Selection strategies for newly registered blood donors in European countries

Ryanne W. Lieshout-Krikke[1], Dragoslav Domanovic[2], Wim de Kort[3], Wolfgang Mayr[4], Giancarlo M. Liumbruno[5], Simonetta Pupella[5], Johann Kurz[6], Folke Knutson[7], Sheila MacLennan[8], Gilles Folléa[9]

[1]Sanquin Blood Supply Foundation, Department of Blood-borne Infections, Amsterdam, the Netherlands; [2]European Centre for Disease Prevention and Control, Department Surveillance and Response Support, Stockholm, Sweden; [3]Sanquin Blood Supply Foundation, Department Donor Studies, Amsterdam, the Netherlands; [4]Austrian Red Cross Blood Transfusion Service, Vienna, Austria; [5]Italian National Blood Centre, National Institute of Health, Rome, Italy; [6]retired from the Federal Ministry of Health, Vienna, Austria; [7]Section of Clinical Immunology, Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden; [8]NHS Blood and Transplant, Department Leeds Centre, Leeds, United Kingdom; [9]French Blood Establishment (EFS), Saint Denis, France

Background. Two selection strategies for newly-registered blood donors are available: a single-visit selection called the standard selection procedure (SSP), and a two-stage selection named pre-donation and donation screening (PDS). This study reviews the selection strategies for newly-registered donors currently applied in European countries.

Material and methods. We collected data on donor selection procedures, blood donation, laboratory screening and HIV, HCV and HBV positive donors/donations from 2010 to 2013 in 30 European countries by using questionnaires. We grouped the countries according to the applied selection strategy, and for each country, we calculated the 4-year prevalence of confirmed positive results indicating the presence of overall and recent HIV, HCV and HBV infections among first-time and repeat donations and among newly-registered donors.

Results. Most of the 24 countries (80%) apply the SSP strategy for selection of newly-registered donors. Twenty-two countries (73.3%) employ a nucleic acid amplification testing in addition to the mandatory serological screening. The survey confirms a higher overall prevalence of HIV, HCV and HBV infections among first-time donations and newly-registered donors than among repeat donations. In contrast, the prevalence of recently acquired HIV and HCV infections was lower among first-time donations and newly-registered donors than among repeat donations, but higher for recent HBV infections ($6.7/10^5$ *vs* $2.6/10^5$ in the SSP setting and $4.3/10^5$ *vs* $0.5/10^5$ in one country using PDS). The relatively low numbers of infected donors selected by PDS impeded accurate assessment of the prevalence of recent infections in first-time donations.

Discussion. The data from European countries provide inconclusive evidence that applying PDS reduces the risk of donations being made in the diagnostic window of first-time donors. The impact of PDS on the risk of window-period donations and blood donor management needs further investigation.

Keywords: donors, infectious diseases, screening, selection.

Introduction

An important way to reduce the risk of transfusion-transmitted infections occurring is a combination of donor recruitment, education, selection and screening the donated blood and blood components. Yet, the donation of infected blood during the "diagnostic window" can result in transfusion-transmitted infection[1-3]. Recently, transmission of human immunodeficiency virus (HIV) was reported to have occurred through an infected, first-time donation in the nucleic-acid amplification testing (NAT) diagnostic window[4]. Transfusion-transmitted infections are more frequently detected among newly-registered donors and first-time donors than among repeat donors[5-11]. However, the risk of newly-registered or first-time donors being in the diagnostic window would be higher only if they have incident infections more frequently than do repeat donors. The higher frequency of transfusion-transmitted infections in new donors is largely a result of accumulation of chronic, yet undiagnosed, infections that are detected at the first visit/donation. Questions have been raised about the potential for reducing the risk of transfusion-transmitted infections further by qualification of newly-registered donors in two steps, using the so-called "pre-donation and donation screening" (PDS). The first step in PDS entails a donor eligibility assessment complemented

with laboratory testing of donor blood for transfusion-transmitted infections[12] before the first donation is taken. After a defined period, the pre-qualified newly-registered donor is invited to make the first donation. At this "donation visit", the donor's eligibility is assessed again. The laboratory screening of blood donated at the "donation visit" may detect recent transfusion-transmitted infections in individuals who were in the window period at the pre-donation visit. In contrast, a standard selection procedure (SSP) is a strategy for qualification of newly-registered donors in which the donor screening and the donation occur during the same, first visit. The aim of this study was to review the current selection strategies for newly-registered donors in Member States of the European Union/European Economic Areas (EU/EEA) and Switzerland.

