Short Term Health Outcomes Following Whole Blood Donation: A Nationwide, Retrospective Cohort Study

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Abstract

Background: Blood donation is associated with a number of adverse events. Most of these are both uncommon and non-severe, leading to mild discomfort for the donor at worst. However, adverse events occurring outside of the donation facility have largely not been studied. In this study, we aim to further the understanding by performing the first large-scale analysis of short-term risks following whole blood donation.

Methods: We set up a nationwide cohort of donors who donated whole blood between 1987 and 2018. Analyses were conducted using conditional logistic regression in a self-comparison design, where each donor was compared only to themselves, considering the 30-day risk of 16 outcomes following whole blood donation. Outcomes included cardiac/vascular diseases such as myocardial infarction, unspecified conditions such as fainting, accidents or external causes of injury, and death.

Results: A total of 963,311 donors were included, 19,670 of whom experienced at least one of the outcomes within 30 days of a blood donation. For fainting and hypotonia we observed transient 2 to 5-fold risk increases on the day of donation and the subsequent 2–3 days. Importantly, the risk increase for the most pronounced effect corresponded to less than 1 additional events of fainting per 200,000 blood donations. Risks of all other outcomes were either unaffected or lower than expected right after blood donation.

Discussion: To conclude, we found no evidence of new or unexpected short-term health effects after blood donation and confirmed that risks of hypotension-related events requiring hospital care are present but small.

1 | INTRODUCTION

Access to safe blood products is paramount for the practice of modern medicine. While transfusions can clearly be life-saving for the recipient, blood donation exposes the donor to small, but non-negligible risks. Given the voluntary nature of blood donation it is imperative to minimize associated risks and to allow donors to make informed decisions prior to participation.

Acute adverse events occurring at the donation facility are well described, and are mostly non-severe such as vasovagal reactions – occasionally followed by subsequent fall injuries – or local nerve injuries and hematomas. Notably though, not all adverse events occur in direct

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conjunction with the donation, and there is likely substantial underreporting. It is inherently difficult to
determine whether an illness or injury was indeed caused 
by the donation or if it simply happened to coincide. For 
example, a myocardial infarction occurring in the days after a blood donation could, for example, be a consequence of the rheological changes caused by the temporary reduction in red cell mass and hypovolemia, but could also be an event bound to take place independent of the donation. The problem of studying health effects of blood donation is further exacerbated by the so-called "healthy donor effect". This effect is caused by the fact that self-perceived good health is a prerequisite for enrolling as a donor, and by the careful exclusion of donors with certain medical conditions or symptoms, as well as donors engaging in behavior entailing risk to blood recipients.

The lack of systematic short- and long-term follow-up, and the healthy donor effect has resulted in uncertainty regarding adverse effects not evident in direct conjunction with the donation procedure. Furthermore, the lack of scale and dependence of self-reporting has hampered the opportunity to capture possibly significant but rare events. In light of more than 110 million blood units being donated each year, the uncertainty about donor risk is problematic. In this study we aim to further the understanding by performing the first large-scale, population-based analysis of short-term risks of a range of health outcomes following whole blood donation.

2 METHODS AND MATERIALS

2.1 Data sources

The study was based on the Swedish portion of the third iteration of the Scandinavian Donations and Transfusions (SCANDAT3-S) database. In brief, the database contains all electronically available data on blood donors, donations, components, transfusions, and transfused patients, dating back to the late 1960s and with nationwide coverage since the mid-1990s. Through linkage with a range of nationwide health data registers, capturing data on all hospital-based in- and outpatient care, as well as all causes of death, both donors and transfused patients can be followed for a range of health outcomes, irrespective of where and when they occurred. For details about the SCANDAT3-S database, see previous publications.

2.2 Setting

The Swedish blood collection centers are part of the public health care system, and regulated nationally by laws set forth by the Swedish Board of Health and Welfare. As with the health care system, the blood collection centers are organized independently by autonomous regions, which may leave room for slightly different regional adaptations within the bounds of national guidelines.

