for donors who have not eaten for several hours. Interestingly, France also encourages a pre-donation snack for donors who have not eaten, but for all donors during heat waves. Most other BCEs have snacks available on site, and donors may choose to have something to eat pre-donation, even if this is not actively promoted.

All BCEs offer a variety of drinks and snacks post-donation, many of which have both high salt and sugar contents, although they were not necessarily chosen based on salt levels. Drinks include water, juices, soft drinks, coffee, tea and hot chocolate. Drink volumes are generally 200 to 500 ml. Snacks include chips, pretzels, cookies, raisins, crackers, nuts and warm plates. Donors are strongly encouraged to consume fluids and a snack, and in some cases, this is particularly true for first-time or novice donors.

Note that this survey was performed before the COVID-19 pandemic, and policies may have changed during the pandemic to reduce the possibility of viral spread at donation sites. For example, donors may be instructed to hydrate and have a snack before coming in to donate and may consume their post-donation refreshments off the blood donation site, rather than consuming them in a refreshment area.

Q9: Do you encourage donors to perform applied muscle tension exercises (AMT)? (Table 4).

- *if so, at what time(s) during donation?*
- *how is the information communicated to the donor?*

Applied Muscle Tension in some form is encouraged in 10 out of 17 BCEs; in four, it is particularly emphasized for younger or first-time donors. Donors are provided with verbal information by staff, in many cases supplemented by a brochure or donor card with pictures. In the Netherlands, verbal instructions are supplemented by

Table 4 Refreshments, AMT and post-donation time on donation chair.

	FLUIDS		SNACKS					
			Pre-donation		Post-donation		AMT	Time in donation chair
BCE region and number	Pre-donation Fluids offered, volume (ml) if specified	Post-donation Fluids offered, volume (ml) if specified	Snacks encouraged	Chosen for salt content	Snacks encouraged	Chosen for salt content	Done, which donors, how	Time in minutes
North America								
1	Water	Variety, 240	Yes	Yes	Yes	Yes	Yes, younger donors, brochure + verbal	1
2	Water if <19, 500	Water, 500	On request	No	Yes	No	Yes, FT donors(brochure) others verbal	No fixed time
3	Water, 500	Variety	Yes	Yes	Yes	No	No	5
4	Water, 500	Variety	Yes	Yes	Yes	No	Yes, card	FT – 5, repeat – 2
Europe								
5	Water, 500	Variety, at ≥500	No	NA	Yes	Yes	Yes, card	2
6	Water, 500	Variety, 500	If has not eaten or heatwave	No	Yes	No	Yes, pamphlet + verbal	FT – sit, then stand
7	Water, 300 for novice donors[a]	Variety, 120–300	no	NA	Yes	No	Yes, posters, verbal; video for FT	FT – have drink
8	Variety, 500	Variety, at ≥500	If has not eaten	No	Yes	No	No	FT – 15, repeat – 10
9	Variety, 400	Variety	Yes	Yes	Yes	Yes	No	FT – 10
10	Variety, 200-400	Variety[c]	No	NA	Yes	No	Yes, especially FT, card + verbal	FT – 10
11	Variety, 250-300	Variety	Variable by site	No	Yes	No	No	FT – 5–10
Asia-Pacific								
12	Water or isotonic, 200-500	Water or isotonic,> 200	If has not eaten	No	Yes	No	Yes, card	About 3
13	Water, 500	Variety, 300	If has not eaten	No	Yes	No	Yes, card	5
14	Variety[b]	Variety	If has not eaten	No	Yes	No	Yes	5
Middle East, South America								
15	Water	Variety	If has not eaten	Yes	Yes	No	No	5
16	Water, 200–400	Water, ≥200	No	NA	Yes	No	No	2–3
17	Water, 500	Juice, 200–250	If has not eaten	No	Yes	No	No	15

AMT = applied muscle tension, BCE = Blood Center Establishment, FT = first-time donor, NA = not applicable.

[a]First 5 donations.

[b]Mobile units – isotonic and packed drinks, fixed sites, water, packed drinks and hot beverages.

[c]First-time donors offered water, juice, coffee or tea before leaving donation chair.

posters and a video is also used to instruct first-time donors. BCEs that provide precise instructions regarding timing advise donors to perform AMT at the end of donation and before sitting or standing up; some also specify to also perform AMT at needle insertion (Australia, Vitalant) and throughout the whole duration of the donation (Japan).

Q10: Do you have any work instructions about how long the donor should stay on the donation chair before going to the refreshment area, or to an additional rest chair before the refreshment area? (Table 4).

- *if so, how long are donors encouraged to stay on the donation chair?*
- *is this different for some donors, such as first-time donors?*

The minimum time on the donation chair post-donation is not always specified or may be specified only for first-time donors. Minimum times range from one-minute sitting with feet down to 15 min. Seven BCEs specify time on the donation chair only for first-time donors, or have more stringent requirements for first-time donors, stipulating that first-time donors should spend from 5 to 15 min on the donation chair. In Japan, donors spend approximately three minutes on the donation chair as their blood pressure and pulse are checked post-donation. Some BCEs also specify that donors should spend time in the refreshment area; the minimum time ranges from 5 to 20 min, depending on the BCE.

Q11: Have you performed any local studies to inform your policies, or evaluate post-implementation results?

- *if so, how have they guided your practices?*

We deliberately invited many BCEs that had published studies to participate in the survey, so it is not surprising that all North American participants, Asia-Pacific participants and five of the seven European participants had performed some type of study to guide their policies. Selected published studies from these BCEs are listed in the references.

Randomized trials: Studies included a randomized, controlled trial on the benefit of AMT and salt and water intake in France (EVASION study), and a randomized study of water prior to donation in new and novice donors in the Netherlands (EPISoDe study) [11,12]. Australia performed a randomized study on the best way to provide information about AMT to donors [13]. The UK had performed a systematic review of mitigation strategies to prevent reactions, and a randomized, controlled trial of various mitigation approaches, such as hydration protocols and methods of performing AMT, is underway [10].

Observational studies, before and after studies, and case–control studies: In the United States, Vitalant has performed several studies on the precise timing of reactions during the donation process to provide insight into reaction mechanisms [2]. Both Vitalant and ARC performed large studies on risk factors for vasovagal reactions, and before and after studies comparing reaction rates after introduction of stricter criteria for minimum EBV in younger donors and mitigation strategies such as AMT and increased promotion of salty snacks and fluids [15,16]. Both Canadian BCEs, Hema-Quebec and Canadian Blood Services, performed studies analysing risk factors for donor reactions, and before and after analysis of the effect of policy changes, such as an increase in the upper age limit for donation on reaction rates [17–20]. A case–control study was performed in France to identify risk factors for reactions [21].

Studies in Hong Kong evaluated risk factors for reactions, and the impact of reducing the collection volume in first-time donors [22].

Canadian Blood Services also evaluated donor attention to the pre-donation pamphlet and streamlined information as a result [23]. Finland is also evaluating the impact of changes in content of the donor pamphlet. Hong Kong evaluated the impact of reactions on donor return rates [24,25].

Finally, an international study by the BEST group compared vasovagal reaction rates in older donors (over 70) compared with 23- to 69-year-old donors in five countries (USA, Canada, UK, Australia and New Zealand) [26].

Conclusion

In summary, regulatory and accrediting agencies have been largely silent regarding precise actions to be taken to mitigate for donor adverse reactions. All BCEs have some form of donor vigilance, with reporting of at least moderate and severe, if not mild, reactions, and most use the ISBT 2014 definitions or a very similar classification scheme. All BCEs provide donors with some information about reactions and mitigation strategies pre-donation, although the exact content varies considerably. Donor minimum age ranges from 16 to 18; maximum age for first-time donors ranges from 59 to 75, with some BCEs having no maximum. Almost all BCEs routinely offer water pre-donation and a variety of refreshments post-donation. Routine provision of a salty snack pre-donation is done by a minority of BCEs and about two thirds encourage AMT. Time on the donation chair post-donation varies from 2 to 15 min but is not always specified. Several BCEs have special provisions for first-time donors, including more information about mitigation steps, additional encouragement to hydrate, minimum EBV or smaller donation volume, and longer time on the

donation chair post-donation. Many International Forum participants have undertaken some form of evaluation or study to inform their local policies.

Indeed, this International Forum highlights the variability in practice between BCEs, underscoring the need for studies in this area to provide a firm evidence basis for best practices to make donation as safe as possible for our volunteer donors.