Material and methods

Definitions

For this study we used the following definitions[13]: a prospective donor is a donor who states his/her wish to give blood or plasma but is not yet registered as a donor, a newly-registered donor is a donor who has been registered as a donor but who has not yet donated blood, a first-time donor is a donor who makes his/her first blood donation, and a repeat donor is a regular or returning donor who has made at least one blood donation before.

In the SSP setting, the prospective donor becomes a newly-registered donor after registration and a first-time donor after blood donation most commonly during the same visit. In the PDS setting, the prospective donor becomes a newly-registered donor after registration and screening at the first (pre-donation) visit and first-time donor after the first donation of blood at the second visit.

Data collection

We sent a questionnaire by e-mail to the National Competent Authorities for Blood or National Blood Services of the EU/EEA Member States that utilise a voluntary unpaid blood donor programme. They were asked to provide data on blood donation, epidemiology, and donor selection procedures for the reporting years 2010 to 2013. We requested one reply per State. There were two separate questionnaires, designed for PDS and SSP. The questions covered (i) the number of donors and donations; (ii) the number of confirmed HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) positive donations/donors; (iii) the procedures used for donor selection (interview, physical check) and laboratory screening for transfusion-transmitted infections; (iv) the minimal and maximal time interval between pre-qualification and attendance for the first-time donation (in the PDS setting); (v) the proportion of pre-qualified newly-registered donors returning for first-time donation (PDS) and first-time donors returning for the second donation (SSP); and (vi) the information provided to blood donors during their first visit.

We took into account only results of confirmed positivity for HIV, HBV or HCV in the screening. To differentiate recent and previous infections within positive results, an additional question on recent infections in newly-registered donors (PDS) and first-time donations (SSP) was asked. As published before[12], acute (recent) HIV or HCV infection is defined as NAT RNA positive only. Recent infection with HBV is defined as NAT HBV DNA positive with or without hepatitis B surface antigen (HBsAg) AND either (i) total hepatitis B core antigen antibodies (anti-HBc) negative or (ii) anti-HBc immunoglobulins (Ig) M positive and self-reported recent HBV risk behaviour during the donor post-test interview.

Data analysis

We compiled the answers to the questionnaire and analysed the selection strategies for newly-registered donors, reporting capabilities of respondents, types of laboratory testing employed, inter-visit intervals, return rates, epidemiological data on blood donation, and noted the other activities during PDS. Prevalence is defined as the frequency of infections identified (including both past and recent infections) over a specified period in a defined population and is expressed per 100,000 donations. We calculated the crude prevalence rates of confirmed positive results for the presence of HIV, HCV and HBV infection in donations/donors. For the comparison of proportions, we used chi-squared test with the significance level $p<0.05$.

Results

Selection strategies

We collected data from 30 respondents from all 28 European Union Member States, Norway and Switzerland. Three countries (the Netherlands, Norway and Sweden) have implemented PDS for all newly-registered donors. Three countries (Italy, Ireland and Greece) apply both strategies. Italy implemented PDS in some blood establishments only. Ireland and Greece applied it to special subpopulations of donors. However, the vast majority of 24 Member States apply the SSP strategy only. Six respondents did not report data for the whole period. Germany reported for three regional Red Cross organisations. From the United Kingdom, we received data for England, Wales and Northern Ireland. Greece provided only information for their platelet donors for whom they apply the PDS strategy and was not included in the analysis.

Countries applying PDS use different specifications for intervals between pre-donation and donation visits:

the Netherlands - the minimum interval is 14 days, the observed median interval is 42 days (interquartile range, 29-89 days); Italy - "If declared eligible, donors are kept waiting for an established period before they can make a donation. The median time interval calculated is 25 days"; Sweden - "No minimum time interval is specified but in practice it is at least 3 weeks, if they do not return within 5 years there is a new pre-qualification"; Norway, 6 weeks; Ireland, 90 days.

In the PDS cohort, the proportion of newly-registered donors who re-appeared for the first donation was 74.4% (median 73.4; interquartile range 71.4-76.3; n=3 answers). Return rates of first-time donors for subsequent donations in the PDS cohort were not investigated in this survey. In the SSP cohort, the return rate of first-time donors was 44.7% (median 40.1; interquartile range, 30.1-65.3; n=16 answers). The return rates of newly-registered donors in the PDS cohort and of first-time donors in SSP cohort are not comparable.