In Sweden, blood donation is voluntary and performed without financial incentives. Healthy individuals ≥18 years and ≥50 kg may be considered for blood donation, but notably a number of additional requirements are enforced to ensure donor and recipient safety. To ensure donor safety, donors need to be free of severe medical conditions and without pharmaceutical treatment that may increase donation associated risk. Further, an hemoglobin concentration ≥125 g/L for women and ≥135 g/L for men is required. During the study period pulse and blood pressure were assessed at the initial visit, and blood pressure thereafter yearly for donors >40 years of age. Arrhythmia or a systolic blood pressure >180 mmHg precluded donation. Donors >65 years of age needed an additional yearly assessment by the blood center medical doctor.

Donors were instructed to be well hydrated and non-fasting upon arrival and were advised to refrain from strenuous exercise 24 hours post donation. Many centers recommended inexperienced donors to remain at the donation facility for at least 15 minutes, post donation. A light meal/snack and non-alcoholic beverages were commonly offered.

The maximum donation frequency was 3 times yearly for women and 4 times yearly for men.

2.3 Outcomes

Outcomes were based on data from the Swedish Patient Register, which is nationally complete since 1987 for inpatient care and since 2001 for hospital-based specialist outpatient care. Coverage for the latter was initially incomplete, but has increased over time. A priori, we decided to study the occurrence of 16 diagnoses of which the risks were hypothesized to be potentially affected by whole blood donation. Selection of outcome groups was based on known risks associated with blood donation as well as mechanistically plausible outcomes, i.e. we hypothesized that the temporary reduction in blood volume, through rheological as well as oxygen carrying capacity pathways, may transiently impact risk of vascular symptoms and outcomes such as angina, myocardial infarction and stroke. Outcome classification was based on diagnoses, coded according to the international classification of disease (ICD), revisions 9 and 10, and included cardiac/vascular conditions (angina, myocardial infarction, atrial fibrillation/flutter, other tachycardias, cerebrovascular stroke, cerebral hemorrhage, and thrombophlebitis), unspecified conditions/symptoms (other
unspecified chest pain, unspecified palpitations, hypotonia, and fainting), accidents or external causes of injury (falls, unspecified/multiple trauma, other unspecified injuries, and motor vehicle accidents). Deaths were ascertained from the Swedish Cause of Death Register. For details about classification, see Supplementary Table 1.

2.4 Study design and statistical analyses

The analyses were based on a cohort of all donors who were recorded to have donated whole blood at least once between January 1st, 1987 and December 31st, 2017. Donors were followed from the time of each whole blood donation for a maximum of 30 days, or until the first occurrence of any of the 16 outcomes, emigration, or end of follow-up (December 31st, 2017), whichever occurred first. A 30-day follow-up was chosen as a compromise between having a short period (where events would have at least some likelihood of having been caused by the donation) and a longer period (to ensure that there would be some follow-up that was not affected by the donation). Donors with multiple donations were thus included in the analyses with multiple follow-up segments. To study the association between time of whole blood donation and the risk of each outcome, we employed a self-controlled study design where each donor served as their own control 17,18. The analysis for each outcome was thus restricted to donors who experienced that outcome within 30 days of any of their donations, i.e. during one of their follow-up segments. Donors who experienced the first event, of each type, more than 30 days after their most recent donation were excluded.

The statistical analyses were conducted using pooled conditional logistic regression, treating each day of follow-up as a separate observation. Ensuing odds ratios were thus estimates of hazard (incidence rate) ratios 19. In this instance, the models effectively investigate the temporal distribution of events, to test whether events were more likely to occur right after a blood donation than later during follow-up. By treating each donor as a separate stratum in the models, all comparisons were done within subjects, rather than between unrelated individuals, thus removing confounding effects from factors that are either fixed (e.g. sex, and genotype), or that change only slowly (e.g., many chronic conditions and age). This self-controlled design can be viewed as a generalization of the well-known case-crossover design, to scenarios with more than two exposure levels 20. We note that the self-controlled design does not remove confounding effects from factors that change more rapidly, such as current health state or from risk behaviors which may differ from day to day.