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INTERNATIONAL FORUM

International Forum on Mitigation Strategies to Prevent Faint and Pre-faint Adverse Reactions in Whole Blood Donors: Responses

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Norway

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Question 1

There are national regulations about pre-donation weight, blood pressure, pulse and haemoglobin levels, and also regulations about donor information, but not more specific measures to prevent complications. In the questionnaire, the donor is asked about previous (repeated) fainting episodes, which will be carefully considered.

The Norwegian Directorate of Health "Helsedirektoratet" has issued standards of transfusion medicine including standards about blood donation.

Question 2

All donor reactions are reported in the local hospital system for adverse events. Serious reactions are reported online to the national haemovigilance system (Hemovigilans.no). Hemovigilans.no publish statistical reports every year.

The following are reported to Hemovigilans:
–reactions with injuries
–faint reactions
–pre-faint reactions; only if prolonged or requiring treatment
–reactions reported by donors post-donation, if serious
–Local reactions are recorded within the hospital system, if serious also to Hemovigilans. Mild and moderate systemic reactions are reported locally within the hospital system

Question 3

No.

Question 4

Yes, general written information for donors provided before donation is in accordance with the specific standard.
–The information provided as a written pamphlet pre-donation, oral form by staff, website link, and we are preparing an information movie.
–Information is routinely given before first donation, and in an ad hoc way at later donations.
–The following elements are included:

- description of the donation process
- information about hydration
- There is no information about salt intake or applied muscle tension (AMT)

Question 5

The minimum age for whole blood donation is 18 years (specific standard) without extra criteria except 5 min extra on donation chair.

Question 6

The maximum age for whole blood donors:
-First-time donors are allowed until 65 (new donors above 60 are interviewed by MD; specific standard)
-Repeat, regular donors above 65 are annually medically evaluated using an extra questionnaire (specific standard). Very healthy individuals can be allowed to donate also above 75 years.

- Donors above 65 are annually evaluated with a questionnaire containing 12 questions to reveal possible age-dependent health issues. If completely healthy, they are approved for another year or until a health issue presents.

Question 7

All donors are offered drinks throughout their stay at the donation site, without distinguishing between pre/post-donation.
–We offer a variety of drinks, from water to coffee, including soda water, soft drinks with or without sugar,

and ice tea. Not milk. We strongly encourage them to drink at least 0.5 l liquid (of their own choice) during their stay at the donation site.

Question 8

(i) Only donors who have not eaten for several hours are routinely offered food. They are offered a sandwich/crispbread or two before donation. For others, snacks are freely available.
   – We offer sandwiches, crispbread, bananas, sweet biscuits and sometimes salty crackers.
   – The snacks are simply available and have not been specifically chosen for their salt content.

(ii) Post-donation on the donation site, no routinely offers but snacks are available as described.

Question 9

We do not encourage donors to perform applied muscle tension exercises (AMT).

Question 10

As a local policy, we have work instructions about how long the donor should stay on the donation chair before going to the refreshment area, or to an additional rest chair before the refreshment area:
–Repeat donors are encouraged to stay on the donation chair for 10 min
–First-time donors for 15 min

Question 11

We have not performed any local studies to inform our policies, or evaluate post-implementation results.

In a study of donors using antihypertensive medication, we asked how much they drink in connection with blood donation. Almost everybody drinks >0.5 L, and the mean intake was 0.65 L.

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Question 1

There is no national standard or regulation that specifically covers mitigation strategies to prevent faint or pre-faint complications. We follow those mitigation strategies in Standards for Blood Banks and Transfusion Services of AABB to develop our local measures.

	No loss of consciousness			
Generalized Symptoms *(Vasovagal Reactions)*	**Loss of consciousness**	**1.**	**Duration**	**Duration: < 60 s** **Duration:>= 60 s**
		2.	**Convulsion or incontinence**	**Without convulsions or incontinence** **With convulsions or incontinence**
		3.	**Injury**	**Without injury** **With injury**
Localized Symptoms	Blood outside vessel		Hematoma Arterial puncture Delayed bleeding	
	Arm pain		Nerve injury/ irritation	Duration < 12 months Duration> 12 months
			Other arm pain	
	Localized infection/ inflammation of vein or soft tissues		Superficial thrombophlebitis Cellulitis	
Apheresis related			Citrate reactions Haemolysis Air embolism	
Allergic reactions			Localized Generalized	

Question 2

All post-donation adverse reactions are documented according to the classification of 'Standard for Surveillance of Complications Related to Blood Donation' of ISBT in 2014 with slight modifications.

The categories of the complications are summarized in the table above.

Question 3

Yes.

Screening nurses shall assess all young repeat donors who aged from 16 to 17 if they have any adverse reaction after their previous donation and record on the blood donation form. For other repeat donors, adverse reactions recorded are reviewed through the blood management

system or being enquired while deciding the donation volume.

Question 4

Donation-related information is provided in the form of pamphlet at all blood drives and in electronic format via official website, Facebook and mobile apps.

The related information will be given to all donors before each donation.

The following elements are included:

–Donor preparation for blood donation including adequate rest the night before donation and adequate fluid intake
–Description of the donation process
–Introduction of applied muscle tension (AMT)
–Information of post-donation advice

Question 5

The minimum age for whole blood donation is 16.

Question 6

The first-time whole blood donor can join blood donation till the day of 66th birthday.

With the annual health assessment and approval by the Blood Transfusion Service medical staff, donors aged 66 or above who have completed any donation in the last 2 years can be accepted for whole blood donation up to their 76th birthday.

Question 7

(i) Yes.
- For blood donation at mobile units where young donors, first-time donors and infrequent donors are the majority, isotonic and packed drinks would be provided for pre- and post-hydration.
- For blood donation at centres, water, packed drinks and hot beverage would be offered.
- The hydration status of blood donors will be assessed, and donors are always recommended to be well hydrated before proceeding to blood donation.

(ii) A drink will be routinely offered to donors after donation.

Question 8

(i) Yes.
- Biscuits are offered as snacks at all blood drives.
- If donors do not have any food consumption within 4 h, they are recommended to take some snacks and drinks before proceeding to blood donation. Otherwise, snacks are simply available for enjoyment before blood donation.

(ii) Yes.
- Biscuits are offered as snacks at all blood drives.
- Snacks are simply available for enjoyment after blood donation.

Question 9

Yes.

Nurses and phlebotomists would introduce AMT during the preparation of venipuncture and advise blood donors to practise during blood donation.

Question 10

Yes.

–Blood donors are recommended to stay in the donation chair for at least 5 min for haemostasis as well as resting. And after that, staff would position the donor to upright position and accompany the blood donor to refreshment area if there is no adverse reaction.
–Blood donors are recommended to stay in refreshment area for 15 min before leaving the venue.
–If the blood donor is a first-time donor or has past history of post-donation adverse reaction, she/he would be suggested to stay in the donation area for a longer period of time with individual assessment.

Question 11

Local studies [1–3] have confirmed that young age, first-time donation status, female gender and low body weight were significant vulnerable factors for vasovagal reactions, and those with reactions were significantly less likely to return.

Less collection per donation as a preventive measure for young first-time donors has shown promising result. Another recent small study on effects of AMT also reveals positive outcome with good acceptance to donors.

Given that high-risk groups can be identified and the availability of evidence-based techniques, prevention strategies can be tailor-made to the local setting with the aim to assure a safe, sufficient and sustainable blood supply.

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Question 1

Yes, we have procedures to mitigate adverse events at blood collection in our SOP.

Question 2

Yes, we record adverse donor reactions into our nationwide system and follow the reaction rates regularly. We record reactions with injuries, faint reactions, pre-faint reactions and reactions reported by donors post-donation. We also record allergic reactions, hyperventilation, cardiac arrest, seizure, etc., with timings and locations.

Question 3

No, we do not ask the donor every time, but our national computer system, which staff at each donation site check for every donor, shows up to five adverse events from that donor's previous donations.

Question 4

Yes, we give donors an information paper and a pamphlet pre-donation, each time, which they have to read before their donation. We verbally explain about adverse events during and after blood collection every time, too. And we give a card with information about adverse events and blood centre contact information.

The materials contain information about hydration, together with information about rest/exercise and the blood centre contact information. During blood collection, we show a card with information about applied muscle tension (AMT) and ask for their participation.

Question 5

The minimum age for whole blood donation is 16 years old for 200 ml whole blood. For 400 ml whole blood, the minimum age is 17 years old for males and 18 years old for females.

There is no extra-criteria in place for younger donors or first-time donors, regardless of their age.

