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Factors associated with fainting – before, during and after whole blood donation

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Background Whole blood (WB) donation encompasses several periods during which some donors faint. Identification of factors associated with fainting during each period should guide intervention strategies. Reducing faint reactions may reduce donor injuries and disability.

Methods Blood donation was divided into three periods: Period 1 – registration; Period 2 – phlebotomy; and Period 3 – post-phlebotomy. Period 3 consists of two sub-periods (3A – on-site and 3B – off-site). For each Period, stratified rates of fainting in relation to various donor and donation characteristics were calculated and multivariable logistic regression analyses to identify factors associated with fainting were conducted. Donor injuries in each period were also analysed.

Results Of the 956 766 donors registered in 2007, 554 534 (58%) donated WB. There were 43 fainting episodes and two injuries in Period 1 and 1520 faints and 73 injuries in Periods 2 and 3. Regression analyses showed that youth and donor first-time status are associated with fainting in all periods; but most significantly in Period 1. Small estimated blood volume is notably not a factor in Period 1 but is significant in Periods 2 and 3. The highest injury rate is seen in Period 3A (0·07 and 0·09/1000 donations) for male and female donors, respectively.

Conclusions Variability in factors associated with fainting across defined periods of the donation process suggest differing underlying mechanisms and the possibility that interventions for the reactions most associated with injury during each time period can be designed. The highest rate of injury per donation occurred in ambulating donors.

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Introduction

Previous studies identified risk factors for mild, moderate and severe reactions in whole blood donors as well as factors associated with immediate and delayed reactions among whole blood and apheresis donors [1–4]. Tomasulo *et al.* [5] have shown that blood donor fainting reactions are not spread evenly over the entire time course of the donation process, but rather are concentrated in three peaks. It is our hypothesis that there are distinct periods during the donation process each with a different risk of injury and set of risk factors. Because some intervention measures have been shown to be effective in reducing the risk of fainting reactions [6,7], it becomes important to identify those donors most likely to react in each period and, if possible, why, so that appropriate interventions can be selected for reactions in each period and for reactions which are associated with injury.

Our study focuses on all fainting reactions across the time course of donation; i.e. vasovagal syncope (VVS) or

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loss of consciousness (LOC), because LOC is likely to be more consistently recognized than categories such as mild, moderate and severe and because LOC is likely to be associated with donor injury. We investigated the proportion of donor injury and outside medical care (OMC) which occurs with LOC reactions in each period to help set priorities for future intervention strategies. We included LOC reactions that occur before venipuncture to determine risk factors during this period, permitting the inclusion of these factors in future intervention strategies to reduce reactions.

Materials and methods

Blood Systems, Inc. is a large, non-profit blood collection, testing and research organization operating in the United States, collecting approximately 1 million allogeneic donations every year at blood centres located in 18 central, southern and western states [United Blood Services (UBS), Blood Centers of the Pacific and Inland Northwest Blood Center]. Donations at the 15 UBS centres represent more than 80% of these donations and 6% of the US blood supply. Blood Systems serves more than 500 hospitals.

We studied LOC reactions at 15 UBS blood centres from 1 January to 31 December 2007. Donor, donation and reaction data (including injury and OMC) acquisition is controlled by Standard Operating Procedure (SOP) and was previously described in detail [4,5]. Donor and donation information was obtained from the blood bank computer system (MAK/Progesa, Paris, France) by accessing the information through the Blood Systems Data Warehouse using Sagent Information Studio 5.5.1 (Troy, NY, USA). The donor records captured donor demographic information (age, gender, race/ethnicity, donation history), biometric characteristics (height, weight) and clinical measurements (pulse, blood pressure, temperature) prior to donation. Donation records included phlebotomy start and end time, collection status, collection site, donation type, etc. Additionally, each UBS blood centre provided required information on all reactions including classification (mild, moderate or severe), symptoms, time of reaction, location of reaction, injuries (lacerations, fractures, etc.) and the use of OMC (e.g. emergency medical services or emergency room visit) using a standardized adverse reaction reporting form. These forms captured detailed information on observed and reported reactions. The data recorded on the adverse reaction forms during the study period were entered by hand into a database. For this analysis, we include LOC reactions associated with a presentation to donate or an allogeneic whole blood donation attempt. We use the term VVS and fainting interchangeably to describe donor's transient LOC of any duration before, during or after blood donation. VVS is associated with arterial hypotension and/or bradycardia. Clinically, these episodes are preceded by various symptoms including light-headedness, dizziness, nausea, sweating, pallor, unclear thinking and visual disturbances. LOC may have been directly observed by staff, reported by the donor, or reported by a third party and may have occurred on- or off-site.