Laboratory screening

All responding countries use serological screening of blood donations to detect the presence of anti-HIV, anti-HCV antibodies, and HBsAg (Table I). Twenty-two countries (73.3%) employ NAT for HIV, HCV and HBV screening of all donations. In two countries, only particular Blood Establishments perform NAT. Ten countries use mini-pool NAT of 6, 24 or 96 samples, seven implemented an individual donor NAT, and in five countries both individual donor and minipool NAT are in use. Twelve countries (40%) have implemented anti-HBc screening, four of them use this test only selectively and in two countries it has been implemented by some Blood Establishments. Twenty-eight countries (93.3%) test for syphilis. Twelve countries have implemented HTLV-I/II screening in general, partly or selectively.

Table I - Mapping of the laboratory tests used for blood donor screening in the period 2010-2013.

Infection	Tests	N. of countries (n=30)
HIV	NAT	22
	ID	7
	ID or MP	5
	MP	10
	Anti-HIV	30
HCV	NAT	22
	ID	7
	ID or MP	5
	MP	10
	Anti-HCV	30
HBV	NAT	22
	ID	7
	ID or MP	5
	MP	10
	HBsAg	30
	Anti-HBc	18
	Partial* anti-HBc	6
Syphilis	Anti-lues	28
HTLV I/II	Anti-HTLV	12
	Partial*	6
Other:		
CMV	Anti-CMV	14
	Partial	11
Malaria	Anti-malaria (partial*)	7
Chagas	Anti-*Trypanosoma cruzi* (partial*)	6
Parvovirus B19	Anti-ParvoB19 (partial*)	1

*Partial screening means selective screening of newly registered donors only or when not implemented in the whole country or implemented during the observed period of this study. HIV: human immunodeficiency virus; NAT: nucleic-acid amplification testing; ID: individual donation testing; MP: mini-pool of 6, 24 or 96 samples testing; HCV: hepatitis C virus; HBV: hepatitis B virus; HBsAg: hepatitis B surface antigen; HBc: hepatitis B core antigen; HLTV: human T-lymphotropic virus; CMV: cytomegalovirus.

Epidemiological data on viral infections

Epidemiological data on HIV, HCV and HBV infections among a total of 7,949,908 first-time donations, 66,046,854 repeat donations and 976,561 newly-registered donors screened by serology alone or in combination with NAT in the 4-year period are presented for the SSP and PDS cohorts in Tables II and III, respectively. Assuming that all infections among repeat donors were recently acquired, data on recent infections among repeat donations were not collected. In the SSP cohort, the overall prevalence of each infection was higher ($p<0.05$) among first-time donations than among repeat donations. We also compared recent infections among 4,822,874 first-time donations to overall infections among 44,397,229 repeat donations from 18 countries that provided complete SSP data (subset of relevant data in Table II). The prevalence of recent infections among first-time donations of 0.4 (0.0-3.2) for HIV and 0.9 (0.0-26.1) for HCV was lower than the overall prevalence of 2.2 (0.2-18.8) for HIV and 2.5 (0.0-147) for HCV ($p<0.05$) among repeat donations. For HBV, the prevalence of recent infections of 6.7 (0.0-34.1) among first-time donations was higher than the 2.6 (0.0-22.6) among repeat donations ($p<0.05$).

In the PDS cohort, the overall prevalence of all three infections among newly-registered donors in the Netherlands, Norway and Sweden was significantly higher than among repeat donations ($p<0.05$). Ireland and Italy did not provide data for repeat donations among donors selected by PDS. The Netherlands reported the prevalence of recent infections to be lower for HIV and HCV but

Table II - Epidemiological data on HIV, HCV and HBV screening in the SSP setting 2010-2013.