Question 6

The maximum age for a whole blood donation is 64 years old, including first-time blood donors. But for donors who have donated blood between 60 and 64 years of age, we accept whole blood donations up to 69 years old.

Question 7

(i) Yes, all the donors are offered water or isotonic fluids pre-donation on the donation site. The volume is not definite, usually between 200 and 500 ml, and we strongly encourage the donors to drink. Also, this information is included in the pamphlets they read before the donation.
(ii) Yes, all donors are routinely offered water or isotonic fluids post-donation on the donation site. The volume is usually >200 ml. The fluid intake is encouraged on the site, and this information is also included in the pamphlets they read before the donation.

Question 8

(i) No, we ask donors if they are hungry pre-donation on the donation site, and offer snacks when they are hungry. They are not strongly encouraged to eat them. The snacks are cookies and sometimes also donuts and are not chosen for their salt content.
(ii) Yes, at fixed donation rooms for all donors we offer snacks post-donation in the refreshment area. The donors are asked to eat them, but are not strongly encouraged. The snacks are cookies and sometimes also donuts and are not chosen for their salt content. For mobile sites, we offer food at most but not all.

Question 9

Yes, we encourage donors to perform applied muscle tension (AMT) exercises during the donation, near the end

and after the donation. It is explained to every donor with a card which includes pictures of AMT.

Question 10

We have no regulation on the duration of stay on the chair/bed after a blood donation. Our instruction is to keep the donor for at least 10 min at the donation site including their time in the refreshment area. We do have a procedure to check the blood pressure and pulse after the blood donation and send the data to our IT system, so the donor stays on the chair/bed for around 3 min. Included in our instructions is to chat with the donor more when it is their first time to make a blood donation.

Question 11

Yes, we did studies about water intake and AMT at various locations before implementing our policies in the SOP nationally.

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Canada

Mindy Goldman & Jennifer McKay

Question 1

There are standards from the Canadian Standards Association, Blood and Blood Components, that state that the status of the donor shall be such that the donation will not harm his or her health and that there should be procedures to educate and inform prospective donors about risks of donation and post-phlebotomy care. However, there are no specific requirements regarding mitigating strategies such as more stringent criteria for younger donors, or fluid and salt loading.

Question 2

We do record reactions with injuries, faint reactions and reactions reported by donors post-donation. Pre-faint reactions are recorded if the donors contact us post-donation to report symptoms. ISBT harmonized definitions are used to categorize donor reactions, and rates are reported in our annual surveillance report.

Question 3

We do not routinely ask returning donors if they had a complication at their last donation. However, first-time donors are called approximately 1-week post-donation to assess their on-clinic experience and how they are feeling post-donation.

Question 4

We provide donors with written pre-donation information in the mandatory pamphlet 'What you must know to give blood: Making donations safe for you, and for those who receive your blood'. The pamphlet describes the donation process and provides information about hydration and salt intake as well as applied muscle tension (AMT). The pamphlet is available on our website at https://www.blood.ca/sites/default/files/10552-BloodInfo_PamphletEN_Final.pdf. Information about salt and water immediately pre-donation and AMT is also provided by staff and volunteers on the donation site (see responses to questions 7, 8 and 9).

Question 5

The minimum age for whole blood donation is 17. First-time donors age 17–23 (up to 23rd birthday) must have an estimated blood volume (EBV) greater than 3.5 L, which is calculated based on sex and reported height and weight. All first-time donors remain on the donation chair for 5 min post-donation before sitting up and proceeding to the refreshment area. First-time donors also receive a follow-up call approximately 1-week post-donation, as noted in question 3.

Question 6

There is no maximum age for first-time or repeat whole blood donors. No extra-criteria are in place for older donors.

Question 7

(i) In the pre-donation pamphlet, donors are encouraged to hydrate and eat a non-fatty meal before donation. The pamphlet also mentions that they will be encouraged to drink water pre-donation. For donors who provide us with their e-mail address and permit us to communicate with them by e-mail (over 65% of donations), an e-mail reminder is sent to the donors a few days before donation with the same information. On the donation site, donors are strongly encouraged to drink 500 ml of water by both staff and volunteers; the water is placed in a prominent location near the waiting area. There are also video screens in the

waiting areas of our fixed sites (over 55% of collections) that include this messaging.

(ii) Post-donation, donors are encouraged to hydrate and drink water, juice, tea or coffee. This is less formal than our pre-donation process, and the amount is not specified.

Question 8

(i) Donors are strongly encouraged to have a salty snack immediately pre-donation, which contains approximately 400 mg of salt. Pretzels and chips are offered on all donation sites, and other types of packaged snacks are offered on some sites as well. Both before and after donation, we aim to have some snacks that are gluten-free, vegan or kosher to cater to the needs of our donors.

(ii) Snacks are also offered post-donation, in a less structured way. They include both salty snacks (as above) and sweet snacks such as cookies.

Question 9

Yes, we specifically encourage AMT, giving donors an information card about it when they sit in the donation chair. Donors are instructed to do the AMT exercises after the needle is removed and while they rest in the donation chair, prior to sitting up and going to the refreshment area. They also may do the exercises at any time during or after donation if they feel lightheaded. AMT is also mentioned in the donor pamphlet, on the video screening in our fixed sites and in the e-mail reminder to donors.

Question 10

First-time donors are encouraged to stay on the donation chair for 5 min post-phlebotomy. Repeat donors may get up from the donation chair 2 min post-phlebotomy, providing that they feel well.

Question 11

We follow reaction rates in our donors when policy changes are introduced [4].

We assessed risk factors for donation by evaluating our donor reaction database and performing a post-donation survey of donors. In the survey, we were able to capture more baseline information that we do not routinely collect, such as donor height and weight, and more reaction information than we routinely collect, such as off clinic reactions and mild reactions. The study contributed to adoption of our policy for more stringent EBV criteria in 17- to 23-year-old donors [5].

We assessed vasovagal reactions in older donors (over 71st birthday) and the contribution that an annual external medical assessment of these donors made to donor safety. After this evaluation, we decided to eliminate the need for the outside medical assessment. Since reaction rates in older donors were no higher than in middle aged donors, we also dropped the upper age limit for infrequent and then for first-time donors [6,7].

We performed a donor survey assessing how much attention donors pay to the mandatory pre-donation pamphlet. Results were sobering, in that many donors, particularly repeat donors, admit to a very cursory look at the pamphlet. Based on this information, we have streamlined the pamphlet, trying to remove unessential information. We also try and repeat the information in the pamphlet regarding donor health in multiple other channels (website, e-mail reminders, on clinic video screen, oral messaging from staff, AMT card) to improve donor participation in mitigation strategies [8].

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Sweden

Maria Kvist

Question 1

The National Board of Health and Welfare regulates blood donation in Sweden. They stipulate that blood donation should be performed in a safe way for donors and that

persons that have health issues making them prone to adverse reactions should not be chosen as donors.

Question 2

Yes.
–reactions with injuries – yes
–faint reactions – yes
–pre-faint reactions – often recorded locally but not reported to the national donor vigilance system
–reactions reported by donors post-donation – yes
–other – faint reactions are reported as immediate or delayed, as well as grade of severity of outcome. (The donor vigilance system also records adverse reactions following international standards).

Question 3

Not in the DHQ but many of the staff ask this during the pre-donation interview.

Question 4

At the donation site, we have only oral information and encouragement on drinking before donation. Our pamphlet will be updated shortly to include advice on drinking before donation. Our website has information of the donation process with recommendations on drinking.

Oral encouragement on drinking is given by staff before each donation.

The following elements are included on the website:
–description of the donation process
–information about hydration

Question 5

The minimum age for whole blood donation is 18 years.

No extra-criteria are in place for younger donors, or first-time donors, regardless of their age.

Question 6

Regulations follow the EU directive on senior donors. No maximum age for experienced donors stipulated in regulations. In Stockholm and many parts of Sweden, there is no maximum for repeat donors but some counties apply their own maximum age.

For first-time donors, the national regulations follow the EU directive that stipulates that first-time donors over the age of 60 can be approved at the discretion of the physician in the blood establishment. In practice, no approvals are made for first-time donation over the age of 65.

For repeat older donors, the national regulations follow the EU directive that stipulates that repeat donors over the age of 65 can donate with permission of the physician in the blood establishment, given annually.

Question 7

(i) All donors are routinely offered water, juice or other fluids.
  – Blood donation centres have a small café with drinks such as water, tea, coffee, milk and juices, sandwiches, and fruit. Donors can take what they want at liberty, before or after donation. Most often the donors are offered a portion of non-carbonated fruit soft drink of 250–300 ml, packaged with a straw so that they drink during the donation. This drink is often the only option at mobile donation services.
  – Drinks are available but most often also encouraged.