We recorded the start time of a reaction associated with LOC in relation to the end of phlebotomy ($T = 0$) using a clock at each donation site which is synchronized with the blood establishment computer system clock. We defined the following periods: Period 1 (Registration and eligibility assessment) – from donor presentation at the collection site through medical health screening; Period 2 (Phlebotomy) – from venipuncture until 4 min after phlebotomy end (presumably when the donor stands up). A donor is likely to be recumbent or semi-recumbent during Period 2. SOP requires that donor sits on the side of the bed for 1–3 min after the removal of the needle; and Period 3 (Post-phlebotomy) – >4 min after phlebotomy end to the last event reported (in the dataset, 265 min after the needle was removed). A donor is likely to be sitting, walking or standing during this period. Period 3 is divided into two sub-periods: Period 3A – LOC occurring on-site, and Period 3B – LOC occurring off-site, outside the vicinity of the blood drive and without staff involvement for immediate donor management.

The donor, donation and reaction data were merged to create a research database. Uneven age group categories were created because younger donors have a higher risk of fainting. Body mass index (BMI) and estimated blood volume (EBV) for each donor were calculated based on self-reported weight, height and gender using published formulas [8,9]. Some merged records had missing information for potentially relevant parameters in the analysis. We did not impute missing values based on other information. If the data were not recorded or available, the individual fainting reaction record did not contribute information to the statistical analysis for a given variable. The data variables with highest frequency of missing values were race (3·3%), height (1·3%); consequently, EBV and BMI were missing in 1·3% of records, and Pre-donation pulse (1·3%). Implausibly extreme values for any parameter were assumed to be data entry errors and were not included in the analysis.

The Period 1 dataset contained 956 766 records of registered donors with the intention to donate – donating and deferred, autologous and allogeneic, apheresis and whole blood. When donors register, they do not indicate for what type donation procedure they have come. In addition, the treatment of donors is similar during Period 1 regardless of the intended donation type. For Periods 2 and 3, intended whole blood (complete and incomplete) donations were studied because whole blood donation is associated with a higher LOC rate compared to apheresis donation [4,5] and

because the physiology and duration of apheresis donations are different. When all data cleaning activities were completed for Periods 2, 3A and 3B, the dataset contained of 554 534 donation records of donors who gave or intended to give allogeneic whole blood during the 12-month study period.

Statistical analysis

The proportion of donors who fainted was calculated by dividing the number fainting by the total number of presentations or donations in each corresponding demographic group or other grouping variable. Rates per 1000 presentations or per 1000 donations depending on the period are reported. Reacting donors in previous periods were excluded from the denominators before calculations are made for subsequent periods.

For each period, separate multivariable logistic models were fit to the data, comparing fainting vs. not fainting to identify factors associated with the risk of reaction in each period. The approach to model building was not the same for all four periods. Because there were a small number of fainting events in Periods 1 and 3B, we preselected age, sex, donor status, donor site and EBV in the multivariable analysis based on previous studies of aggregate reaction rates in which these factors were significant [1–4]. Variables that were significant ($P \leq 0{\cdot}05$) were kept in each model. For period 3B reactions, we also conducted likelihood ratio tests to assess whether each variable represented a statistically significant improvement to the overall model. We report odds ratios (OR) and 95% confidence intervals (CI) of all variables included in the final models.

For Periods 2 and 3A, unadjusted (univariate) ORs and 95% CIs were initially computed for each factor and provided an assessment of the crude association of each variable with the risk of fainting. All the variables that were significant in univariate analyses were included in a single overall multivariable model for each period. The adjusted OR for each factor was derived using a multivariable modelling approach that included risk factors and confounders of the relationship between fainting and each variable. Potential factors that were no longer significant ($P > 0{\cdot}05$) when included in each multivariable model were removed in a stepwise manner until only the significant factors remained. For all models, in most cases the reference group for a categorical variable was the group with the highest frequency.

While our focus was on fainting in order to devise future intervention strategies, we assessed frequency of injuries and need for OMC during the three different donation periods to begin to understand the periods during which injury and disability occur from LOC. The proportion of injury and OMC was calculated by dividing the number fainting with injury and fainting with OMC events by the total number of fainting in each corresponding period. Data cleaning and statistical analysis were performed using STATA 11 SE (Stata Corporation, College Station, TX, USA), and results were graphed using Excel 2007 (Microsoft Corporation, Redmond, WA, USA).

