Risk factors for complications in donors at first and repeat whole blood donation: a cohort study with assessment of the impact on donor return

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Background. First-time donation is among recognised risk factors for vasovagal reactions to blood donation and reactions are known to reduce donor return. We assessed associations between potential risk factors and vasovagal reactions and needle-related complications in first-time whole blood donation in comparison to repeat donation and analysed the impact of complications on donor return.

Materials and methods. We performed a cohort study on whole blood donations in The Netherlands from 1/1/2010 to 31/12/2010 using data extracted from the blood service information system. Donation data up to 31/12/2011 were used to ascertain donor return.

Results. In 2010 28,786 donors made first whole blood donations and there were 522,958 repeat donations. Vasovagal reactions occurred in 3.9% of first donations by males and 3.5% of first donations by females compared to in 0.2% and 0.6%, respectively, of repeat donations. Associations of vasovagal reactions with other factors including age, body weight, systolic and diastolic blood pressure were similar in first-time and repeat donors. Needle-related complications occurred in 0.2% of male and 0.5% of female first-time donations and in 0.1% and 0.3%, respectively, of repeat donations. Among first-time donors, the return rate within 1 year was 82% following an uncomplicated first donation, but 55% and 61% following vasovagal reactions and needle-related complications, respectively; the corresponding percentages among repeat donors were 86%, 58% and 82%.

Discussion. Among first-time donors, females suffered less than males from vasovagal reactions. Other risk factors had similar associations among first-time and repeat donors. Vasovagal reactions and needle-related complications in both first-time and repeat donors are followed by reduced donor return.

Keywords: blood donation, vasovagal reaction, needle-related complication, donor retention, first-time donor.

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Introduction

In the last two decades the occurrence of adverse reactions to whole blood donation and component apheresis has been increasingly studied[1-3]. Suggested risk factors for vasovagal reactions (VVR) include young age, low body weight or small size (small estimated blood volume), female sex and first-time donor status[4-8].

The occurrence of an adverse reaction reduces the likelihood of a donor returning and becoming a repeat donor[9-12]. It is important for blood centres to minimise donor complications, particularly at the first donation, in the interests both of donor safety and of maximising the number of returning donors.

Hitherto the studies of risk factors have analysed first-time status as one among various parameters. This does not answer the question of whether the risk factors are the same for first-time donors and repeat donors. Analyses of risk factors for donation complications among first-time donors have been performed only for a limited number of parameters[13]. In 2010, we examined risk factors for the occurrence of vasovagal reactions, local needle-related complications or procedural problems among first-time whole blood donors in comparison to repeat donors, and assessed the impact of the different types of donation problems on donor return.

Materials and methods

Study design and population

We performed a cohort study including all first-time and repeat whole blood donations in 2010. Records of whole blood and plasmapheresis attendances to the end of 2011 were examined to evaluate the impact of problems at the index donation on donor return.

Data extraction

We extracted data from existing databases on all whole blood donations in 2010 including recorded donor complications and procedural problems.

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Parameters included collection centre (fixed site or mobile site), donor age, sex, donation type, month, pre-donation haemoglobin and blood pressure, successful (≥450 mL) or incomplete collection, time of day, donor height and weight; however, height and weight were not obligatory data in 2010 and 2011 so they are not known for all donors. Data on daily outdoor maximum temperature in the centre of the country were downloaded from the national meteorological institute website. In addition, all donor complication reports into the national quality management database were examined.

For each donor we determined whether they returned for screening and potential donation (whole blood or plasmapheresis) within 1 year. We also noted whether the donor had been deferred permanently before a subsequent donation and the coded reason for deferral. For all donors who made their subsequent whole blood donation up to the end of 2011, we extracted information on whether this donation had been successful and what donor complication or collection problem, if any, was recorded.