(ii) All donors.
  – At their liberty.
  – Drinks are available but most often also encouraged.

Question 8

(i) Yes, but not at all mobile donation services.
  – Sandwiches, fruit and cookies.
  – No.
  – Available.

(ii) Yes but limited at mobile donation services.
  – Sandwiches, fruit, nuts and cookies. Limited at mobile donation services.
  – No.
  – Available.

Question 9

No

Question 10

Yes.
–A few minutes in the donation chair.
–first-time donors are recommended to rest 5–10 min in the donation chair.

Question 11

No.

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Canada – Quebec

Nancy Robitaille & Jessyka Deschênes

Question 1

In Canada, the Canadian Standards Association (CSA) issues standards on blood and blood components every 5 years and Health Canada published the Blood Regulations, in 2014. Although the CSA standards CSA-Z902-15 have eligibility criteria for donor selection for allogeneic blood collection, there is no clause covering mitigation strategies to prevent faint or pre-faint reactions [9]. The Blood Regulations has no specific clause on mitigation strategies. However, it does require that: 'An establishment that has reasonable grounds to believe that a donor has experienced a serious adverse reaction during a donation or within 72 h after a donation must notify the Minister of the adverse reaction within 24 h after it learns of the death of the donor or within 15 days after it learns of the adverse reaction in any other case' [10].

Question 2

In 2015, Héma-Québec, the sole blood centre for the province of Quebec, implanted a new donor hemovigilance system using the definitions from the 'Standard for surveillance of complications related to blood donation' issued by ISBT, AABB and IHN [11]. All information pertaining to adverse reactions related to blood donations is collected either during donation by Héma-Québec personnel or reported post-donation by donors. Reactions are reported using a standardized form, and an annual report is produced. Both local and systemic reactions are recorded. Local reactions include ecchymosis/hematoma, arterial puncture, re-bleeding, allergic reaction at puncture site, immediate and delayed nerve injury and painful arm. Systemic reactions consist of the following: vasovagal reactions (VVR: including faint and pre-faint reactions with or without loss of consciousness (LOC)), major cardiovascular, apheresis-specific reactions and delayed local reactions (local inflammation/infection, thrombophlebitis, deep venous thrombosis, arteriovenous fistula, compartment syndrome and pseudoaneurysm of the brachial artery).

Question 3

The donor questionnaire contains the following question: 'Did you have complications after your last blood donation (fainting or allergy at puncture site)?' This question is asked to repeat donors for whole blood and apheresis donation.

Question 4

Written information about the donation process, hydration and salt intake is provided to all donors at registration, prior to the blood donation. Similar information can be found on Héma-Québec's website. No information about applied muscle tension is provided. Regular reminders about hydration and salt intake are provided by staff to blood donors at different checkpoints during the donation process (registration, donor questionnaire, pre-donation and post-donation).

Question 5

The Civil Code of Québec forbids blood donation by minors. Therefore, the minimum age requirement for whole blood donation is 18. Héma-Québec has specific criteria in place to prevent VVR. All donors must weigh at least 50 kg to be eligible to donate. For donors aged between 18 and 22, the total blood volume (TBV) is calculated. A minimum TBV of 3200 ml is required to donate. Those with a TBV between 3200 and 3500 ml are allowed to donate a maximum of 450 ml whole blood. Those with a TBV $\geq$ 3500 ml can donate 485 ml whole blood. A TBV $\geq$ 3500 ml is required for apheresis donation for all donors, and the annual volume limit is established according to the donor's weight.

Question 6

As of December 2019, there is no maximum age limit for either first-time or repeat donors. No other eligibility criteria are in place specifically for older donors. However, it is worth mentioning that data from Héma-Québec's donor vigilance system show that older donors, defined as those $\geq$71 years of age, have the lowest rate of VVR (mild to severe). In 2018-2019, the VVR rate in older donors following whole blood donation was 0.93 per 100 donations. In comparison, the highest rate was for donors aged 18-22 years at 14.32 per 100 donations and the rate for all donors was 4.32 per 100 donations [12].

Question 7

All donors are routinely offered 500 ml of water pre-donation, and staff is instructed to strongly encourage donors to drink the recommended amount (500 ml) throughout the donation process. In addition, water, juices or other beverages are available post-donation in the refreshment area. For environmental reasons, donors are encouraged to bring a reusable water bottle.

Question 8

All donors are offered a salty snack containing 450 mg of sodium pre-donation and are strongly encouraged by staff to eat it before their donation or throughout the donation process. Pre-donation snacks are chosen specifically for their salt content. Additionally, various snacks, sweet or salty, are also offered post-donation at the refreshment area; however, no specific salt content is required.

Question 9

At the present time, applied muscle tension exercises are not proposed nor advertised.

Question 10

Donors in permanent donor clinics are instructed to rest for 5 min on the donation chair before going to the refreshment area. Donors at mobile drives also have a 5-min rest period but this will take place in a chair located in a rest area supervised by volunteers.

Question 11

A local retrospective study was performed to evaluate the impact of pre-donation hydration and salt intake on mild and severe VVR. We compared the rates of occurrence of VVR with LOC and without LOC 6 months before and after the implementation of prevention measures. The data show that 6 months after implementation, the risk of VVR with LOC was reduced by 11.60%, and the risk of VVR without LOC was reduced by 12.60%. More than a year later, these risk reductions were decreased even more at 21.29% and 14.55%, respectively, demonstrating the effectiveness and relevance of this practice. Furthermore, additional data on the rates of VVR according to total blood volume (TBV) has led us to reconsider the minimum TBV required to be eligible to donate blood for donors of all ages. Our objective is that a minimum TBV of 3500 ml be required for donation in order to further decrease the incidence of VVR in our donors.

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United Kingdom

Emanuele Di Angelantonio, Amy McMahon & David Roberts

Question 1

National Health Service Blood and Transplant (NHSBT) – only one blood donation service for the whole of England.

Question 2

Yes, as indicated below:
–reactions with injuries – Yes
–faint reactions – Yes
–pre-faint reactions – Yes
–reactions reported by donors post-donation –Yes

Question 3

Donors are routinely asked, 'Did everything go well with your last donation?'

Question 4

Yes, in the form of written pamphlet pre-donation, written pamphlet post-donation and oral form by staff.
–Yes, prior to each donation
–We include the following elements:

- description of the donation process
- information about hydration
- information about applied muscle tension (AMT)

Question 5

The minimum age for whole blood donation is 17 years old.

–Women under 20 years old are expected to have an estimated blood volume of more than 3500 ml. First-time donors must be aged between 17 and 66 years old.

Question 6

-First-time donors – 66 years old.
-Repeat, regular donors – none.
-If a donor is over 70 years old, they must have donated blood in the previous 2 years.

Question 7

(i) Yes
  – Encouraged to drink 500 ml water pre-donation
  – Encouraged
(ii) Yes, water, juice, tea or coffee
  – Encourage to have at least two drinks
  – Encouraged

Question 8

(i) No
(ii) Yes
  – Potato chips, biscuits and fresh fruit
  – Yes
  – Encouraged

Question 9

Yes.
–During and post-donation.
–A handout is provided during the donation.

Question 10

Yes.
–2 min following needle withdrawal.
–Same for all donors.

Question 11

One ongoing national study.
–In progress.

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Iran

Mahtab Maghsudlu

Question 1

The national standards of Iranian Blood Transfusion Organization (IBTO) require all blood centres to ensure the safety of blood donors during and after blood donation. The blood centres are also required to have a procedure in place for the prevention of reactions.

It is worthy to note that the donor vigilance programme was initially established in 2012 under my supervision.

Question 2

A donor vigilance system was established in 2012 at the national level. Initially, classification of reactions was in accordance with 2008 ISBT standards for surveillance of complications related to blood donation [13]. Then, it was revised based on 2014 revised ISBT classification [14]. Any reactions in donors are documented in blood donor's information software.

Categories are covered as follows:
–Vasovagal reactions with injury
–Vasovagal reactions without injury
–Adverse reactions reported by donors post-donation

Question 3

Donors are not verbally asked if they had a complication at their last donation; however, if they report a complication in their last donation, it will be recorded in blood donors information software. There is a routine procedure to request blood donors to inform the blood centre if she/he has any complication during the first 24 h following blood donation. We believe that asking the donor about his/her reactions may make him/her increasingly sensitive to these issues and imposing stress during his/her current donation.