Results

Frequency of fainting events

For the 12-month study period, there were 956 766 donor registrations with intent to donate, and 554 534 (58%) of which were intended whole blood donations. Among registered donors, there were 43 LOC events during registration and medical health screening for a rate of 0·04/1000 registered donors (Period 1). There were 1520 LOC events in Periods 2 and 3 (LOC rate of 2·7/1000 donations). During Periods 2 and 3, 78 injuries were reported (Injury rate of 0·14/1000) of which 73 (94%) were associated with LOC. Of the 1520 fainting reactions, 39% (593), 51% (772) and 10% (155) occurred in period 2, 3A and 3B, respectively. No donor had more than one LOC reaction associated with any donation. Rates of LOC during the donation periods are reported in Table 1 and Fig. 1b. The rate of off-site reactions (Period 3B) associated with fixed site donations is low compared to LOC rates associated with donations on mobile buses and mobile inside set-ups. Low EBV is associated with a profoundly increased rate of off-site reactions when compared to donations by individuals with more than 4 or 5 l EBV.

Multivariable analysis results by period

For Period 1, the final model included age, sex and donor status. EBV and donor site were found to be non-significant and were not retained in the model. In Period 1, the likelihood of LOC was higher in younger donors compared to donors 25–65 years of age (Table 2 and Fig. 2). The adjusted ORs and 95% CIs were 11·1 (4·6–27·3), 10·3 (4–27) and 4·9 (1·0–23·8) for 17–18, 19–22 and 23–24 years old donors respectively. First-time status showed a higher risk compared to repeat donor status (OR 4·3, 2·1–8·8). Gender and low EBV were not risk factors in this period.

For Period 2, the final logistic model included donation site, age group, gender, race/ethnicity, first time/repeat status, EBV, systolic blood pressure, collection status and blood centre as covariates. Donation at fixed sites and on bus mobiles had significantly lower risk of LOC compared to donation at mobile set-ups: 0·5 (0·4–0·7) and 0·8 (0·6–0·9), respectively. There was a significantly increasing risk with younger age: 17–18, OR 2·1 (1·7–2·6); 19–22, OR 2·0

Table 1 Characteristics of the blood donor population and their donations: fainting cases across time course of donation

	Registrations by category	Period 1 *N* = 956 766		Whole blood donations by category	Period 2 *N* = 554 534		Period 3A *N* = 553 941		Period 3B *N* = 553 169	
Donor and donation characteristics	**Number**	**Number**	**Rate/ 1000**	**Number**	**Number**	**Rate/ 1000**	**Number**	**Rate/ 1000**	**Number**	**Rate/ 1000**
Overall	956 766	43	0·04	554 534	593	1·1	772	1·4	155	0·3
Reaction location										
On-site		43			593		772		–	
Off-site		–			–		–		155	
Donation site										
Fixed site	361 286	8	0·02	175 920	91	0·5	183	1·0	12	0·1
Mobile bus	228 379	12	0·05	149 726	129	0·9	159	1·1	70	0·5
Mobile set-up	367 101	23	0·06	228 888	373	1·6	439	1·9	73	0·3
Association type										
High school	89 081	17	0·19	49 780	137	2·8	191	3·8	45	0·9
College/University	56 181	8	0·14	32 962	73	2·2	77	2·3	17	0·5
Others	811 504	18	0·02	471 792	383	0·8	504	1·1	93	0·2
Age group (years)										
17–18	107 179	23	0·21	57 879	187	3·2	285	4·9	50	0·9
19–22	76 028	11	0·14	42 065	83	2·0	114	2·7	20	0·5
23–24	30 274	2	0·07	17 061	27	1·6	28	1·6	4	0·2
25–65	675 800	7	0·01	397 209	272	0·7	303	0·8	69	0·2
>65	67 442	0	0·00	40 292	23	0·6	42	1·0	12	0·3
Missing	43	0	0·00	28	1	35·7	0	0·0	0	0·0
Sex										
Male	453 240	26	0·06	227 351	184	0·8	154	0·7	8	0·0
Female	503 526	17	0·03	327 183	409	1·3	618	1·9	147	0·5
Race/Ethnicity										
Black, non-Hispanic	34 139	0	0·00	19 724	2	0·1	6	0·3	2	0·1
Hispanic	148 662	4	0·03	81 151	87	1·1	154	1·9	38	0·5
Other or mixed, non-Hispanic	16 212	2	0·12	8921	15	1·7	17	1·9	1	0·1
Asian or Pacific Island, non-Hispanic	12 336	1	0·08	7065	7	1·0	16	2·3	3	0·4
White, non-Hispanic	713 224	32	0·04	419 130	460	1·1	550	1·3	100	0·2
Missing	32 193	4	0·12	18 543	22	1·2	29	1·6	11	0·6
Donation Status										
Repeat	736 856	11	0·01	426 055	275	0·6	406	1·0	84	0·2
First time	219 910	32	0·15	128 479	318	2·5	366	2·9	71	0·6
Weight, Kg (lbs)										
49·9–54·0 (110–119)	24 445	3	0·12	16 639	46	2·8	75	4·5	28	1·7
54·4–58·5 (120–129)	49 322	3	0·06	34 791	79	2·3	121	3·5	18	0·5
59·0–65·3 (130–144)	111 089	5	0·05	76 466	142	1·9	186	2·4	44	0·6
65·8–70·0 (145–154)	86 501	9	0·10	55 904	59	1·1	91	1·6	22	0·4
70·3–90·3 (155–199)	378 693	12	0·03	218 765	184	0·8	230	1·1	36	0·2
90·7–117·5 (200–259)	250 878	9	0·04	128 907	72	0·6	66	0·5	7	0·1
≥117·9 (260)260	50 113	0	0·00	22 802	11	0·5	3	0·1	0	0·0
Missing	5085	2	0·39	260	0	0·0	0	0·0	0	0·0
Height, m (inches)										
<1·47 (58)	2146	0	0·00	1483	4	2·7	4	2·7	0	0·0
1·47–1·52 (58–60)	24 969	0	0·00	17 036	20	1·2	42	2·5	12	0·7