Setting: blood supply organisation

In The Netherlands there has been a national, non-commercial blood service since 1998. All donations are from volunteer, non-remunerated blood donors. At their first attendance potential donors are interviewed and a blood sample is taken for testing; the first donation takes place on a subsequent visit. At the intake interview, haemoglobin level and blood pressure are measured and venous accessibility is assessed. Recording of weight and height became obligatory in 2012. At the time of this study body weight was noted as above 50 kg or below; actual values for weight and height were often but not always recorded. Blood donation is permitted from the age of 18 years up to and including 69 years (new donors must be <65 years); body weight must be above 50 kg. Arterial blood pressure values should be between 100/60 mmHg and 160/100 mmHg; subjects with values outside this range, down to 90/50 mmHg and up to 180 mmHg systolic, may only be accepted on the basis of a specific assessment by the physician. All donors, donations, tests, processing and distribution data are recorded in the blood service computer system eProgesa (MAK systems, Paris, France).

Whole blood donors are sent invitation cards according to supply needs (walk-in attendances of registered donors provide a small minority of collections.) Women may donate up to three times a year, men up to five times; all donors donate the standard volume of 500 mL plus test samples, in total not exceeding 550 mL. A physician is present at all collections. As a general principle a first-time donor donates whole blood at least once before apheresis is considered; apheresis is not further discussed in this article.

Recording of donor complications and procedural problems

The occurrence of donor complications or procedural problems is recorded in eProgesa using codes. A new coding system was introduced in the first half of 2010 to improve its usefulness for analysis. Donor complications are classified into types that can be mapped to the International Society for Blood Transfusion surveillance classification based on clinical signs and symptoms[14]. Complications which involve outside medical care are also reported separately in the quality management database. The (obligatory) recording of complications and procedural problems is intended to capture all cases occurring on site. Donors are encouraged, through written and verbal information at the first interview, to inform the blood service about problems occurring off site. In addition, the standard questionnaire filled in by returning donors includes a question on whether the previous collection went well and staff are instructed to retrospectively record any complications which are mentioned.

We classified donor complications into broad categories: needle-related complications (painful arm, arterial puncture and haematoma) and vasovagal reactions (pre-fainting [consisting of pallor, dizziness, sweating, nausea and/or vomiting] as well as fainting [loss of consciousness] with or without complications, injury or hospital admission). The phase of occurrence of a reaction was noted (during collection, afterwards in the centre or afterwards off site). We also examined the outcomes of procedural problems: failed stab (no blood flow following an attempt to insert the needle into a vein for collection; a repeat attempt in the other arm is permitted if no blood enters the tubing), flow problems (e.g. low flow or collection terminated because maximum collection time of 15 minutes is exceeded) or miscellaneous problems (e.g. machine failure). The term venepuncture-related problem is used for the combined outcome of needle-related complication, failed stab and/or flow problems.

Statistical analyses

For all calculations the total number of (needle in) collections was used as the denominator. Rates of events per 1,000 were calculated for first-time and repeat donations separately. Multivariable logistic regression analysis to assess the associations of different variables was performed using IBM SPSS Statistics version 18 (IBM corporation, New York, USA). Associations are expressed by means of the odds ratio (OR) and 95% confidence interval (CI). Because of the low rate of the outcomes being studied, the odds ratio can be interpreted as a relative risk.

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Results

Whole blood collections, recorded donor complications and procedural problems

A total of 551,744 whole blood collections were performed from 1st January 2010 to 31st December 2010; 28,786 (5.2%) came from first-time donors. Table I summarises the key metrics of this cohort in comparison to the collections from repeat donors.

During the study period a total of 4,183 (0.76%) donor complications were recorded: 1,173 (4.1%) in first-time donors and 3,010 (0.58%) in repeat donors. All rates were higher in first-time donors. Table II shows data on vasovagal reactions: the rate for first-time donations was approximately nine times higher than for repeat donations, being 3.6 and 0.39%, respectively. Vasovagal reactions in first-time donors occurred during (as opposed to after) collection in 74% of reacting female donors and 80% among males whereas the percentages of reactions during collections from repeat donations were lower (57% and 65% in reacting female and male donors, respectively). The rate of vasovagal reactions with loss of consciousness (fainting) was 1.0% in female and 1.2% in male first-time donors, compared to 0.2% for female and 0.1% for male repeat donations; however, the gender difference in the group of first-time donors was not statistically significant.

