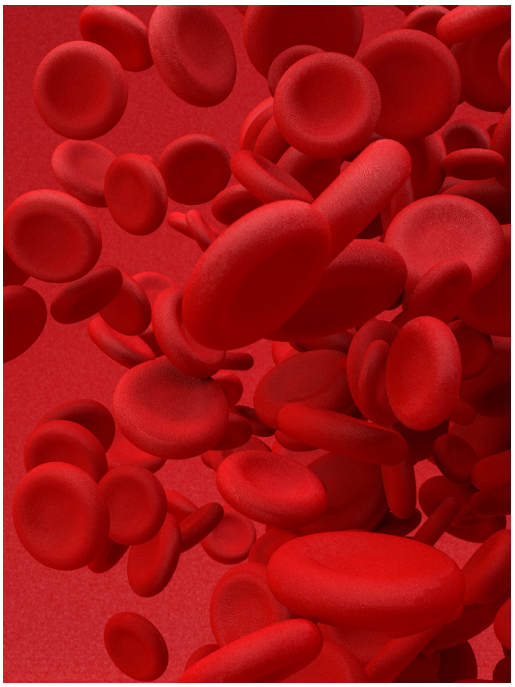

Beyond the iron gate: Therapeutic donation at Lifeblood for patients with haemochromatosis

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Background and objective
Australian Red Cross Lifeblood (Lifeblood) provides therapeutic venesection for patients who meet evidence-based eligibility criteria. Many of these patients have iron overload due to hereditary haemochromatosis (HHC). This study aimed to gain knowledge into the demographic characteristics of donors with haemochromatosis and to investigate their knowledge, compliance and experiences with their condition.

Methods
An online survey was sent to therapeutic donors who had provided at least one donation in the five years prior to December 2022. Data were analysed using descriptive statistics.

Results
HHC donors self-reported high compliance with their prescribed venesection schedules. They reported being very knowledgeable about HHC, with most attending Lifeblood as they know their blood will be used. Further, they reported their doctor had little difficulty referring them to Lifeblood.

Discussion
These findings will enable the development of more tailored communications with therapeutic donors to enhance their donation experience and potentially improve treatment compliance.

THERAPEUTIC VENESECTION is considered first-line treatment for patients with iron overload.[1] Although there are several genetic disorders that might lead to iron accumulation, clinically significant haemochromatosis is predominately associated with C282Y homozygosity. Treatment reduces symptoms associated with iron overload, such as fatigue, and improves cognition. It also reduces organ damage from iron accumulation, particularly in the liver.

Australian Red Cross Lifeblood (Lifeblood) provides a referral-based therapeutic venesection program. Doctors can refer their patients electronically using the High Ferritin App,[2] and venesections are performed at Lifeblood donor centres. Doctors continue to manage their patients' condition and adjust venesection schedules as required.

Acceptance into the Lifeblood therapeutic program requires evidence of C282Y homozygosity or C282Y/H63D compound heterozygosity combined with elevated ferritin levels. Individual assessment of patients without these genetic variants is also possible if they have evidence, from FerriScan® or a liver biopsy, of iron overload. Additional screening questions regarding general health are asked to determine if a patient is suitable to donate blood, noting Lifeblood centres do not have onsite doctors. Lifeblood is committed to donor wellbeing and all donors are assessed to ensure that donation in a Lifeblood facility is safe. Therapeutic donors who fall outside Lifeblood's guidelines are referred back to their doctor who can arrange venesection elsewhere. Examples where this might occur include donors who have experienced previous cerebrovascular accident and heart failure.

Blood donated by therapeutic donors is used to manufacture blood products for the Australian community if the donor is eligible (>80% of donations). Where recipient safety risks exist, hereditary haemochromatosis (HHC) donors might still undergo venesection and Lifeblood can discard these collections. For example, malaria area exposure precludes clinical use of collected red cells until a negative antibody test is obtained 120 days after exposure. HHC donors can continue to donate in this period but their red cells will not be used clinically.

During the de-ironing or treatment phase, HHC donors are permitted to be venesected more frequently than allogeneic donors. For example, HHC donors with ferritin levels greater than 1000 µg/L can donate weekly, gradually reducing the frequency of donation until they reach an acceptable ferritin level (50–100 µg/L)[3] and then revert to three-monthly maintenance donations.