Table 1 (*Continued*)

1·55–1·63 (61–64)	219 772	9	0·04	152 434	194	1·3	318	2·1	90	0·6
1·65–1·70 (65–67)	241 632	8	0·03	143 584	170	1·2	232	1·6	37	0·3
1·73–1·83(68–72)	352 307	20	0·06	185 065	146	0·8	142	0·8	13	0·1
>1·83 (72)	98 218	4	0·04	47 775	45	0·9	23	0·5	0	0·0
Missing	17 602	2	0·11	7157	14	2·0	11	1·5	3	0·4
Body mass index (kg/m^2)										
<18·5 underweight	5442	1	0·18	6717	20	3·0	26	3·9	3	0·4
18·5–22·49 low normal	139 183	20	0·14	103 815	205	2·0	262	2·5	57	0·6
22·50–24·99 high normal	163 007	7	0·04	84 247	103	1·2	148	1·8	32	0·4
25·00–29·99 overweight	348 116	8	0·02	199 190	163	0·8	218	1·1	45	0·2
30–39 obese	247 181	5	0·02	134 392	83	0·6	100	0·7	15	0·1
≥40 extreme obesity	35 634	0	0·00	18 782	5	0·3	7	0·4	0	0·0
Missing	18 203	2	0·11	7391	14	1·9	11	1·5	3	0·4
Estimated blood volume (ml)										
<3500	42 878	3	0·07	29 621	69	2·3	121	4·1	41	1·4
3500–3999	156 718	7	0·04	110 811	189	1·7	281	2·5	59	0·5
4000–4499	165 113	6	0·04	108 355	122	1·1	166	1·5	39	0·4
4500–4999	146 334	9	0·06	82 948	61	0·7	79	1·0	6	0·1
≥5000	427 520	16	0·04	215 408	138	0·6	114	0·5	7	0·0
Missing	18 203	2	0·11	7391	14	1·9	11	1·5	3	0·4
Pre-donation pulse (bpm)										
<65	156 809	1	0·01	98 166	110	1·1	93	0·9	16	0·2
65–90	600 944	9	0·01	393 364	403	1·0	525	1·3	112	0·3
>90	99 122	0	0·00	55 632	66	1·2	143	2·6	24	0·4
Missing	99 881	33	0·33	7372	14	1·9	11	1·5	3	0·4
Pre-donation S-BP (mmHg)										
<100	32 978	2	0·06	23 771	41	1·7	58	2·4	13	0·5
100–140	715 399	9	0·01	462 883	523	1·1	671	1·5	132	0·3
>140	115 149	1	0·01	67 866	29	0·4	43	0·6	10	0·1
Missing	93 240	31	0·33	14	0	0·0	0	0·0	0	0·0
Pre-donation D-BP (mmHg)										
<70	204 572	4	0·02	136 483	209	1·5	285	2·1	51	0·4
70–85	518 232	4	0·01	334 607	337	1·0	432	1·3	89	0·3
>85	137 937	3	0·02	83 416	47	0·6	55	0·7	15	0·2
Missing	96 025	32	0·33	28	0	0·0	0	0·0	0	0·0
Collection status										
Incomplete				17 606	149	8·5	11	0·6	3	0·2
Complete				536 907	444	0·8	761	1·4	152	0·3