Country	First-time donations							Repeat donations			
	N. of donations	*HIV*		*HCV*		*HBV*		*N. of donations*	*HIV*	*HCV*	*HBV*
		Total (prev./10⁵)	*Recent (prev./10⁵)*	*Total (prev. /10⁵)*	*Recent (prev./10⁵)*	*Total (prev. /10⁵)*	*Recent (prev./10⁵)*		*Total (prev./10⁵)*	*Total (prev. /10⁵)*	*Total (prev./10⁵)*
Austria	209,761	8 (3.8)	1 (0.5)	60 (28.6)	0 (0.0)	122 (58.2)	5 (2.4)	1,363,102	16 (1.2)	16 (1.2)	5 (0.4)
Belgium	186,389	8 (4.3)	0 (0.0)	73 (39.2)	1 (0.5)	176 (94.4)	1 (0.5)	2,095,733	16 (0.8)	5 (0.2)	10 (0.5)
Bulgaria#	138,303	17 (12.3)	NA	350 (253.1)	NA	2,090 (1,511.2)	NA	531,571	13 (2.4)	465 (87.5)	2,842 (534.6)
Croatia	49,170	4 (8.1)	0 (0.0)	32 (65.1)	0 (0.0)	52 (105.8)	6 (12.2)	666,979	7 (1.0)	13 (1.9)	31 (4.6)
Cyprus#	36,870	6 (16.3)	0 (0.0)	9 (24.4)	0 (.0)	18 (48.8)	0 (0.0)	73,649	0 (0.0)	0 (0.0)	0 (0.0)
Czech Rep†	113,576	7 (6.2)	NA	80 (70.4)	NA	43 (37.9)	NA	1,519,471	10 (10.7)	17 (1.1)	27 (1.8)
Denmark	91,375	1 (1.1)	0 (0.0)	11 (12.0)	0 (0.0)	26 (28.5)	4 (4.4)	1,188,770	3 (0.2)	2 (0.2)	9 (0.8)
Estonia	31,074	12 (38.6)	1 (3.2)	157 (505.2)	0 (0.0)	34 (109.4)	0 (0.0)	206,640	10 (4.8)	27 (13.1)	13 (6.3)
Finland	70,409	1 (1.4)	0 (0.0)	24 (34.1)	0 (0.0)	3 (4.3)	0 (0.0)	947,744	3 (0.3)	15 (1.6)	5 (0.5)
France	1,770,492	49 (2.8)	NA	466 (26.3)	NA	948 (53.5)	NA	10,402,304	70 (0.7)	51 (0.5)	36 (0.3)
Germany*	553,992	39 (7.0)	0 (0.0)	278 (50.2)	0 (0.0)	618 (111.6)	0 (0.0)	7,242,799	72 (1.0)	35 (0.5)	23 (0.3)
Hungary#	175,375	9 (5.1)	NA	371 (211.5)	NA	350 (1,99.6)	NA	1,520,124	47 (3.1)	93 (6.1)	42 (2.8)
Ireland (a)	45,643	1 (2.2)	0 (0.0)	2 (4.4)	0 (0.0)	5 (11.0)	0 (0.0)	540,506	1 (0.2)	0 (0.0)	0 (0.0)
Italy (a)	1,137,695	163 (14.3)	0 (0.0)	1,029 (90.4)	13 (1.1)	2,054 (180.5)	39 (3.4)	11,098,098	263 (2.4)	136 (1.2)	550 (4.9)
Latvia	43,883	32 (72.9)	1 (2.3)	733 (1,670.4)	5 (11.4)	245 (558.3)	1 (2.3)	173,310	16 (9.2)	159 (91.7)	14 (8.1)
Lithuania	49,818	24 (48.2)	0 (0.0)	710 (1,425.2)	13 (26.1)	269 (540.0)	7 (14.1)	106,120	20 (18.8)	156 (147.0)	24 (22.6)
Luxembourg	5,110	0 (0.0)	0 (0.0)	4 (78.3)	0 (0.0)	0 (0.0)	0 (0.0)	89,288	1 (1.1)	0 (0.0)	0 (0.0)
Malta[1]	8,651	0 (0.0)	0 (0.0)	4 (46.2)	0 (0.0)	7 (80.9)	0 (0.0)	57,853	0 (0.0)	1 (1.7)	0 (0.0)
Poland	755,270	92 (12.2)	0 (0.0)	2,371 (313.9)	6 (0.8)	3,293 (436.0)	2 (0.3)	4,083,694	99 (2.4)	190 (4.6)	82 (2.0)
Portugal	83,466	57 (68.3)	1 (1.2)	134 (160.5)	0 (0.0)	113 (135.4)	6 (7.2)	670,363	117 (17.4)	270 (40.3)	76 (11.3)
Romania#	281,235	122 (43.4)	NA	1,565 (556.5)	NA	8,609 (3,061.1)	NA	936,546	44 (4.7)	35 (3.7)	116 (12.4)
Slovakia#	100,041	4 (4.0)	NA	43 (43.0)	NA	74 (74.0)	NA	537,415	1 (0.2)	20 (3.7)	6 (1.1)
Slovenia	31,570	1 (3.2)	0 (0.0)	8 (25.3)	0 (0.0)	32 (101.4)	0 (0.0)	335,144	7 (2.1)	0 (0.0)	29 (8.6)
Spain	709,925	187 (26.3)	13 (1.8)	722 (101.7)	7 (1.0)	1,301 (183.3)	242 (34.1)	4,694,645	269 (5.7)	77 (1.6)	235 (5.0)
Switzerland	110,019	4 (3.6)	1 (0.9)	63 (57.3)	0 (0.0)	130 (118.2)	12 (10.9)	1,342,991	8 (0.6)	7 (0.5)	16 (1.2)
England/ Wales/ Northern Ireland	658,305	31 (4.7)	0.0	225 (34.2)	0 (0.0)	256 (38.9)	4 (0.6)	7,560,945	31 (0.4)	20 (0.3)	17 (0.2)
Total	7,447,417	879 (11.8)	NA	9,524 (127.9)	NA	20,868 (228.2)	NA	59,976,162	1,144 (1.9)	1,810 (3.0)	4,208 (7.0)