Those with high serum ferritin but without evidence of iron overload might be referred to Lifeblood as volunteer allogeneic donors provided significant causes of hyperferritinaemia have been excluded.[1] There is no evidence of clinical benefit in these cases but they can donate every three months and contribute to the supply of blood products. In contrast to HHC donors, allogeneic donors will be deferred if risk to recipient safety is identified.

Previous published data have demonstrated the safety of using products collected from haemochromatosis patients[4] and donations from therapeutic donors currently provide a significant number of usable donations annually. Enhancements to communications and other elements of the donation experience are likely to improve compliance with venesection schedules, which would benefit both the donor and the community. Some of these donors, when provided with additional information, might also be able and willing to contribute to Australian plasma requirements.

Lifeblood provides about one-third of all therapeutic venesections in Australia. Venesections occurring in other facilities (eg general practice and specialist rooms) are discarded. Therefore, improving the donor experience might encourage others to donate at Lifeblood and have their products contribute to the blood supply. Communication with referrers to ensure they are aware of Lifeblood's therapeutic program and the community benefits of their patients donating with Lifeblood is also important.

This paper reports on research conducted with the aim of gaining knowledge into the demographic characteristics and knowledge of HHC donors at Lifeblood. Specifically, this paper reports on where they donate; reasons for being investigated for HHC; knowledge of HHC; experience of donating at Lifeblood and elsewhere; compliance with prescribed venesection schedules; and the proportion of HHC donations made at Lifeblood and other providers.

Methods

Participants

All eligible HHC donors (N=17,792) at Lifeblood were emailed an invitation to complete an online survey. Donors were eligible to be invited if they were aged 18 years and older, had a valid email address and had provided at least one therapeutic donation in the last five years. Donors were excluded if they were a Lifeblood staff member.

Donors provided implied consent by clicking on the link in the survey. Approval for the study was obtained from Lifeblood's Human Research Ethics Committee (2022#30).

Survey and data capture

The survey evaluated a donor's knowledge of haemochromatosis, their self-reported compliance with their treatment regime using a modified MARS-10[5] (nine out of the 10 questions asked, and wording changed for donation; five-point scale, 1 [Always] to 5 [Never]); other facilities they had donated at; why they choose to donate at Lifeblood; and whether their general practitioner (GP) had any difficulties with the referral process. The survey is included as Appendix 1 (available online only).

The online survey and donor research records were managed using REDCap (Research Electronic Data Capture), a secure web platform supporting data capture for research studies.[6] Routinely collected Lifeblood data were extracted, including age, sex, number of prior donations, blood type and date of last donation.

Finally, publicly available Medicare item number data were extracted for the estimated number of therapeutic donations made at external providers during the 2022–23 financial year.[7] These data were compared with the number of therapeutic donations made at Lifeblood during the same period.

Statistical analysis

Statistical analyses were performed using Stata (StataCorp LLC, 2019; College Station, TX, USA). Demographic and donation characteristics were described by means (± standard deviation [SD]) for normally distributed data, medians (interquartile ranges [IQR]) for non-parametric ordinal data, and totals (percentages) for categorical data. Univariate means testing was performed to examine differences between the two identified segments (responders vs non-responders) using t tests for continuous variables and Chi-square goodness-of-fit test for frequency variables. Open-response variables were coded inductively in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) by one author and checked by a second one. Statistical significance was defined at $P<0.05$.

Results

A total of 4350 (24.4%) donors participated in the survey. Table 1 provides an overview of their characteristics.

Respondents were predominately male (62.9%) and aged 56.71 years (SD ± 12.57). Compared to non-responders, our cohort was significantly older (aged 56.71 vs 51.28 years), and more females responded (37% vs 32%). The ABO blood group distribution and geographical distribution were similar to those of the general donor panel and did not vary significantly between responders and non-responders.

The mean age of diagnosis with HHC was 51.86 years (SD ± 12.89). Diagnosis occurred through investigations due to a high iron level (53.2%), a family member being diagnosed (28%), and incidental findings (24.1%). Table 2 provides an overview of reasons why respondents were investigated for HHC.

Knowledge of haemochromatosis

Responders reported that they were knowledgeable about haemochromatosis (median: 5 (IQR: 4–6) on a seven-point scale; 7 [Very knowledgeable] to 1 [Not knowledgeable at all]), and understood the importance of venesection to remove excess iron (Median: 7 (6–7) on a seven-point scale; 7 [Very important] to 1 [Not at all important]).