Among all the reported vasovagal reactions in the period July-December 2010 (the period after full implementation of the new codes which record the time of occurrence of a reaction), 53 of the total number of vasovagal reactions in all donors commenced off site (3.3%), the majority in female donors (4.6% of vasovagal reactions in women) and five of the total in first-time donors. In all, 34 complications required further medical care: 26 vasovagal reactions (six of these were delayed reactions after the donor had left the centre and three were with injury; five of the total were in first-time donors), two donors with painful arm or nerve injury who in due course made a full recovery, five cases of local inflammation (phlebitis) and one donor who presented at hospital with a cardiac arrhythmia within 24 hours of giving blood.

Table II presents the analyses regarding associations between risk factors and vasovagal reactions. Female donors were less likely than men to experience a vasovagal reaction at their first donation except above the age of 45 years (overall OR 0.86, 95% CI 0.63-0.98). At repeat donations, females were more likely to have a vasovagal reaction (OR 2.2, 95% CI 2.0-2.4). Younger donors had more vasovagal reactions than donors aged 35 years and older. The odds of vasovagal reactions were lower with greater body weight: OR 0.75, 95% CI 0.64-0.88 for >70 kg *vs* ≤70 kg in first-time donors after adjustment for sex and age group. The odds for a vasovagal reaction showed a rising trend with increasing haemoglobin level in both male and female first-time donations, with or without adjustment for age group and other variables; this was also seen in repeat donations. Regarding blood pressure, analysed only for above- and low-normal ranges *vs* normal values, in the group with the highest blood pressures there were marginally lower odds for vasovagal reactions. The time of day

Table I - Donor and donation characteristics of whole blood collections in 2010.

	First time		Repeat		Total	
	N	%	N	%	N	%
Overall	28,786		522,958		551,744	
Successful	27,126	94%	514,958	98%	541,684	98%
Sex						
Male	10,059	35%	308,662	59%	318,721	58%
Female	18,727	65%	214,296	41%	233,023	42%
Age (years)						
Mean; median	32; 29		47; 49		46; 48	
18-19	3,827	13%	5,587	1%	9,414	2%
20-24	6,907	24%	31,747	6%	38,654	7%
25-35	6,994	24%	62,927	12%	69,921	13%
35-45	5,116	18%	96,607	18%	101,723	18%
45-55	4,078	14%	146,895	28%	150,973	27%
55-65	1,850	6%	144,064	28%	145,914	26%
65-69	14	0%	35,131	7%	35,145	6%
Type of facility						
Fixed	23,258	81%	407,288	78%	430,546	78%
Mobile (setup or bus)	5,528	19%	115,670	22%	121,198	22%

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Table II - Rates of recorded vasovagal reactions (VVR) in first time and repeat whole blood donors.

Variables	First time						Repeat					
	Females 18,753		Males 10,066		Odds Ratio (95% CI)		Females 214,296		Males 308,655		Odds Ratio (95% CI)	
VVR:N, rate in group (%)	656	3.5%	395	3.9%	Females*: 0.86 (0.76-0.98)		1,362	0.6%	692	0.2%	Females*: 2.2 (2.0-2.4)	
VVR, successful collection	335	1.8%	193	1.9%			977	0.5%	443	0.1%		
Subgroup during collection†	253	2.7%	159	3.1%			420	0.4%	232	0.2%		
Subgroup LOC‡	98	1.0%	60	1.2%	Females*: 0.87 (0.63-1.2)		227	0.2%	90	0.1%	Females*: 2.9 (2.2-3.7)	
Age (years)					OR in females*	OR in males*					OR in females*	OR in males*
18-19	117	4.2%	53	5.0%	1.5 (1.1-1.9)	1.8 (1.3-2.4)	80	2.5%	34	1.4%	6.0 (4.8-7.6)	10.7 (7.5-15.3)
20-24	168	3.4%	82	4.1%	1.2 (1.0-1.5)	1.4 (1.1-1.9)	298	1.5%	120	1.0%	3.7 (3.2-4.2)	7.2 (5.9-8.9)
25-34	182	4.2%	135	5.1%	1.5 (1.2-1.9)	1.8 (1.4-2.4)	310	0.9%	182	0.6%	2.2 (1.9-2.5)	4.6 (3.8-5.5)
35-69	189	2.8%	125	2.9%	1.0	1.0	674	0.4%	356	0.1%	1.0	1.0
Weight§					OR in females•	OR in males•					OR in females•	OR in males•
≤70 kg	369	4.2%	70	5.6%	1.0	1.0	826	0.8%	139	0.5%	1.0	1.0
>70 kg	163	3.1%	247	4.0%	0.75 (0.62-0.91)	0.73 (0.55-0.97)	352	0.4%	439	0.2%	0.62 (0.55-0.70)	0.49 (0.40-0.60)
Haemoglobin (mmol/L)^												
Threshold+0.5	217	3.1%	50	3.1%	1.0	1.0	530	0.6%	129	0.2%	1.0	1.0
0.6-1.5	367	3.6%	213	3.8%	1.2 (1.0-1.4)	1.2 (0.9-1.7)	703	0.6%	344	0.2%	1.1 (1.0-1.3)	1.3 (1.1-1.7)
>1,5	72	4.5%	132	4.6%	1.5 (1.1-2.0)	1.4 (0.9-2.0)	129	0.7%	219	0.4%	1.3 (1.0-1.6)	2.3 (1.8-2.9)
Blood pressure (mmHg)					Odds ratio• (95% CI)						Odds Ratio• (95% CI)	
Diastolic ≤60 and/or systolic ≤100	52	3.4%	24	4.4%	0.9 (0.7-1.2)		99	0.9%	24	0.4%	1.0 (0.8-1.3)	
Mid range	589	3.5%	355	4.0%	1.0		1,226	0.6%	617	0.2%	1.0	
Diastolic >90 and/or systolic >160	15	2.8%	16	2.7%	0.8 (0.7-1.0)		37	0.3%	51	0.2%	0.8 (0.6-1.0)	