NA: not available; * Data from three blood establishments; #donations not tested with NAT; †donations tested in a few blood establishments; prev.: prevalence; (a) standard selection strategy not used in the whole country or for all types of donors. HIV: human immunodeficiency virus; HCV: hepatitis C virus; HBV: hepatitis B virus; SSP: standard selection procedure.

higher for HBV among the newly-registered donors than among repeat donations ($p<0.05$). Italy reported only overall infections among first-time donations. There were no infections among first-time donations in the Netherlands during the observed period (Table III).

Discussion

This survey confirms a higher overall prevalence of HIV, HCV and HBV infections among first-time donations and newly-registered donors than among repeat donations[14]. In the PDS cohort the prevalence of transfusion-transmitted infections among first-time donations is diminished due to the exclusion of newly-registered donors who tested positive at the pre-donation stage. The reduction of infected first-time donations that are collected and screened may lower the risk of sporadic false negative results or laboratory errors[15] and lessen the number of discarded donations. Besides reducing the wastage of resources, the pre-donation exclusion also avoids needless discomfort for positive newly-registered donors. Some African countries with a very high prevalence of infectious diseases, such as malaria, have implemented the PDS strategy to prevent discarding a large portion of donations[16].

The residual risk of existing transfusion-transmitted infections in the SSP setting is known and can be estimated by using incidence/window period mathematical models[17,18]. Strategies for further risk reduction may be directed to decreasing the incidence of infections in the donor or general population or to reducing the risk by the two-stage screening of newly-registered donors in the PDS setting. A reduction of such a risk can be assumed if the rate of incident infections among first-time donors is lower than in repeat donors in large studies[19]. In populations with a low prevalence of infection, an estimation of the residual risk of infectious donation requires a longer observation period to detect positive donations[14]. The prevalence ratio of risk situations for recent transfusion-transmitted infections (gathered from the Donor Health Questionnaire) between newly-registered and repeat donors can also give an indirect estimate of the risk of window-period donations[20]. However, evidence in our survey for such an advantage remains weak, due to lack of necessary data and the small number of countries using a PDS strategy. Thus, a limitation of our survey is the lack of data describing confirmatory testing strategies. This precludes an assessment of the comparability of confirmed positive results and evaluation of reported positivity rates among countries. Further research and more data are needed to assess the potential capacity of PDS to reduce the residual risk in first-time donations.

Table III - Epidemiological data on HIV, HCV and HBV screening in the PDS setting 2010-2013.

Country	Newly registered blood donors							First time donations				Repeat donations			
	Number	*HIV*		*HCV*		*HBV*		*Number*	*HIV*	*HCV*	*HBV*	*Number*	*HIV*	*HCV*	*HBV*
		Total (prev./10^5)	*Recent (prev./10^5)*	*Total (prev./10^5)*	*Recent (prev./10^5)*	*Total (prev./10^5)*	*Recent (prev./10^5)*		*Total (prev./10^5)*	*Total (prev./10^5)*	*Total (prev./10^5)*		*Total (prev./10^5)*	*Total (prev./10^5)*	*Total (prev./10^5)*
Ireland	5,369	0 (0.0)	0 (0.0)	10 (186.3)	0 (0.0)	11 (204.9)	0 (0.0)	NA	NA	NA	NA	NA	NA	NA	NA
Italy*	580,988	74 (12.7)	NA	428 (73.7)	NA	758 (130.5)	NA	394,892	8 (2.02)	5 (1.26)	21 (5.31)	NA	NA	NA	NA
Netherlands	140,972	2 (1.4)	0 (0.0)	20 (14.2)	0 (0.0)	57 (40.4)	6 (4.3)	107,599	0	0	0	3,259,611	5 (0.2)	1 (0.003)	17 (0.5)
Norway**	73,774	1 (1.4)	NA	32 (43.4)	NA	27 (36.6)	NA	NA	NA	NA	NA	860,125	0 (0.0)	3 (0.3)	1 (0.1)
Sweden**	175,458	1 (0.6)	NA	73 (41.6)	NA	58 (33.1)	NA	NA	NA	NA	NA	1,950,956	1 (0.1)	11 (0.6)	3 (0.2)
Total	976,561	78 (7.9)	NA	563 (57.6)	NA	911 (93.3)	NA	NA	NA	NA	NA	NA	NA	NA	NA