(1·7–2·6) and 23–24, OR 1·8 (1·2–2·7), though the ORs were lower than in Period 1. Females had a lower risk compared to male donors, OR 0·6 (0·5–0·8). First-time donors had a higher risk; 2·5 (2·1–3·1) compared to repeat donors. There was an increased risk of fainting among donors with EBV <4500 ml with the highest risk for those <3500, OR 3·2 (2·2–4·8); 3500–3999, OR 2·9 (2·0–4·0) and 4000–4499, OR 2·0 (1·5–2·8). Incomplete donation status compared to complete donation status was highly associated with LOC OR 8·0 (6·6–9·7).

For Period 3A, the final multivariable model included donation site, age, race/ethnicity, donor status, EBV, pulse, collection status and centre. Younger and older donors, compared to 25–65 y/o, had a higher risk of fainting. This period showed a higher OR in the 17–18 group, 3·9 (3·2–4·7) than in Period 3B during which the OR in the 17–18 group was 2·5 (1·7–3·8). First-time donor status was associated with a higher risk compared to repeat, 1·9 (1·6–2·3). In this period, all EBV groups <5000 ml had a significantly higher risk of VVS with increased risk in the lower EBV groups: <3500, 4·6 (3·5–6·0); 3500–3999, 3·4 (2·8–4·3); 4000–4499, 2·4 (1·9–3·0); 4500–4999, 1·5 (1·2–2·1).

For Period 3B, the final model included donation site, age, sex, donor status and EBV. Based on likelihood ratio tests, both sex and EBV were significant independent factors associated with LOC. Women had a higher risk in this period, 2·9 (1·2–7·4). Similar to Period 2, EBV < 4500 ml was a significant risk. The highest risk was among the lower

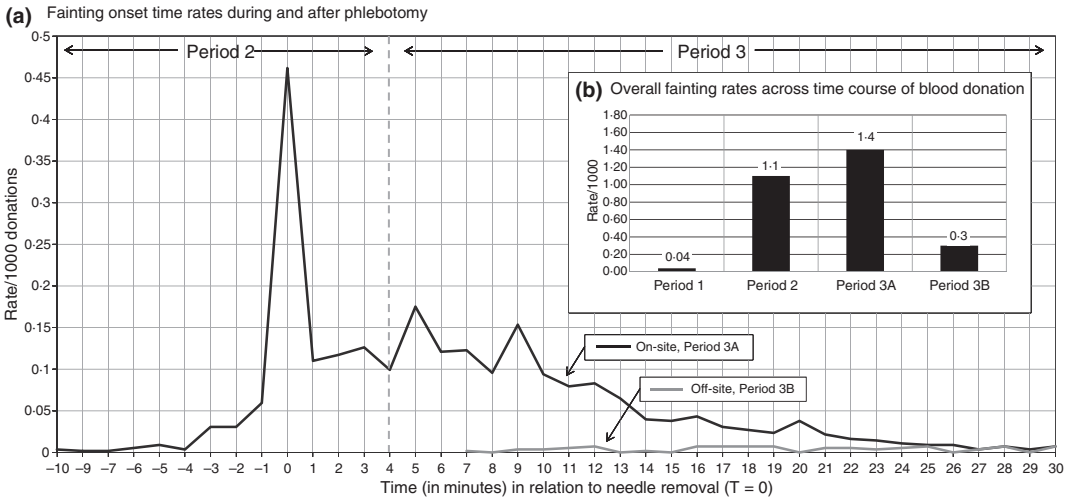

Fig. 1 Fainting onset time distribution and rates across time course of whole blood donation. (a) Fainting onset time rates during and after phlebotomy. (b) Overall fainting rates across time course of blood donation. Notes: Panel a includes fainting records with onset time of reactions, n = 1482; >30 min not shown, maximum fainting onset time: on-site = 160 min and off-site = 265 min. Panel b includes all fainting records, n = 1520, with missing onset time classified accordingly based on location of reaction and other record information.