*Adjusted for age (categorical) and observation period; †data available for July-December 2010; ‡Loss of consciousness, data available for July-December 2010; §Known for 466,342 (85%) donation records; ^Donation permitted from 7.8 mmol/L for females (12.6 g/dL) and 8.4 mmol/L for males (13.5 g/dL); •Adjusted for other variables (categorical) in multivariable model.

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and maximum daily outdoor temperature had no clear association with the occurrence of vasovagal reactions in first-time or repeat donations. The data on type of collection facility showed lower odds for vasovagal reactions for donors donating in mobile collection sites than in fixed sites (adjusted OR 0.7 [95% CI 0.6-0.9] in first-time and 0.8 [95% CI 0.7-0.9] in repeat donors); however, there were few mobile collection sites and the data for setup sites and bus collections were combined, so the statistically significantly lower odds ratio should interpreted cautiously.

The overall rate of needle-related complications for first-time donations was 0.5% in female and 0.2% in male first-time donors in comparison to 0.3% and 0.1%, respectively, for female and male repeat donations. Likewise the rates of flow problems and failed stab for first-time donations were approximately double those for repeat donations and higher in female donors. Associations of donor sex, age and body weight with needle-related complications, flow problems and failed stab in the first-time group are presented in Table III. In addition to the increased rates in females, a failed stab was more likely in heavier donors. There were no apparent associations of haemoglobin level, blood pressure, type of centre, temperature or time of day with needle-related complications (data not shown).

Donor return

In the cohort of first-time donors 130 females (0.7%) and 36 males (0.2%) were permanently deferred without making subsequent donations because of complications or unsuitable veins. A total of 287 female and 65 male donors in the repeat donor cohort were permanently deferred because of complications or problems with venous access, for rates of 0.1% and 0.02% per donation or 0.3% and 0.1% per donor among female and male donors respectively. The return rate was 77% among female first-time donors, 81% among male first-time donors, 85% among female repeat donors and 91% among male repeat donors. Among all donor attendances, return was associated positively with male sex (females OR 0.59; 0.58-0.60) and negatively with first-time donation (OR 0.67; 0.65-0.69), age groups 20-24, 25-34 and 35-44 (but not 18-19 years) in comparison to over 45 years. If the first collection was successful despite a complication or problem during the collection or recovery period, a vasovagal reaction led to reduced donor return (return rate 61% in females and 67% in males) but there was no reduction from venepuncture-related problems. If the first donation was not successful, all types of problems were associated with lower donor return but the reduction was strongest for vasovagal reactions. The same effects were seen in repeat donors (return data not shown).