Question 4

A general written information focusing on recommendations for mitigation of systemic and local reactions is given to each donor prior to each donation. It is a take-home message and focuses on hydration in to avoid

fainting. There are different materials (pamphlet, banner, web-based link) in all blood centres focused on donation process available in the registration area.

Following elements are included:

–Description of donation process
–Information about hydration

Because the Iranian populations consume much more sodium than health authorities recommend, this strategy is not used in IBTO.

Question 5

The minimum age for whole blood donation is 18 years, and there are no extra-criteria in place for them.

Question 6

The maximum age for first-time whole blood donors is 60 years; for repeat and regular donors, the maximum age is 65 years and beyond if approved by a blood donor's physician. There are no extra-criteria in place for them.

Question 7 (i) & 7 (ii)

All donors are routinely encouraged to drink 2 glasses of water before donation, which is available in the registration area. All blood donors are offered a package after donation which contains a juice drink (200–250 ml). Water is also available to drink.

Question 8

As previously mentioned, all blood donors receive a package following blood donation that contains a piece of cake and a juice drink. There is no routine to offer snacks before donation. However, all physicians are required to ask blood donors about having eaten during the last 6 h. If a donor has not eaten anything in the last 6 h, she/he will be offered snacks.

Question 9

This method is not used in IBTO.

Question 10

Based on the approved working instruction (WOI) of IBTO, a donor must stay on the donation chair for 15 minutes, and then, she/he is guided to the refreshment area. This is required for all donors, including first-time donors.

Question 11

Monitoring the recorded data and implementing corrective or preventive actions is an important part of a donor vigilance system; therefore, monitoring of data is routinely done. However, no study has been conducted so far, since complications appear to be underreported.

References

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Finland

Johanna Castrén

Question 1

Finnish Red Cross Blood Service

Question 2

Yes, as indicated below:
–reactions with injuries – Yes
–faint reactions – Yes
–pre-faint reactions – Yes
–reactions reported by donors post-donation – Yes
–other – convulsions and by every category above; the need of medical care outside of the blood service.

Question 3

No.

Question 4

Yes.
–Written pamphlet pre-donation, oral form by staff, information on website.
–Oral form by staff prior to every donation, written short information prior to every donation, written more

detailed information for first-time donors and in an ad hoc way.
–The following are included:

- description of the donation process – Yes
- information about hydration – Yes
- information about salt intake – No
- information about applied muscle tension (AMT) – Yes, in the more detailed information leaflet and in an ad hoc way.

Question 5

The minimum age is 18 years.
–Yes, extra time on donation chair, information leaflet (more detailed information about AMT and hydration).

Question 6

-First-time donors – age 59.
-Repeat, regular donors – age 70.

- In the age group 66-70, you need to donate at least every 24 months.

Question 7

(i) Yes
  – Water, juice or coffee/tea, 1–2 glasses.
  – Strongly encouraged.
(ii) Yes.
  – For first-time donors staff offer one glass of water/juice/coffee/tea before the donor leaves the donation couch.
  – For all donors, strongly encouraged.

Question 8

(i) No
  – Snacks have not been specifically chosen for their salt content.
  – There are snacks available.
(ii) Yes.
  – Sandwiches, cookies, sweets and nuts.
  – Snacks have not been specifically chosen for their salt content.
  – Strongly encouraged.

Question 9

Yes.
–All first-time donors and donors in an ad hoc way.
–Card, and verbal if needed.

Question 10

Yes.
–For first-time donors 10 min, for regular donors no timeline given.
–See above.

Question 11

Yes.
–Small, non-scientific studies. Changes in the content of the information leaflets. (One ongoing study project).

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France

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Question 1

Yes.

ANSM (Agence Nationale de Sécurité du Médicament, the French competent authority) regulations and EFS (Etablissement Français du Sang, the French transfusion public service) standards and instructions. Of note, EDQM (European Directorate for the Quality of Medicines and Health Care of the Council of Europe) guide to the preparation, use and quality assurance of blood components, contains standards that are contributive to the prevention of faint or pre-faint occurrence, and therefore complications (such as maximum volume of blood to be collected, maximum percentage of blood volume collected), standards to which ANSM regulations and EFS standards abide.

Question 2

Yes.
–reactions with injuries
–faint reactions
–pre-faint reactions
–reactions reported by donors post-donation

All grade I (low grade) to grade IV (death) donor adverse events (including those mentioned above) are recorded through a unique French database vigilance system, irrespective of imputability (regulatory requirement for grade II to IV; EFS requirement for grade I to IV).

Question 3

Yes, returning donors are asked about complications, per EFS instructions.

Yes, general written information is provided per EFS instructions.

Pre-donation written pamphlet, digital communication (screens at donor site, EFS website link and EFS mobile phone application).
–It is given prior to each donation.
–the following elements are included:

- description of the donation process – Yes
- information about hydration – Yes
- information about salt intake – No (except in the event of heatwaves)
- information about applied muscle tension (AMT) – Yes

Question 5

The minimum age for whole blood donation is 18.
–No specific measure for younger donors or first-time donors.

Question 6

-First-time donors – Age 70 (after 60, specific MD approval is required), per ANSM regulations
-For repeat, regular donors – Age 70 (after 65, specific MD approval is required), per ANSM regulations

- Yes, MD approval after 60 (first-time donors) or 65 (repeat donors), per ANSM regulations

Question 7

(i) Yes, all donors, per EFS instructions.
  – 500 ml plain water.
  – Strongly encouraged.
  – Yes, all donors.
  – Approximately 500 ml.
  – Strongly encouraged.

Question 8

(i) No, (only in case of a heatwave or an empty stomach).
  – Cookies, pastries, bread, fruits, chocolate bars and fruit juice.
  – No.
  – Strongly encouraged.
(ii) Yes.
  – Warm plates, sandwiches, cookies, pastries and chocolate bars.
  – No.
  – Strongly encouraged.

Question 9

Yes, per EFS instructions.
–During donation.
–Written pamphlet and verbal instructions.

Question 10

Yes, per EFS instructions.
–A few minutes (of note, donors are required per EFS instructions to stay at least 20 min at collation and 40 min for granulocyte collection before leaving the donation site).
–Not specifically, although the EFS instructions, in particular for the first-time donors, strongly recommend that the donors get up slowly from the donation chair, stay a few minutes sitting on the donation chair with the legs dangling and stand up only if all is ok.

Question 11

Yes.

Evasion study: prospective randomized study evaluating hydration (plain water, isotonic water) and AMT [15].

Case–control study examining risk factors for fainting [16].
–Introduction of AMT

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United States

Hany Kamel, Marj Bravo & Mary Townsend

Question 1

No.

Question 2

Yes, as follows:
–reactions with injuries
–faint reactions
–pre-faint reactions
–reactions reported by donors post-donation
–other – needle-stick injuries

Question 3

No.

Question 4

Yes.
–Pamphlet and oral.
–Young donors.
–The following elements are included:

- description of the donation process
- information about hydration
- information about salt intake
- information about applied muscle tension (AMT)

Question 5

The minimum age for whole blood donation is 16.
–Blood volume ≥3500 ml; information about hydration, salty snacks and muscle tensing.

Question 6

-First-time donors – no maximum.
-Repeat, regular donors – no maximum.

- There are no extra-criteria in place for older donors.

Question 7

(i) All donors.
  – Water, no volume specified.
  – Encouraged.
(ii) All donors.
  – 8 oz.
  – Encouraged.

Question 8

(i) All donors.
  – Salty.
  – Yes.
  – Encouraged.
(ii) All donors.
  – Salty.
  – Yes
  – Encouraged.

Question 9

Yes, only young donors.
–Needle insertion, end of donation, needle withdrawal, anytime feeling faint, when standing up.
–Brochure, verbal.

Question 10

Yes.
–One minute with feet dangling off side of bed.
–All donors.

Question 11

Yes.
–Many studies published; we now provide salty snacks and fluids to donors before, during and after donation; and we teach muscle tensing to young donors.

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Israel

Eilat Shinar, Veronica Gendelman & Hana Raz

Question 1

Yes.
–The Israeli Ministry of Health.

Question 2

Yes, as follows:
–reactions with injuries
–faint reactions

–pre-faint reactions
–reactions reported by donors post-donation
–upon receiving report from the donors.

Question 3

No.

In cases of severe reaction, a deferral is entered into the record system to prevent the next donation.