Table 2 Comparing predictors of fainting across time course of blood donation, 2007 data

	Onset time of event			
	Period 1 Registration	**Period 2 Phlebotomy**	**Period 3A Post-phlebotomy and on-site**	**Period 3B Post-phlebotomy and off-site**
Donation activity	Registration and medical health screening	During phlebotomy up to 4 min from tube clamping/needle removal	>4 min from tube clamping/needle removal, on-site	>4 min from tube clamping/needle removal, off-site
Most likely position	Ambulatory	Recumbent/ Semi-recumbent	Ambulatory	Ambulatory
Approach in multivariable analysis (MVA)	Predictor selection	Step-wise	Step-wise	Predictor selection
Variables used in final MVA	Age Sex Donor Status (EBV not included in final model because it was not significant)	Donation Site Age Sex Race/Ethnicity Donor Status EBV Systolic BP Collection Status Centre	Donation Site Age Race/Ethnicity Donor Status EBV Pulse Collection Status Centre	Donation Site Age Sex Donor Status EBV
Fainting	43	593	772	155
Registrations/Donations	956 766	554 534	553 941	553 169

EBV, estimated blood volume.

EBV groups: <3500, 14·1 (5·1–39·0); 3500–3999, 6·4 (2·4–17·4); 4000–4499, 5·0 (1·9–13·4). The risk of low EBV was highest in period 3B compared to other periods. Age remained significant only in those <23 y/o; 17–18, 2·5 (1·7–3·8) and 19–22, 1·9 (1·1–3·2). First-time donors had a higher risk as well, 1·5 (1·0–2·1).

Injury and outside medical care

Of the 43 LOC events in Period 1, two male donors were injured and one male and one female donor needed OMC (Table 3). Of the 1520 LOC events occurring during and after donation (Period 2 and 3), 73 (20 men and 53 women)