Recurrence of complications at subsequent donation

In all 83% of female donors and 88% of male donors who experienced a vasovagal reaction at the first donation had an uncomplicated second donation. For females the rate of vasovagal reactions at the second donation was 10.5% compared to 2.4% among donors who had uncomplicated first donations, i.e. 4.4 times higher. In male donors the rate of recurrence was 9.7% compared to 1.7% vasovagal reactions in male donors who had had an uncomplicated first donation, i.e. 5.7 times higher. All these rates were higher than in the whole group of repeat donations (0.6 and 0.2% respectively, Table II). Among the donors who made a

Table III - Rates of venepuncture-related problems at first whole blood donation (total N =28,786).

Variables	Needle related complication*				Flow problems				Failed stab†			
N; rate (%)	117	0.4%	OR (95% CI)‡		819	(2.8%)	OR, 95% CI‡		314	(1.1%)	OR, 95% CI‡	
Incomplete N§ (% of total)	93	0.3%			731	(2.5%)			205	(0.7%)		
Sex												
Female	93	0.5%	2.1	1.3-3.2	670	3.6%	2.0	1.5-2.6	253	1.3%	2.9	1.9-4.4
Male	24	0.2%		1.0	149	1.5%		1.0	61	0.6%		1.0
Age group (years)												
18-19	20	0.5%	1.2	0.7-2.1	141	3.7%	1.5	1.2-1.8	51	1.3%	1.4	1.0-1.9
20-24	29	0.4%	1.0	0.6-1.6	234	3.4%	1.3	1.1-1.6	94	1.4%	1.4	1.1-1.9
25-34	24	0.3%	0.8	0.5-1.4	183	2.6%	1.1	0.9-1.3	68	1.0%	1.1	0.8-1.4
35-69	44	0.4%		1.0	261	2.4%		1.0	101	0.9%		1.0
Weight^												
50-70 kg	53	0.5%		1.0	400	(4.0%)		1.0	118	(1.2%)		1.0
>70 kg	43	0.4%	0.93	0.60-1.4	235	(2.0%)	0.7	0.6-0.8	137	(1.2%)	1.5	1.2-2.0

*Haematoma, arterial puncture, painful arm; †Failed stab: failed venepuncture, either leading to failure of collection or to successful collection after repeat venepuncture; ‡Odds ratio and 95% confidence interval, adjusted for sex and age group (categorical); §Collection <450 mL (standard = 500 mL excluding samples); ^Weight known for 21,633 donations.

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second whole blood donation during the study period the occurrence of a vasovagal reaction on that occasion was associated with younger age (OR 1.7, 95% CI 1.3-2.4 for 18-19 year olds compared to donors older than 34 years) and lower body weight (1.6, 95% CI 1.3-2.1 for weight <70 kg after adjustment for sex and age group). There was no sex difference in vasovagal reactions at second donation after adjustment for the other factors. In repeat donors who made a subsequent whole blood donation after a vasovagal reaction at the index donation the rate of recurrence of the vasovagal reaction was 6% in both male and female donors.

Among the 4.4% of female and 2.2% of male donors who experienced needle-related complications (haematoma, painful arm or arterial puncture), flow problems or failed stab at first donation, 83% had second donations without problems; the rates of venepuncture-related problems were 12% and 11%, respectively, in comparison to 2.7% and 1.2%, respectively, for female and male second-time donations overall. Among the repeat donors the rate of recurrent venepuncture-related problems was 10% in female donors compared to 2.4% among female repeat donors; these figures were 5% *vs* 1.2% in male repeat donors.

Discussion

Vasovagal reactions

In our cohort we found that female first-time donors had fewer vasovagal reactions than male donors, whereas the opposite was the case in repeat donations. The rates of more severe reactions, with loss of consciousness, were similar in first-time male and female donors but showed a trend in the same direction. The associations with lower values for donor age, body weight and blood pressure in first-time donors were similar to those in repeat donors.