The exposure of interest in the analyses was time since most recent whole blood donation which was assessed both as a categorical variable (categorized as day 0–1, day 2–3, day 4–6, day 7–13, and day 14–30, with day 7–13 set as the reference) and as a continuous variable modelled with a restricted cubic spline with 3 degrees of freedom. In addition, models included categorical terms for day of week, calendar month and a binary term for public holidays (including Christmas, New Year's Eve and New Year's Day, Easter, as well as Midsummer). Robust standard errors were used to generate 95% confidence limits. For outcomes with a clear risk increase in the first days after a blood donation, we estimated incidence rate differences by multiplying odds ratio estimates for each follow-up period, from the categorical analyses, with the event rate in the reference period (i.e. days 7–13) and subtracting from this product the event rate in the reference period. This yielded incidence rate differences comparing each follow-up period compared with the reference period. These risk differences were also accumulated across the full 30-day follow-up after a blood donation. Confidence limits for risk differences and cumulative risk differences were constructed using a bootstrap approach, with 1000 resamples.

Because blood donations are almost exclusively done during office hours, follow-up on the day of donation would be shorter and as such the probability of becoming ill and admitted to hospital would be lower. To account for this problem, the conditional logistic regression analyses were set up to incorporate weights, which were calculated as the inverse of the time, measured in fractions of a day, from the blood donation until midnight on that day. To exemplify, for a donor who donated blood at noon (12.00 AM), 0.5 days of follow-up remained on that day, whereby that day of follow-up was assigned a weight of 2. Full follow-up days were assigned a weight of 1. Missing values for exact time of blood donation (39%) were replaced with mean time of other donations at that day. All data processing was done using SAS, version 9.4 (SAS Institute, Cary, NC, USA). Statistical analyses were done with R version 4.0.3 (R Foundation, Vienna, Austria). The conduct of this study was approved by the regional ethics committee in Stockholm, Sweden.

3 RESULTS

A total of 963,311 donors were included in the analyses. Of these, 19,670 experienced a total of 28,432 events.
Characteristics of the study population are presented in Table 1. Donors with events were less frequently female (31.9 vs. 48.3%), were older at the time of their first donation (median age 35.1 vs. 30.7 years) and had a larger number of donations (median 27 vs. 7), as compared to donors without events.

Details of observed events are presented in Table 2. Different types of injuries and accidents constituted the most frequent types of events, with 14,429 donors sustaining Other unspecified injuries, 6114 seeking medical care for Falls and 2591 seeking medical care after Motor vehicle accidents. The proportion of donors with events who were women varied considerably between types of events, from 13.6% for Myocardial infarction to 43.8% for Hypotonia. The temporal distribution of events was conspicuous, with most types of events only occurring very rarely in the first days after the most recent donation. There were two clear exceptions, with a higher proportion of events occurring early on, with 16.0 and 6.3% of donors experiencing Fainting and Hypotonia receiving their diagnosis on the day of donation, respectively. Of the 74 donors with a hospital diagnosis of Fainting on or the day after a blood donation, 36 (49%) had performed 1–10 donations, 19 (26%) had performed 10–19 donations, and 19 (26%) had performed 20 or more donations. Furthermore, 39 (53%) were female, and the median age was 42 years (IQR, 28–56).