NA: not available; * newly-registered donors not tested with NAT; ** donations not tested with NAT; prev.: prevalence. HIV: human immunodeficiency virus; HCV: hepatitis C virus; HBV: hepatitis B virus; PDS: pre-donation and donation screening.

The higher proportion of recent HBV infections among newly registered PDS donors and first-time SSP donations as compared to repeat donations might be explained by the detection of occult HBV infections or changing epidemiology of HBV infection in blood donors[21]. However, complementary studies are needed to better understand the possible causes of these findings.

It has been hypothesised that the PDS strategy attracts test-seekers who could contribute to transfusion-transmitted infection positivity especially among newly-registered donors. If this is true, most of the infected test-seekers will be excluded by donor selection or sensitive laboratory screening at the pre-donation stage. However, the impact of test-seekers and the negative experience of the donation[22] on the return rate of first-time donors to the next donation need further investigation in both selection settings.

Our survey shows that several national blood services have limited ability to record and report requested epidemiological data, could use various definitions, particularly for first-time donor/donations and employ different laboratory tests in addition to the mandatory screening. Such diversity suggests a need to harmonise and revise the screening strategies taking into account the various effectiveness of laboratory tests[23], and to develop a guide for epidemiological data collection in blood management.

Using the PDS strategy may improve blood donor management by safeguarding blood donors' health through the pre-donation screening for diseases such as thalassaemia. Exclusion of thalassaemic individuals prevents such individuals from making blood donations that may be harmful to their health. This strategy is relevant in Mediterranean countries and has been implemented in the southern regions of Italy. Double-checking of the donors' personal data and blood grouping may improve the quality and safety of the donation process in the PDS setting. Moreover, repeated information and the time between visits may have an impact on the newly-registered donors, strengthening their decision to become blood donors.

The costs and resources needed for the implementation of a PDS strategy may be restraints and would require precise cost-benefit analysis. The necessity of PDS is questionable in areas with low/very low prevalence and/or incidence of transfusion-transmitted infections. NAT screening in France during the last 13 years did not produce a statistical difference in the incidence of HIV and HCV infections between first-time and repeat donations[24]. Additional limitations of the PDS strategy are related to its applicability in different blood collection organisational models (e.g. mobile *vs* fixed sites) and the possible loss of donations from "one-visit-only" donors.

Conclusions

Most of the European countries in this survey apply SSP for the selection of newly-registered donors and, in a high proportion of cases, use NAT screening in addition to serological tests. Given the highly varying epidemiology and characteristics of European countries, results should be individually analysed and interpreted at this stage. However, it remains difficult to assess the risk reduction related to PDS, as induced by a decrease in the rates of incident infection and consequently the risk linked to the window period. The low prevalence and incidence of observed markers in donor population of some countries on the one hand and variability in reporting of positive results, definitions of donor types and screening tests on the other hand prevented us from collecting sufficient data to assess and compare a residual risk in PDS and SSP. The cost-effectiveness and possible impacts of PDS on blood donor management need to be investigated. Regular and accurate monitoring of incident infections through NAT-only positive tests is strongly advocated in European Union Member States in order to collect data to evaluate further the potential value of PDS and the effectiveness of the donor selection process.

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Authorship contributions

RWL-K, DD and GF designed the study. DD circulated and collected the questionnaires. RL-K performed the analysis. RWL-K, DD and WdK analysed

and interpreted the data. RWL-K, DD and GF wrote the manuscript. All other Authors critically reviewed, edited and approved the manuscript.

The Authors declare no conflicts of interest.

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Correspondence: Ryanne W. Lieshout-Krikke
Sanquin Blood Supply Foundation
Plesmanlaan 125
1066 CX Amsterdam, The Netherlands
e-mail: r.lieshout@sanquin.nl