An increased risk of vasovagal reactions in male first-time donors has not previously been focused on, although collection centre staff are usually well aware that men can faint at or even before their first donation[8]. Interestingly, in a study by Eder *et al*. which also included donors younger than 18 and analysed the effect of introducing deferral of young candidate donors with a calculated blood volume of less than 3.5 L[13], it was found that the rate of vasovagal reactions recorded by the blood centre in first-time 18-19 year old blood donors was approximately 10% in females and 6% in males, i.e. a higher rate in female than male donors in contrast to the findings in our study. Among donors of 20 years and older in the same organisation, the rates were approximately 7% in female and 5% in male first-time donors[5]. Given the overall higher rate of reactions in these studies, it is possible that additional milder reactions occurred which were not captured by our reporting. In a study by Wiltbank *et al*., including donors from the age of 17 years, the rates of mild and moderate (but not severe) vasovagal reactions tended to be higher in male than in female first-time donors in univariate analysis according to estimated blood volumes, but the differences were not statistically significant; rates were higher in females in other comparisons[6]. Most other studies did not analyse the role of sex as a risk factor separately in the first-time donor population[7,8,12,15].

Haemoglobin level and vasovagal reactions

The trend of increasing vasovagal reactions associated with haemoglobin level in the first donation cohort after adjustment for sex and age was unexpected. Although the confidence intervals for the odds ratios at some haemoglobin levels crossed unity, indicating a lack of statistical significance, there was a consistent, increasing trend, robust to adjustments for the other included variables. A similar association was seen in the repeat donors. Preliminary findings of an association with haemoglobin level have been reported by other investigators (Bravo/Tomasulo, oral communication, Montreal April 2012[15]). The observed trend may be due to unmeasured confounding factors. An explanation might be sought in smoking since smokers have higher haemoglobin levels. At our centre there have been recent studies surveying donors' characteristics (including smoking) and donors' attitudes towards returning[11,16]. In a supplementary analysis of study data, no difference was found in the percentage of smokers between donors who reported having had a vasovagal reaction at their last attendance (Veldhuizen, personal communication, 2012). This makes smoking unlikely as an explanatory factor. Dehydration marginally increases the haemoglobin level and is also associated with vasovagal reactions[17]. Newman measured a decrease in haemoglobin of 0.13 g/dL following a drink of 475 mL of water, so it is conceivable that the effect of the state of hydration on haemoglobin is large enough to contribute to the observed association[18]. Stress haemoconcentration is a third possible explanation of the association: a reduction of plasma volume and resultant increased haemoglobin level have been described in acutely stressed subjects[19,20] while a contribution of stress in inducing vasovagal reactions is well recognised[21-23]. Further work is needed to examine the association with haemoglobin and possible further confounders.

Needle-related donor complications, flow problems and failed stab

Female donors were roughly twice as likely as males to have needle-related complications, flow problems or failed stab. The overall higher rate of needle-related complications in first-time donors (both female and male) than in repeat donors is probably explained by

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selection. For some donors the first attempt at donation is a test of suitability of the venous access and some donors were subsequently deferred; others self-selected and did not return.

Donor return

Following a vasovagal reaction both male and female donors were less likely to return, the greatest reduction being seen in male donors whose first donation was unsuccessful. Reduced donor return following vasovagal reaction has been previously described[9-11]. Our results make it clear that the reduction is stronger following a vasovagal reaction in combination with an unsuccessful donation, a factor which was also noted by the REDS-II group[24]. It is possible that reactions during collection were more severe and that this led to poorer return. Another likely factor was suggested in a recent study by Veldhuizen *et al.* which indicated that repeat male donors in particular report lower self-efficacy when (self-reported) reactions have occurred[11].

Donors with venepuncture-related problems at their first donation were also less likely to return, especially if the first donation was unsuccessful. The effect of experiencing a failed donation attempt in contrast to a successful donation with a complication (other than a vasovagal reaction) does not appear to have been systematically examined, although the role of donor motivation and the psychological impact of donation complications has been highlighted[10,11]. With regards to needle-related complications, Newman, reporting on a telephone survey in 2006, described that bruises or sore arm have an impact which is less strong than vasovagal reactions but which can have an additive effect with fatigue following blood donation to reduce return rates by 65%[9]. In a recent survey of lapsed donors in The Netherlands, fatigue was mentioned among physical reactions after donation which led donors to stop donating[25]. Fatigue is not captured by a collection centre-based study such as ours.