When fitted in a conditional logistic regression model, comparing each donor only to themselves, these data resulted in statistically significantly elevated risks early on after whole blood donation for Fainting, with odds ratios of 4.8 (95% confidence interval [CI], 3.2–7.3) and 3.0 (95% CI, 1.8–4.8) on day 0 and day 1, as compared to days 7–13. A similar pattern was observed for hypotonia, however with no statistically significantly elevated risks on day 0 and 1, and an odds ratio of 3.4 (95% CI, 1.1–9.9) for days 2–3, as compared to days 7–13. Again, statistically significantly lower risks were seen on days 0 and/or 1 for a range of outcomes,
## Table 2

Details about observed events in donor population

| Outcome                      | Number of donors with event | Number of women (%) | Number of donations, median (IQR) | Age at time of event, median (IQR) | Timing of event, in relation to most recent donation, N (%) |
|------------------------------|-----------------------------|---------------------|-----------------------------------|------------------------------------|----------------------------------------------------------|
|                              | Number                      | %                   | Median (IQR)                      | Median (IQR)                       | Day 0 | Day 1 | Day 2–3 | Day 4–6 | Day 7–13 | Day 14–30 |
| **Cardiac/vascular conditions** |                             |                     |                                   |                                    |      |      |        |         |          |            |
| Angina                       | 458                         | 82 (17.9)           | 28 (13–51)                       | 58 (51–62)                         | 13 (2.8) | 8 (1.7) | 17 (3.7) | 57 (12.4) | 109 (23.8) | 254 (55.5) |
| Myocardial infarction        | 601                         | 82 (13.6)           | 35 (17–54)                       | 58 (53–63)                         | 13 (2.2) | 16 (2.7) | 48 (8.0) | 85 (14.1) | 159 (26.5) | 280 (46.6) |
| Atrial fibrillation/flutter  | 709                         | 104 (14.7)          | 27 (11–49)                       | 57 (49–62)                         | 32 (4.5) | 33 (4.7) | 53 (7.5) | 76 (10.7) | 177 (25.0) | 338 (47.7) |
| Other tachycardias           | 254                         | 90 (35.4)           | 18 (7–37)                        | 50 (39–57)                         | 9 (3.5)  | 8 (3.1)  | 19 (7.5) | 27 (10.6) | 47 (18.5)  | 144 (56.7) |
| Cerebrovascular stroke       | 351                         | 78 (22.2)           | 29 (12–51)                       | 57 (51–63)                         | 6 (1.7)  | 10 (2.8) | 24 (6.8) | 41 (1.7)  | 80 (22.8)  | 190 (54.1) |
| Cerebral hemorrhage          | 36                          | 10 (27.8)           | 20 (9–35)                        | 58 (49–62)                         | 0 (0.0)  | 1 (2.8)  | 3 (8.3)  | 4 (11.1)  | 4 (11.1)   | 24 (66.7)  |
| Thrombophlebitis             | 572                         | 196 (34.3)          | 22 (9–41)                        | 52 (43–59)                         | 4 (0.7)  | 7 (1.2)  | 25 (4.4) | 47 (8.2)  | 133 (23.3) | 356 (62.2) |
| **Unspecified conditions/symptoms** |                         |                     |                                   |                                    |      |      |        |         |          |            |
| Unspecified chest pain       | 717                         | 210 (29.3)          | 15 (7–31)                        | 51 (45–57)                         | 18 (2.5) | 29 (4.0) | 33 (4.6) | 83 (11.6) | 201 (28.0) | 353 (49.2) |
| Unspecified palpitations     | 136                         | 58 (42.6)           | 23 (9–42)                        | 54 (44–61)                         | 7 (5.1)  | 1 (0.7)  | 12 (8.8) | 15 (11.0) | 37 (27.2)  | 64 (47.1)  |
| Hypotonia                    | 32                          | 14 (43.8)           | 19 (6–42)                        | 50 (39–60)                         | 2 (6.3)  | 2 (6.3)  | 7 (21.9) | 2 (6.3)   | 7 (21.9)   | 12 (37.5)  |
| Fainting                     | 306                         | 113 (36.9)          | 16 (6–34)                        | 47 (35–57)                         | 49 (16.0) | 25 (8.2) | 27 (8.8) | 23 (7.5)  | 56 (18.3)  | 126 (41.2) |
| **Accidents and external causes of injury** |                         |                     |                                   |                                    |      |      |        |         |          |            |
| Falls                        | 6114                        | 2383 (39.0)         | 17 (6–35)                        | 46 (33–55)                         | 150 (2.5) | 171 (2.8) | 375 (6.1) | 626 (10.2) | 1442 (23.6) | 3350 (54.8) |
| Unspecified/multiple trauma  | 808                         | 248 (30.7)          | 13 (5–28)                        | 40 (29–50)                         | 19 (2.4) | 17 (2.1) | 44 (5.4) | 104 (12.9) | 164 (20.3) | 460 (56.9) |
| Motor vehicle accidents      | 2591                        | 930 (35.9)          | 14 (5–30)                        | 42 (30–52)                         | 51 (2.0) | 100 (3.9) | 186 (7.2) | 249 (9.6) | 577 (22.3) | 1428 (55.1) |
| Other unspecified injuries   | 14,429                      | 4910 (34.0)         | 13 (4–30)                        | 43 (31–53)                         | 327 (2.3) | 437 (3.0) | 917 (6.4) | 1406 (9.7) | 3507 (24.3) | 7835 (54.3) |
| **Other**                    |                             |                     |                                   |                                    |      |      |        |         |          |            |
| All-cause mortality          | 318                         | 47 (14.8)           | 19 (7–36)                        | 50 (41–57)                         | 2 (0.6)  | 15 (4.7) | 19 (6.0) | 32 (10.1) | 59 (18.6)  | 191 (60.1) |
Estimates of odds ratios for association between time since most recent donation and risk of each outcome