Question 4

Yes.
–Written information in the Door Health Questionnaire and in MDA website link.
–Each donation.
–The following elements are included:

- description of the donation process
- information about hydration

Question 5

Seventeen (17) years with parental permission.
–Younger donors (12–17 years) are accepted for autologous units only.

Question 6

There is no maximum age, BUT
-For first-time donors: 18–60 years. Above 60 years, an approval from the treating physician is required and collection should be done in a fix site, and in the presence of an EMS provider, qualified to provide at least basic CPR.
-For repeat, regular donors: Above 65 years, an approval from the treating physician is required annually and collection should be done in a fix site, and in the presence of an EMS provider, qualified to provide at least basic CPR.

- extra time on donation chair.

Question 7

(i) We suggest they drink 1–2 glasses of water.
  – We suggest they drink 1–2 glasses of water.
  – Gently encouraged.
(ii) Yes.
  – A glass or more.
  – Strongly encouraged and served.

Question 8

(i) No.
(ii) Yes, in certain donation sites.
  – Cookies.
  – No.
  – Simply available.

Question 9

No.

Question 10

Post-donation rest of 10 min in total.
–About 2–3 min.
–No.

Question 11

Analysis of faint reactions is performed yearly.
–Results are presented to MDA blood services management and to the phlebotomists.

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Brazil

Silvano Wendel & Roberta Fachini

Question 1

In Brazil, the Ministry of Health defines the technical regulations to be complied with by all Hemotherapy Services and its compliance is supervised by the National Health of Surveillance Agency.

The technical regulation only defines that each service should have a standard operating procedure with specific instructions for the prevention, identification and treatment of adverse reactions in blood donors, including the availability of medicines and equipment needed to provide the adequate medical assistance to these donors.

Additionally, the training and standardization of health professionals regarding procedures for emergency care follow the guidelines for advanced life support from the Brazilian Society of Cardiology.

However, there is not in the national regulation specific mitigation strategies to prevent faint or pre-faint complications (https://portalarquivos2.saude.gov.br/images/pdf/2018/marco/29/PRC-5-Portaria-de-Consolida----o-n---5---de-28-de-setembro-de-2017.pdf).

Question 2

The technical regulation to be complied with at the national level defines that the Hemotherapy Service should record all adverse events that occur during a blood donation, including the medical procedure established for its attendance, as well as notify the adverse events considered serious to the National Health of Surveillance Agency (http://portal.anvisa.gov.br/documents/33868/404938/guia_hemovigilancia15.pdf/495fd617-5156-447d-ad22-7211cdbab8a7).

We classify, record and follow the adverse reaction rates according to the categories below:

–Local reactions: characterized by only local symptoms of blood leakage or pain, caused directly by inserting the needle (blood leakage, pseudoaneurysm, arteriovenous fistula and compartmental syndrome; nerve injury; thrombophlebitis or allergy for locally used solutions).

–Systemic reactions: most of these reactions are vasovagals, with symptoms of faint or pre-faint, and which can be triggered by psychological factors such as the blood vision, fear or apprehension, or may constitute a neurophysiological response to the donation.

–We also registered any reactions reported by donors post-donation.

Question 3

Yes. As part of our clinical screening for every blood donor candidate, the question whether the candidate has previously donated blood and if he/she has had any discomfort or reaction during or after his/her previous donation. Depending on what the donor reports, we provide pre-puncture and post-donation care guidelines to try to prevent recurrence of this reaction.

For example, to increase oral hydration even more during the day, and not to undergo great physical effort, such as gym exercises.

Question 4

Yes. Our Service provides the donor candidate with full details of the entire clinical screening and blood donation process itself. We have a general written information, which is offered before all donations, explaining all the donation process, and the importance of the adequate hydration and of the salt intake, during the day.

This inform is offered by a written pamphlet during the pre-donation period, and it is emphasized orally by staff. All of these contents are also available in our website link.

Question 5

The blood donor must be between 16 years and 69 years old, 11 months and 29 days.

Candidates for blood donation aged between 16 and 17 years old must have formal written consent from their legal guardian for each donation that they make.

In cases of technically special needs (donors with rare phenotypes, familiar with irregular antibodies whose frequency of negative antigen blood is higher in the same family members), an applicant whose age is under 16 years or over 70 years will be accepted for donation purposes after examination by the doctor of the Hemotherapy Service.

Additionally, the limit for the first donation shall be 60 years, 11 months and 29 days.

To be approved for donation, the applicant must have a weight of at least 50 kg. Candidates weighing less than 50 kg may be accepted for donation purposes, after medical evaluation, provided that the volume of anticoagulant in the collection bag is proportional to the volume to be collected.

The total blood volume to be collected should be a maximum of 8 mL/ kg weight for women and 9 mL/ kg weight for men. The volume allowed by donation is 450 mL ± 45 mL, to which up to 30 mL may be added for the laboratory tests required by laws and technical standards.

Question 6

To repeat or regular donors, the maximum age for whole blood donation is 69 years, 11 months and 29 days.

In cases of technically justifiable needs, over 70-year-old donors might be accepted for donation purposes after examination by the doctor of the hemotherapy service, with corresponding risk and benefit assessment. It is necessary to present a report that justifies the need for the donation, recording it in the donor form.

For the first-time donors, the maximum age acceptable for donation is 60 years, 11 months and 29 days.

There are no extra-criteria in place for older donors.

Question 7

For all donors or a subset of donors (such as first-time donors) are routinely offered water pre-donation on the donation site. We do not specify the volume to be drunk, but it is strongly encouraged.

Post-donation, all donors are kept in our service at least 15 min and they receive juice, coffee or milk, depending on their preference. This conduction is strongly encouraged, too.

Question 8

The offering of pre-donation salty snacks does not occur routinely. Our procedure provides for the donor to be questioned if he has adequately fed and ingested liquid on the date of the donation and, if he reports that the last meal was more than three hours, the donor is obliged to take salty snacks and to drink enough liquid at this time, pre-donation.

On the other hand, always after blood collection, the donor remains at the Blood Bank for at least 15 min. At this time, it is strongly recommended that he/she eats salty snacks and/or drinks water, coffee, milk or juice, according to his/her preference.

All snack options offered to our donors have the sodium concentration specified, but they were not chosen from a thorough analysis of what should be the ideal value (reference). Some examples that demonstrate how this sodium concentration can vary: turkey breast sandwich with 1015 mg of sodium and cheese sandwich with 102 mg of sodium.

Question 9

The only muscle exercise that the donor is advised to do during the donation is the flexion–extension of the fingers of the upper limb that has been punctured for blood collection.

This instruction is communicated by the nurse verbally and immediately before the venous puncture.

Question 10

There are no differences regarding first-time or repeated donors about how long they should stay on the donation chair before going to the refreshment area provided the donation went on normally. However, we always advise donors to stay for approximately 5 min in their chair after the end of donation, as an extra safety caution.

Question 11

The practices described in this paper have been instituted for many years, and no case–control studies have been done to justify any of them, as well-controlled evaluation post-implementation.

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The Netherlands

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Question 1

Since July 2019, at Sanquin new and novice donors (up to their 5th donation) are offered a 300 ml cardboard drinking cup with a cartoon picture and text printed on it, encouraging them to drink water before they donate.

Question 2

Yes, we record all of the adverse donor reactions mentioned above in the blood service information system. For all complications, we record severity (low degree of morbidity – not life threatening; moderate-to-severe morbidity – hospital admission, prolongation of disease or disability; life-threatening or fatal outcome) and the time at which the complication. For each reaction, the code shows when it occurred (during donation, after donation at the blood collection centre or after donation outside the collection centre). Serious reactions and all cases where outside medical care was required are additionally assessed for imputability to the donation and recorded in the quality management system.

Question 3

We ask returning donors if their last donation went well on the Donor Health Questionnaire, which they all complete before donation.

Question 4

Information about blood donation, including the donation process and avoiding complications, is actively provided to new donors through the website and a short video which is reviewed on a tablet at the collection centre immediately before the first interview. Printed and verbal information about planning and preparing for their first donation is given to them on that

occasion (in the Netherlands, donors attend first for interview and testing only, and are subsequently invited separately for their first donation). We encourage all donors to eat and drink enough prior to each donation (via invitation and website). New and novice donors (up to 5 donations) are encouraged to drink additional water before donation (at blood collection site). Posters with information about AMT are available at each blood collection site.

Question 5

The minimum age for blood donation is 18 years. New and novice donors (up to 5 donations) are encouraged to drink additional water before donation.