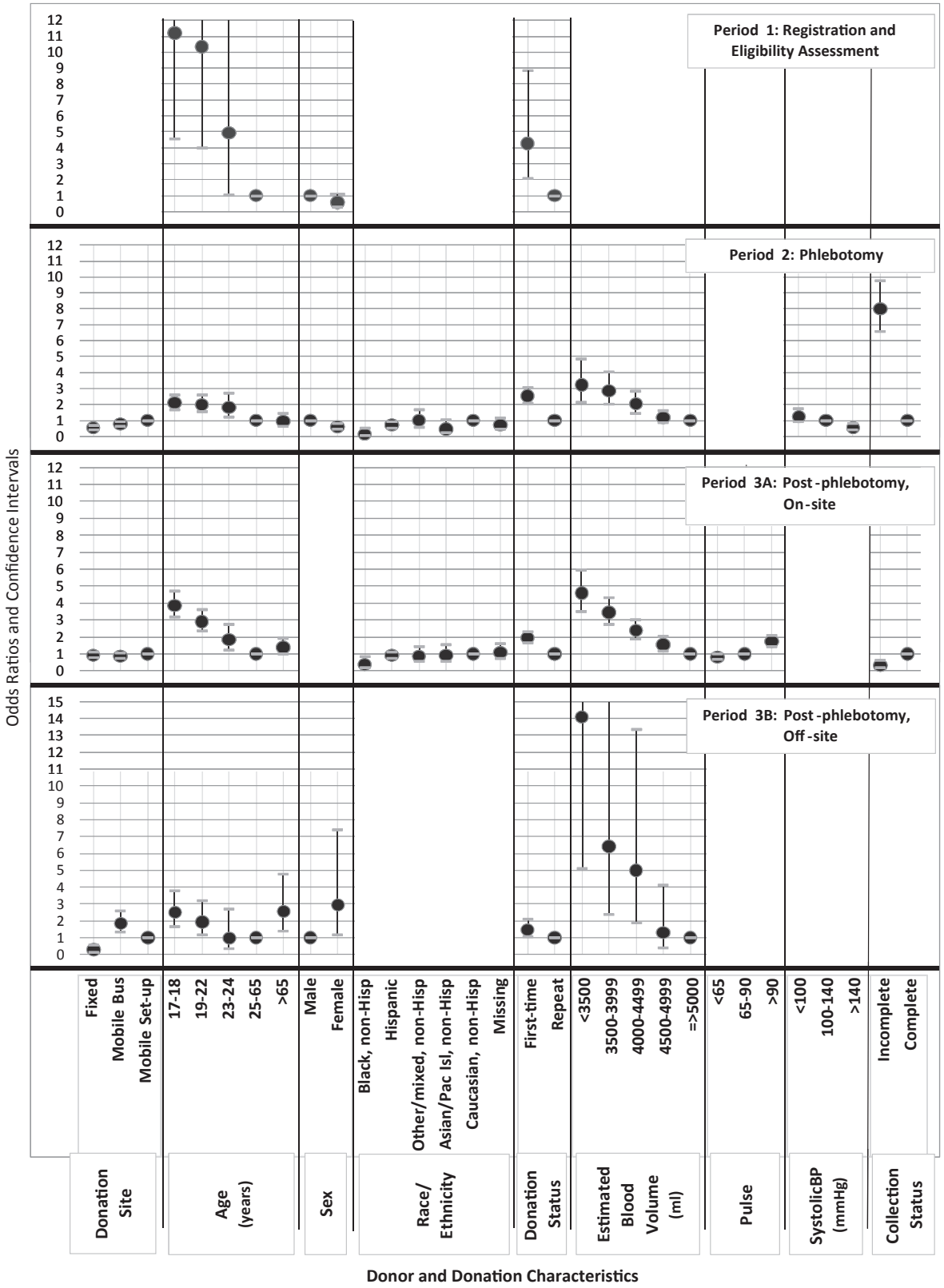

Fig. 2 Multivariable analyses of factors associated with fainting – before, during and after whole blood donation.

Table 3 Injury and OMC, by gender, associated with fainting reactions

	Period 1				Period 2				Period 3A				Period 3B			
	Male *N* = 453 240		Female *N* = 503 526		Male *N* = 227 351		Female *N* = 327 183		Male *N* = 227 167		Female *N* = 326 774		Male *N* = 227 013		Female *N* = 326 156	
	Number	Rate[a]	Number	Rate[a]	Number	Rate[a]	Number	Rate[a]	Number	Rate[a]	Number	Rate[a]	Number	Rate[a]	Number	Rate[a]
Fainting	26	0·06	17	0·03	184	0·81	409	1·25	154	0·68	618	1·89	8	0·04	147	0·45
Injury	2	0·004	0	0·00	3	0·01	7	0·02	17	0·07	30	0·09	0	0·00	16	0·05
OMC	1	0·002	1	0·002	7	0·03	30	0·09	19	0·08	62	0·19	5	0·02	40	0·12
Injury (% of all fainting)	7·7		0·0		1·6		1·7		11·0		4·9		0·0		10·9	
OMC (% of all fainting)	3·8		5·9		3·8		7·3		12·3		10·0		62·5		27·2	

OMC, outside medical care

[a]Rate is expressed as number of events per 1000 registration in Period 1 and per 1000 donations in Periods 2 and 3.

donors were injured and 163 (31 men and 132 women) required OMC. The rate of injury for men and women combined in Period 1 is extremely low (2 per million donor registration). The injury rate was low in male and female donors in recumbent/semi recumbent position, Period 2 (0·01 and 0·02 per 1000 donations respectively). The highest injury rate is seen in Period 3A (0·07 and 0·09/1000 donations for male and female donors, respectively). When considering only those donations in which LOC occurred, the total rate of injury per fainting reaction was lowest during Period 2, increased in Period 1 and 3A and peaked in Period 3B.

Discussion

Blood donors are subjected to psychological and haemodynamic challenges during the blood donation process. During the study period, 94% of injuries observed/reported, in association with vasovagal reactions, occurred in donors who experienced LOC. Our data show variation in factors associated with fainting across different periods and suggest variation in underlying mechanisms leading to LOC. It is possible that period-specific interventions may be useful in reducing fainting reactions that might lead to injury.

During Period 1 (registration and screening), the donor is walking or sitting. The data suggest the risk factors to be mainly demographic characteristics of donors; young age and first-time status and the stimuli for fainting may be primarily psychological. During Period 1, the donors' blood volume does not change and the only procedures experienced by the donors are the interview, the vital signs and a finger stick to determine haemoglobin level. During phlebotomy (Period 2), the strong association of incomplete donation status with LOC may reflect the fact that the reaction prompted the discontinuation of the donation process. The most important donor factor associated with LOC is small EBV. This is consistent with the fact that the majority of LOC events during this period occur at the time of needle removal (Fig. 1), suggesting relative hypovolemia as a contributing factor. In addition, first-time donor status and young age are also significant predictors of LOC. Donors who faint in the recumbent position have lower potential for injury.