![Image of a table showing estimates of odds ratios for association between time since most recent donation and risk of each outcome. The table includes columns for Day 0, Day 1, Day 2–3, Day 4–6, Day 7–13, and Day 14–30, with rows for different outcomes such as Cardiac/vascular conditions, Unspecified conditions/symptoms, Accidents and external causes of injury, and Other.](image)

including angina, thrombophlebitis, unspecified chest pain, as well as all different types of accidents and external causes of injury. For details, see Table 3. Estimates from categorical analyses not incorporating weights are presented in Supplementary Table 2. Overall, effects were very similar to the analyses presented in Table 3.

When the conditional logistic regression analyses were repeated with time since most recent donation fitted instead as a restricted cubic spline function, the pattern of low risk early after whole blood donation, and thereafter increasing risk, was again evident (Figure 1). As in the categorical analyses, the same two exceptions analyses were observed, i.e. for the occurrence of fainting (panel K) and to some extent also for hypotonia (panel J), though the trend was less clear for the latter on account of small number of events.

Lastly, the estimated cumulative incidence difference of needing hospital care for Fainting after donating blood was 0.43 per 100,000 donations (95% CI, 0.1–0.7). On the day of the donation and the day after, the risk differences were 0.23 (95% CI, 0.14–0.33) and 0.12 (95% CI, 0.05–0.20) events per 100,000 donations.

### DISCUSSION

In this nationwide, retrospective cohort study with complete ascertainment of disease outcomes for more than 1 million blood donors over a 30-year period, we describe for the first time occurrence of short-term health risks in the 30 days following a whole blood donation. Overall, the observed patterns were largely the expected, with increased risks only seen for fainting and hypotension outcomes likely related to transient hypovolemia or vasovagal reactions, which have been well-described previously. Of note, effect sizes were modest and rapidly returned to baseline levels. We found no evidence of increased risks of more severe adverse outcomes among those selected a priori. Indeed, the pattern was rather the opposite, with risks of the more severe outcomes being at their very lowest right after donating blood and thereafter increasing gradually.