Question 6

Donors can register as blood donors up to the age of 65. Repeat donors can now continue to donate up to and including the age of 79 – the maximum age was raised from 69 in 2018. Donors above the age of 65 must be checked by a donor physician each year.

Question 7

Hot and cold drinks (including water, but no isotonic drinks) are available in cups, mugs or glasses (customary sizes, 120–330 ml) in the refreshment area at the donation site. As mentioned before, 300 ml pre-donation water drinking is actively encouraged up to the fifth donation. In the pre-donation interview, all donors are asked about recent drink and food intake and staff will recommend taking a drink or snack before donation as appropriate.

All donors are advised to eat and drink something after their donation. Drinks (as described above) and snacks are offered at the donation site by a staff member or volunteer. Instant soup and broth are also served depending on the donor's preference.

Question 8

Snacks are not offered pre-donation, but are available at the donation site.

Snacks are available to all donors post-donation and include instant soup or broth, currant buns, bread rolls with ham or cheese, gluten-free muesli/chocolate bars, honey cake, and small or semi-large cookies/cakes. The savory snacks have not been chosen based on actual salt content but on practicality and palatability.

Question 9

Posters with instructions on AMT are displayed at the donation sites. The poster images show donors performing AMT during the collection to prevent dizziness. Staff attending donors with (pre)faint reactions verbally give instructions for AMT during recovery as well as later on the day, if necessary, referring to the posters as reinforcement. AMT is also mentioned in website information for donors as well as the above-mentioned video for new donors.

Question 10

Repeat donors can leave the donation chair after checking if they donot feel faint or dizzy. They are encouraged to eat and drink something in the refreshment area and stay there for 10 min or so. First-time donors remain on the donation chair for longer and are offered a cold drink before they are allowed to leave the donation chair. Donors with a previous vasovagal reaction (this information is coded on the printed attendance form) will also be kept in the chair for longer.

Question 11

Yes, the EPISoDe study was performed to check whether drinking water prior to donation prevented donor complications in younger (up to age 30) new and novice donors [17]. The results showed that donors who drank water prior to donation experienced less donor complications. This led to the implementation of the policy in which new and novice donors (up to 5 donations) are offered additional water prior to donation.

Reference

17 Wiersum-Osselton J, Romeijn B, van den Brekel E, et al: Can we prevent vasovagal reactions in young inexperienced whole blood donors? A placebo controlled study comparing effects of a 330 vs 500 mL water drink prior to donation. Transfusion 2019;59:555–65.

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Kathleen M. Grima

Question 1

Yes.

Incorporated into our system documents specifically to include the following:
–Muscle Tension to Prevent Reactions.
–Students Guide to Blood Donation.
–ARC website instructions on what to do before, during and after blood donation – https://www.redcrossblood.org/donate-blood/blood-donation-process/before-during-after.html.
–Website information for first-time donors – https://www.redcrossblood.org/donate-blood/how-to-donate/common-concerns/first-time-donors.html.
–Reference on setting up hydration station for high schools.
–Training for staff on how to identify, manage and prevent further complications.

Question 2

We track all reactions in eBDR and can pull subsequent reports on reaction rates. We also capture all major reactions on Donor Complication Injury Record. All complication types are captured. Data are reviewed and entered into the ARC Hemovigilance database.

reactions with injuries – Yes
faint reactions – Yes, we categorize faint and pre-faint reactions as prolonged recovery if the donor is still experiencing symptoms or low blood pressure for longer than 30 min.
pre-faint reactions – Yes, see above.
reactions reported by donors post-donation – Yes.
other – Yes, any and all reactions are recorded.

Question 3

No.

Question 4

Yes, AABB ASSOCIATION BULLETIN #08-04.
–Written for students, oral by staff (e.g. hydration station and muscle tension) and website links.

- Students Guide to Blood Donation.
- ARC website instructions on what to do before, during and after blood donation – https://www.redcrossblood.org/donate-blood/blood-donation-process/before-during-after.html.
- Website information for first-time donors – https://www.redcrossblood.org/donate-blood/how-to-donate/common-concerns/first-time-donors.html.
- Muscle Tension to Prevent Reactions.
- Reference on setting up hydration station for high schools.

–Given to young donors as part of the pre-reading materials at each donation. Available to all donors on the website.
–Information on elements included:

- description of the donation process – Yes
- information about hydration – Yes
- information about salt intake – No
- information about Applied Muscle Tension (AMT) – Yes for young donors in the Students Guide to Blood Donation

Question 5

Age 17–16 if permitted by state law and with parental permission.

Yes, (AABB ASSOCIATION BULLETIN #08-04).
–Students Guide to Blood Donation is part of the required reading for donors who are student age (under the age of 19).

Higher estimated blood volume is in place for the following:

Question 6

No maximum age except for donors in NY state – 75 is upper limit but are allowed to donate with an additional evaluation.
-First-time donors NO – see above.
-Repeat, regular donors? NO – see above.

- No extra-criteria are in place for older donors.

Question 7

(i) Young donor < 19 or at high schools routinely offered water.
  – Water – 1 16.9oz bottle and more if requested.
  – Strongly encouraged.
(ii) All, Yes.
  – 1 bottle – 16.9oz or more if requested.
  – Strongly encouraged.

Question 8

(i) No – only if requested by donor.
  – N/A.
  – No.
  – Simply available upon request.

Donor Type	Product Type	Age	Gender	Acceptable Height	Acceptable Weight (lb)
Allogeneic	Whole Blood	19 & over	Male or Female	N/A	110 to bed weight limit
		Under 19	Female	4'10"	146 to bed weight limit
				4'11"	142 to bed weight limit
				5'	138 to bed weight limit
				5'1"	133 to bed weight limit
				5'2"	129 to bed weight limit
				5'3"	124 to bed weight limit
				5'4"	120 to bed weight limit
				5'5"	115 to bed weight limit
				5'6" and taller	110 to bed weight limit
		Under 19	Male	4'10"	118 to bed weight limit
				4'11"	114 to bed weight limit
				5' and taller	110 to bed weight limit
	Apheresis except 2RBC	N/A	Male or Female	N/A	110 to bed weight limit
	ALYX 2RBC	N/A	Male	5'1" and taller	150 to bed weight limit
		N/A	Female	5'5" and taller	175 to bed weight limit
	MCS+ 2RBC	N/A	Male	5'1" and taller	130 to bed weight limit
		N/A	Female	5'5" and taller	150 to bed weight limit

(ii) Yes.
- Variety of what is available – usually donated – cookies, pretzels, raisins, crackers.
- No.
- Strongly Encouraged.

Question 9

Yes, especially recommended for young donors.
–During the actual time, the donor is donating the unit.
–Written for young donors and verbal for all others (covered in staff training).

Question 10

No – we ensure the donor is feeling well and allow them to leave after bandaging.

Question 11

Yes.
–Changes in height and weight requirements for young donors reduced reaction rates substantially.

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Australia

Joanna Speedy

Question 1

In Australia, we are required to comply with the Therapeutic Goods (Standard for Blood and Blood Components) (TGO 102) Order 2019. TGO 102 includes that the requirements in relation to blood and blood components are specified in the Guide to the preparation, use and quality assurance of blood components, 19th edition, 207, published by the Council of Europe (CoE Guide).

The CoE Guide includes the following general principles in relation to donor adverse events:

-Prospective donors must be informed of the possible adverse reactions of blood donation and how they can be prevented.
-Training of the personnel collecting blood should include preventing and recognising the (early) signs of adverse reactions and their rapid treatment.
-The source of an adverse reaction should be identified and corrective and preventive measures considered.
-Data should be collected and analysed in order to initiate corrective actions that could prevent or reduce the

frequency or minimize the severity of adverse reactions in the future.

-A donor who has experienced vasovagal reactions should be informed about the risk of delayed fainting. The donor should not drive a vehicle or resume work or any hazardous occupation or hobby in the ensuing 12 h if delayed fainting could put the donor or other persons at risk.

Note: the specification of 12 h is new in the CoE 19th edition. Lifeblood is in the process of reviewing this gap, as we currently recommend 8 h for driving based on the known occurrence of greatest risk for delayed VVR.

There are no standards or regulations that cover specific information on hydration, applied muscle tension or meals.

Question 2

Lifeblood's donor vigilance system monitors adverse events in blood donors that have a temporal relationship to blood donation. The system underpins Lifeblood's comprehensive and continuous improvement approach to the mitigation and management of donor adverse events to improve donor safety and experience and is integral to Lifeblood's Clinical and Quality Governance Framework.