At the beginning of Period 3A, the donor's posture changes from recumbent to upright. The time course shows two peaks of LOC events at 5 and 9 min after the time of needle removal. We believe that the peak at $T = 5$ represents fainting occurring at the time the donor leaves the donor chair and that at $T = 9$ occurs as the donor is ambulating in the refreshment area. Young age, small EBV and first-time donor status are the main factors associated with fainting during this period. Of note, donors with a Predonation pulse >90 beats per minute and donors older than 65 years of age were also at significantly higher risk of fainting. Events during this period show the highest rate/donation of donor injuries and need for OMC. In Period 3A, the rate of injury and OMC per 100 fainting events was higher than in Period 2.

Ten per cent of fainting episodes associated with whole blood donations occurred off-site (Period 3B). Low EBV, female gender, younger age and first-time donor status are the characteristics associated with higher risk. This group has a higher ratio of injury risk/LOC event possibly due to the fact that LOC occurs outside the area of staff observation. It is also possible that the more serious events requiring OMC are disproportionately reported to the blood centre.

Period 2, when the donor is recumbent, has a lower male and female rate of injury per LOC reaction and a lower rate

of injury per donation than Period 3A and 3B. The potential for injury is likely to be lower if the donor reacts while recumbent. Period 3A shows a higher ratio of rate/donation for injury and OMC compared to other periods which may be attributed to the upright posture at this stage in the donation process. An interesting finding of this study is that the risk of LOC reaction was lower in Periods 2, 3A and 3B for donations that occurred at fixed sites vs. donations occurring on buses or at mobile, inside set-ups (Table 1 and Fig. 1). While it is more likely that older and repeat donors attend fixed site donation clinics leading to lower reaction rates, this lower risk was apparent in the multivariable analysis that controlled for these characteristics as well as in the rate analysis. A point of future investigation may be the donor's position during donation. The elevation of the donor's head, pelvis, knees and feet in relation to the position of the donor's heart varies with the chairs or beds used for donation and there can be different impacts on donor blood volume related to body position. Body position during donation may influence the delayed reaction rate.

There was wide and statistically significant variation in the rate of fainting reactions among the 15 UBS blood centres (Data not shown). In the multivariable analyses, the blood centre was a consistent risk factor, with some centres having low while others had high risks for LOC reaction. Results showed a significantly decreased risk of reaction across various centres compared to the reference centre in the logistic regression analyses (the centre with the largest number of donations). In previous studies, rates of donor adverse events varied significantly among blood centres that use standardized training, procedures and classification systems [2,3]. The cause of this variation is unknown and will continue to present a challenge in interpreting data as blood collection facilities participate in donor vigilance systems. There may be other confounding factors for which we have not collected data and which we have not included in the models. Further research is needed.

Limitations to our analysis include the likelihood that while changes in position play a role in creating risk of fainting reactions, no record was made of donor position at the time of reaction or the time the donor stood up. Conclusions about position were based on timing and on operational procedures. In addition, there were missing data elements and specifically there were a small number of records with no time for the onset of the reaction. However, for all these reactions we were able to determine the location. We also are unable to confirm with precision, the recording of the reaction onset times. All the reactions recorded for Period 3B were not observed by staff and were voluntarily reported. Under-reporting of off-site reactions is possible [10,11]. While we focused on fainting which should be consistently reported because it is clinically apparent, we cannot be sure that all LOC events were reported. The decision to utilize OMC was not consistent. Blood centre staff participated in the decision to call for help or to refer a donor to the emergency room when reactions occurred on-site, but when reactions occurred off-site, the use of OMC was likely to be inconsistent. For Periods 1 and 3B, due to the small number of events in these two groups, multivariable analysis was limited to a selected group of variables known to have an impact on VVS, it was not possible to replicate the same multivariable model building procedures as we did in Periods 2 and 3A.

Summary

This study shows that the rates of fainting reactions are not consistent and that the risk factors associated with such reactions are not the same across the time course of blood donation. A key finding of this study is that while donor age and experience are constant risk factors in all periods, higher per cent blood volume donated (based on a fixed donation volume and lower corporeal EBV) and gender are not risk factors before phlebotomy. High per cent EBV donated increases in significance as time passes after the end of phlebotomy. This suggests that low EBV donors, who give a greater per cent of their blood volumes, are at greater risk of reactions which occur when they are upright and which could lead to injury. Reducing the risk of injury from fainting reactions which occur after blood donation may be accomplished by preventing the impact of relative hypovolemia which results from donation.

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