Overall, findings were quite consistent and although we only observed a comparatively small number of events for some of the investigated outcomes, risk estimates were generally sufficiently precise to rule out even small excess risks associated with whole blood donation.
For example, we only observed 2 deaths on the day of donation during the entire study period. Notable strengths of the investigation include the reliance on prospectively collected, high quality register data, and the use of state-of-the art statistical methods, whereby donors serve as controls only to themselves, thus reducing confounding from factors that stay constant or change only slowly. Still, as is evident in Figure 1, for most outcomes we observe a striking pattern of low risk right after donating blood, which then increases gradually. We do not

FIGURE 1 presents the odds ratio of each respective outcome in relation to the number of days passed since the most recent whole blood donation. The shaded areas represent 95% confidence intervals [Color figure can be viewed at wileyonlinelibrary.com]
think this should be interpreted as being driven by beneficial effects of donating blood. Instead, in our view, a more plausible interpretation is that this pattern is driven by the combination of eligibility criteria for donating blood (i.e. that the donor needs to be healthy at the time of donation), and donor self-selection (i.e. that donors will be less likely to donate blood when they feel ill). As such, the observed pattern is a manifestation of the healthy donor effect, which was clearly not fully removed by the use of a design where donors were only compared to themselves and thus remain partly unaccounted for. Consequently, the main limitation of our analyses is the possibility that possible deleterious health effects of donating whole blood were masked by the fact that donors were self-selected to be particularly healthy at the time of donating blood. To exemplify, while we observe no statistically significantly increased risk of atrial fibrillation/flutter right after whole blood donation, with odds ratios of 0.9 and 1.1 on days 0 and 1, respectively, it is possible that the risk would have been elevated had we been able to compare to donors who also self-selected themselves to donate blood at the same time, but who didn’t donate. Still, even though this phenomenon prevents us from drawing strong, causal conclusions based on these data, such a possibility is somewhat speculative and from a pragmatic point of view, we argue that our results still serve as evidence that whole blood donation is generally very safe.

Although data quality was generally very high, there were limitations in data availability. For one, while we had the actual time of donation in most instances, the date of hospital admission or visit was only recorded by calendar date. Because this introduces an uncertainty in the follow-up time for each donor, we introduced weights in the regression model that captured the shorter follow-up time for each donor, we introduced weights. Because this introduces an uncertainty in the date of hospital admission or visit was only recorded by calendar date. Consequently, we find no evidence of new or unexpected outcomes were either unaffected or lower than expected. Furthermore, the reliance on high-quality public health care registers for outcome ascertainment should ensure that we capture events severe enough to warrant a hospital contact, as well as all deaths, it also means that we are quite likely to miss less severe but still possibly important events.

Two specific observations deserve particular mention. First, contrary to what we expected, the median number of prior donations was considerably higher among donors who experienced at least one of the studied outcomes. Although this is likely at least partly explained by the fact that donors with an event were older and more frequently male – both overall and when considering specifically outcomes, such as fainting or hypotonia – it also means that such adverse outcomes could occur among donors also after a relatively large number of donations. Hence, any efforts towards preventing such side-effects must include also experienced donors, with the caveat that our results did not include outcomes that did not lead to hospital contact. Second, we find scale of the transiently decreased risks observed right after a blood donation quite fascinating. It is perhaps unsurprising that we saw decreased risks of death and myocardial infarction, but the consistency of how risks were decreased also for external causes of injury has bearings on our understanding of donation-associated behavior. It seems to indicate that donors’ low-risk behavior – perhaps related to alcohol consumption, or other behavior which might be linked to risk of these outcomes and which donors might abstain from at the time of donating blood – extend several days after a blood donation, which must be considered both when assessing donation-associated adverse events and when conducting research into health outcomes among blood donors.

To summarize, in this nationwide retrospective cohort study of short-term risks among whole blood donors, we find excess occurrence only of fainting and hypotonia shortly after donating blood. Risks of all other outcomes were either unaffected or lower than expected. Consequently, we find no evidence of new or unexpected short-term health effects after blood donation. It should serve as a comfort to all involved in blood collection that although we did observe increased risks of hypotension...
related outcomes right after blood donation, these corresponded to very low absolute risks, indicating that the risk of harm to the individual donor is very small.