We record both incentre and off-site reactions. The table below provides a summary of the events recorded for whole blood donors. The vasovagal category refers to all faints and pre-faint events, and for each of these events, we capture whether there has been loss of consciousness and/or injury.

Vasovagal reactions
Phlebotomy-related events
Arterial Puncture
Cellulitis
Delayed Bleeding
Haematoma
Nerve Injury/Irritation
Other injury
Painful arm
Thrombophlebitis
Other Event
Anaphylaxis
Chest Pain
Local Allergic Reaction
Other event/injury

Question 3

Yes, returning donors are asked if they had any side-effects after leaving the donor centre on their previous visit.

If yes and this event has not previously been recorded, the event is recorded at this time.

Question 4

Information provided prior to attending:

–Appointment SMS reminders often include a reminder about hydration and eating prior to donating and a link to our website lifeblood.com.au where donors can find out more about the donation process and how to prepare for the donation.

Information provided incentre:

–Information on donation risks and mitigation strategies (attached below) is provided in written form to all donors incentre at the time of completing the donor questionnaire. This includes specific information on the risk of fainting and strategies to reduce this risk, including pre- and post-donation hydration, snacks, incentre recovery and post-donation avoidance activities.

All new donors also receive a written information sheet which explains the relevant donation process (ie whole blood, plasma or platelets), ways to reduce the risk of fainting and bruising and who to contact if they have problems or questions after donating.

All donors receive an AMT instruction card.

Question 5

The minimum age for whole blood donation is 18 years for both males and females. There are no extra criteria in place based on age alone or first time status alone for whole blood including eligibility criteria (eg weight/height), messaging regarding mitigation strategies, volume collected or resting period after donation. Staff are however aware of the increased risks of fainting in new donors and also younger donors and are hypervigilant with respect to advising and supervising these donors.

Question 6

First-time donor – maximum age is 75 years for both males and females.

Repeat donors –

-Donors aged 76 years or older who have completed a donation of any type in the last 2 years are permitted to donate whole blood
-Donors aged 76 years who have not donated in the last two years but have made at least one prior donation, can be accepted depending on whether there is a history of a previous faint/pre-faint.

There are no additional criteria in place for older donors.

Question 7

Pre-donation:

All whole blood donors are provided/offered 500ml water on arrival.

Hydration advice is provided to all donors in written form as per question 4 and also often sent via SMS as part of an appointment reminder.

Staff also ask donors about their hydration preparation as part of the general interview process.

Post-donation:

Following collection, all donors are advised by staff to stay in refreshments for 15–20 min and have a cool drink and snack before leaving. This is also included in our written information and recommends donors drink 300mL in refreshments. A variety of drinks are currently available across most donation centres including, water, juice, milk drinks, sport drinks, tea and coffee.

Question 8

Pre-donation:

Lifeblood recommends ALL donors having something savoury to eat in the 3 h before their donation.

This is communicated to donors in written form as per question 4 and also often sent via SMS as part of appointment reminder.

Staff ask donors about their food intake as part of the routine assessment.

Most donor centres have snacks (pretzels and/or biscuits) available for donors pre-donation which are encouraged if the donor has not had something to eat in the last few hours.

Post-donation:

Post-donation we recommend ALL donors remain on site and have a “savoury snack” along with a drink. We provide a variety of snacks including some high salt foods such as pretzels.

Question 9

Yes AMT is encouraged in all whole blood donors. All whole blood donors are provided with an AMT instruction card prior to their donation (attached in Question 4). We encourage this activity at needle in, needle out, before getting up or if they feel dizzy, hot or nauseous.

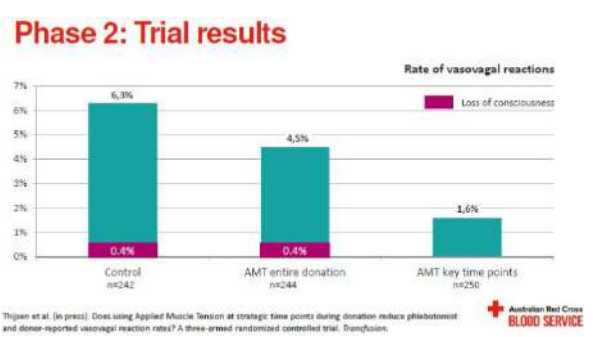
Question 10

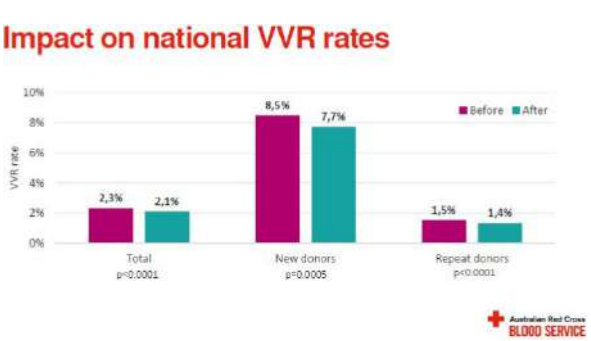
Our procedure is for all donors to remain in the chair for minimum of 5 min after the needle is removed and then get up slowly under their own strength.

Donors are advised to stay in refreshments for 15–20 min and to have something to eat and drink.

Question 11

Introduction of AMT and pre-donation water loading has been implemented based on both international and local studies. A summary of the results is provided in the images below.





To determine the best way of providing this information to donors, Lifeblood compared three approaches: emailing a link to instructions on our website, emailing a link to a video and the provision of a small instruction card provided by staff in the donor centre at the time of the donation. While the video performed well in our preliminary testing, when we conducted a randomized controlled trial, we found that very few donors actually clicked on the link pre-donation. It was much more effective to provide the card in the donor centre, which is the approach that we then implemented.

Evaluation following national implementation.

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Denmark

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Question 1

Yes.

The Danish Society of Clinical Immunology.

Standards of Transfusion Medicine, version 5, 2019, https://dski.dk/wp-content/uploads/2019/07/tms-5-0-2019.pdf.

Question 2

–reactions with injuries –Yes
–faint reactions – Yes
–pre-faint reactions – Yes
–reactions reported by donors post-donation - Yes
–other – Yes.

We also report all kinds of blood vessel injuries, nerve injuries, apheresis-related complications and other serious complications. Furthermore, we grade the complications after severity and imputability.

Danish legislation requires that serious complications are reported to the Competent Authorities (The Danish Patient Safety Authority.)

Question 3

No.

Question 4

No.
–Oral by staff.
–Prior to first donation, and subsequent ad hoc.

- description of the donation process – Yes (written information).
- information about hydration – Yes (written information)
- information about salt intake – No
- information about applied muscle tension (AMT) – No

Question 5

17 years.
–No

Question 6

-60 years old (to be changed to 65 in 2020).
-69 years old.

Yes. Donors older than 65 years have to answer some supplementary cardiovascular-related questions regarding chest pain, swollen legs, dizziness, etc. to ensure they are healthy.

Question 7

(i) Yes.
  – Water, juice, soda and drinking chocolate in cups that contains 400 ml.
  – Strongly encouraged.
(ii) Yes.
  – Not specified.
  – Strongly encouraged.

Question 8

(i) Yes.
  – Potato crisps, nuts, fruit and chocolate.
  – Potato crisps and nuts are chosen because of high content of salt.
  – Simply available.
(ii) Yes.
  – Potato chips, nuts, fruit and chocolate.
  – Potato chips and nuts are chosen because of high content of salt.
  – Simply available.

Question 9

No.

Question 10

Yes, but only for first-time donors.
–Repeat donors can leave the donation chair whenever they feel ready for it.
–First-time donors are encouraged to stay 10 min on the donation chair, and afterwards 10 min in the refreshment area.

Question 11

No.

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Vox Sanguinis

See also http://www.isbtweb.org/congresses/

4.5.2021	IPFA/PEI – The International Workshop on Surveillance and Screening of Blood-borne Pathogens
13–15.5.2021	The Canadian Society for Transfusion Medicine (CSTM) are holding their annual scientific conference virtually in 2021.
26–27.05.21	21st Congress of the European Society for Hemapheresis
5–9.6.2021	ISBT In Focus, the 31st regional congress of the ISBT, will be a virtual event in 2021
17.9.2021	11th BIC International Conference – Advances in Haemostasis and Bleeding Disorders
22–24.9.2021	Deutsche Gesellschaft für Transfusionsmedizin und Immunhämatologie e.V.
23–26.9.2021	16th International Congress on Myelodysplastic Syndromes (MDS 2021)
13–16.11.2021	32nd Regional congress of ISBT, Brisbane, Australia