Studies are consistent in reporting reduced return rates following donor reactions but the methods of measuring donor return vary: visits per year[9], return within 1 year as in this study[10,12], visits within 13 months[26] or 1 year from eligibility[27]. The baseline rates reported by other authors are generally lower than in our study. For instance France *et al.* reported return rates of 42% for first-time donors and 70% for repeat donors overall. Eder *et al.* found a baseline return rate of 35% following uncomplicated first donation; interestingly this group found -as we did in our cohort- that donors below the age of 20 years had higher return rates than older donors with the exception of the highest age band. In the REDS-II study the return rate for donors without reactions was 60-70%, depending on the centre[24].

Strengths and limitations

Our new coding system has made more detailed analysis of donor complications and of diverse collection problems possible. However, a limitation of routinely recorded information is the likelihood of variable and under-reporting. The information is poorly detailed and does not allow in-depth analysis of possible causes. In the course of the observation period an increasing tendency was observed in the recorded donation complications and collection problems. There was also a tendency to a slight increase in unsuccessful collections. A small number of serious complications (0.8% of the total or 0.6 per 10,000 donations; 95% CI 0.4-0.8 per 10,000) required outside medical care; these could not be usefully analysed in this study because of its relatively small size, but such complications are a cause of serious morbidity. The study by Eder *et al*., reporting on over six million donations, recorded a higher rate of outside medical care of 3.2 per 10,000, however this cohort comprised a larger proportion of young donors (14% compared to 2% below the age of 20 years in our study) and of first-time donors[2]. In the future, larger studies should address the rare but serious complications.

As explained above, in the Netherlands all first-time donors have an interview and blood testing prior to the day on which they make their first donation. In the Netherlands there is also a strong focus on donor management and high donor retention with only 5.2% of whole blood donations coming from first-time donors. These aspects may affect the generalizability of our findings since the occurrence of vasovagal reactions, needle-related complications and other problems at the first donation may have a greater impact in terms of lost subsequent donations in settings in which a higher proportion of collected blood comes from walk-in and/or new donors. Differences in age distribution between our cohort and those in other countries will also reduce comparability of overall rates, although this problem has been partly addressed by presenting age-stratified analyses.

Practical implications of the study

Blood centres have the opportunity and challenge to move towards interventions to reduce donor complications, based on current knowledge of which donors are at risk. Our study shows that it is worth investing more effort in avoiding venepuncture-related problems at the first as well as subsequent blood donations. Both male as well as female first-time donors should be considered "at risk" of vasovagal reactions. A number of interventions have been found to be effective at reducing the rate of vasovagal reactions, especially in first-time or inexperienced donors. Examples of such interventions are drinking 500 mL of water shortly

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before the donation, salt replacement, social distraction, instruction in applied muscle tension and the application of deferral or an adjusted collection volume based on weight/height or estimated blood volume, particularly for young donors[13,18,21,22,28,29]. The data on recurrence rates for complications provide insights which are relevant for both written and oral information provided to donors.

Conclusion

In conclusion, our analysis of risk factors for vasovagal reactions at first-time whole blood donation, in contrast to repeat donation, showed that male donors were more likely to have a reaction than female donors, although with regards to more severe reactions with loss of consciousness there was only a trend to a higher incidence in males. The associations between other risk factors and vasovagal reactions were similar among first-time and repeat donors. Female donors were at higher risk of needle-related complications at both first and repeat whole blood donations. Reduced donor return was seen following vasovagal reactions, as well as following venepuncture-related problems leading to unsuccessful collection. Most donors (over 80%) who did come back after complications at their first donation had uncomplicated second donations.

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Authors' contributions

Johanna C. Wiersum-Osselton analysed the data, drafted the manuscript and is guarantor for the article. Tanneke Marijt-van der Kreek supervised the implementation of new codes and monitored complication recording. Wim de Kort is responsible for donor services including the medical care of donors. Johanna C. Wiersum-Osselton, Johanna G. van der Bom and Anneke Brand designed the analyses, to which Tanneke Marijt-van der Kreek and Wim de Kort gave practical input. Ingrid Veldhuizen provided additional data information. All authors critically reviewed the manuscript and agree to its submission for publication.

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