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AUTHOR CONTRIBUTIONS
FT and GE conceived the study. AS and GE designed the analyses. GE conducted the analyses. JZ and GE collected the data. FT and GE wrote the first draft. All authors contributed to the revision of the manuscript.

CONFLICTS OF INTEREST
None

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REFERENCES
1. Sorensen BS, Johnsen SP, Jorgensen J. Complications related to blood donation: a population-based study. Vox Sang. 2008; 94:132–7.
2. Zervou EK, Ziciadis K, Karabini F, Xanthi E, Chrisostomou E, Tzolou A. Vasovagal reactions in blood donors during or immediately after blood donation. Transfus Med. 2005;15:389–94.
3. Trouern-Trend JJ, Cable RG, Badon SJ, Newman BH, Popovsky MA. A case-controlled multicenter study of vasovagal reactions in blood donors: influence of sex, age, donation status, weight, blood pressure, and pulse. Transfusion. 1999;39:316–20.
4. Newman BH. Vasovagal reaction rates and body weight: findings in high- and low-risk populations. Transfusion. 2003;43: 1084–8.
5. Sultan S, Baig MA, Irfan SM, Ahmed SI, Hasan SF. Adverse Reactions in Allogeneic Blood Donors: A Tertiary Care Experience from a Developing Country. Oman Med J. 2016;31:124–8.
6. Narbey D, Fillet AM, Jbilou S, Tiberghien P, Djoudi R. Case-control study of immediate and delayed vasovagal reactions in blood donors. Vox Sang. 2016;111:257–65.
7. Meena M, Jindal T. Complications associated with blood donations in a blood bank at an Indian tertiary care hospital. J Clin Diagn Res. 2014;8:JC05–8.
8. Newman BH, Pichette S, Pichette D, Dzaka E. Adverse effects in blood donors after whole-blood donation: a study of 1000 blood donors interviewed 3 weeks after whole-blood donation. Transfusion. 2003;43:598–603.
9. Amrein K, Valentin A, Lanzer G, Drexler C. Adverse events and safety issues in blood donation—a comprehensive review. Blood Rev. 2012;26:33–42.
10. Newman BH, Waxman DA. Blood donation-related neurologic needle injury: evaluation of 2 years’ worth of data from a large blood center. Transfusion. 1996;36:213–5.
11. Kamel H, Tomasulo P, Bravo M, Wilibank T, Cusick R, James RC, et al. Delayed adverse reactions to blood donation. Transfusion. 2010;50:556–65.
12. Atsma F, de Vegt F. The healthy donor effect: a matter of selection bias and confounding. Transfusion. 2011;51:1883–5.
13. The 2016 global status report on blood safety and availability. Geneva: World Health Organization; 2017.
14. Zhao J, Rostgaard K, Hjalgrim H, Edgren G. The Swedish Scandinavian donations and transfusions database (SCANDAT3-S) - 50 years of donor and recipient follow-up. Transfusion. 2020;60: 3019–27.
15. Zhao J, Dahlen T, Brynolf A, Edgren G. Risk of hematological malignancy in blood donors: A nationwide cohort study. Transfusion. 2020;60:2591–96.
16. Ludvigsson JF, Andersson E, Ekbom A, Feychting M, Kim JL, Reuterwall C, et al. External review and validation of the Swedish national inpatient register. BMC Public Health. 2011;11:450.
17. Hultcrantz M, Modlita B, Vasan SK, Sjolander A, Rostgaard K, Landgren O, et al. Hemoglobin concentration and risk of arterial and venous thrombosis in 1.5 million Swedish and Danish blood donors. Thromb Res. 2020;186:86–92.
18. Allison PD. Fixed effects regression models. Los Angeles: SAGE; 2009.
19. D’Agostino RB, Lee ML, Belanger AJ, Cupples LA, Anderson K, Kannel WB. Relation of pooled logistic regression to time dependent Cox regression analysis: the Framingham Heart Study. Stat Med. 1990;9:1501–15.
20. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. Am J Epidemiol. 1991;133:144–53.

SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of this article.

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