Table 3 provides an overview of the sources of information responders reported using to access information about haemochromatosis. Over 72% of respondents reported their doctor as their main source of information, followed by the internet (62.7%). Only a minority did not access information (6.7%).

Table 1. Characteristics of surveyed donors

	Non-responders (n=13,442)	Responders (n=4350)	Total (N=17,792)	*P* value
Age, mean (SD)	51.28 (13.78)	56.71 (12.57)	52.61 (13.69)	<0.001
Gender, n (%)				
Male	9112 (67.8)	2736 (62.9)	11,848 (66.6)	<0.001
Female	4330 (32.2)	1614 (37.1)	5944 (33.4)	
ABO, n (%)				
A negative	777 (5.8)	251 (5.8)	1028 (5.8)	0.84
A positive	4018 (29.9)	1320 (30.3)	5338 (30.0)	
AB negative	64 (0.5)	23 (0.5)	87 (0.5)	
AB positive	349 (2.6)	108 (2.5)	457 (2.6)	
B negative	228 (1.7)	77 (1.8)	305 (1.7)	
B positive	1176 (8.7)	357 (8.2)	1533 (8.6)	
O negative	1115 (8.3)	387 (8.9)	1502 (8.4)	
O positive	5715 (42.5)	1827 (42.0)	7542 (42.4)	
State, n (%)				
ACT	453 (3.4)	147 (3.4)	600 (3.4)	0.52
NSW	3965 (29.5)	1270 (29.2)	5235 (29.4)	
NT	120 (0.9)	30 (0.7)	150 (0.8)	
Qld	2759 (20.5)	852 (19.6)	3611 (20.3)	
SA	718 (5.3)	256 (5.9)	974 (5.5)	
Tas	577 (4.3)	194 (4.5)	771 (4.3)	
Vic	3300 (24.5)	1106 (25.4)	4406 (24.8)	
WA	1550 (11.5)	495 (11.4)	2045 (11.5)	
Prior therapeutic donations made, mean (SD)	19.48 (18.69)	25.09 (21.60)	20.85 (19.59)	<0.001
Prior allogeneic donations made, mean (SD)	1.29 (4.65)	2.27 (7.95)	1.53 (5.65)	<0.001

ACT, Australian Capital Territory; Qld, Queensland; NSW, New South Wales; NT, Northern Territory; SA, South Australia; SD, standard deviation; Tas, Tasmania; Vic, Victoria; WA, Western Australia.

Only a small portion of respondents reported they were members of not-for-profit support and advocacy group, Haemochromatosis Australia (HA) (7.4%), and fewer than 2% utilised a digital application to track their ferritin level. The My Iron Manager app[8] was used more often by those who reported using an app (66.7%), followed by a Microsoft Excel spreadsheet (14.5%).

Donating at Lifeblood

One-third of responders reported previously having therapeutic venesection performed elsewhere. Of those, 42.5% reported venesections being performed at a general practice/specialist clinic, 28.9% at a public hospital, 28.5% at a pathology service and 10% at a private hospital. When asked if they would attend those providers again, the majority reported they would not (67.5%), with only 20.5% saying they would, and 12% were unsure.

Most responders reported choosing Lifeblood because their blood would be used (62.5%) or their doctor recommended it to them (48.3%). A further 17.6% reported attending as the service was free, 17.4% because they had a centre close by and 12.8% because they had previously donated blood. For the 11.2% who selected 'Other', when asked to specify, convenience and good customer service were reported as reasons.

Most responders reported that their referring doctor had no difficulty with the Lifeblood referral process (74.4%). For those who reported issues, the main reasons were difficulty completing the form (56.3%), their doctor had not heard of the High Ferritin App (26.5%) or their doctor had submitted incomplete or incorrect paperwork (19.9%).

Treatment compliance

Respondents self-reported high compliance with their venesection schedule, noting appointments were rarely missed, and that they always donated as prescribed. More than half (54%) reported they had never missed a donation appointment. Those who had missed a donation appointment cited a variety of reasons (refer to Table 4), including other commitments (8.5%), health reasons (7.7%), difficulties getting an appointment (5.3%) and distance to travel (4.9%).

Discussion

This study provides significant information regarding the Lifeblood therapeutic program and the experience and attitudes of HHC donors. Lifeblood is the single largest provider of therapeutic venesection in Australia, performing approximately one-third of all therapeutic phlebotomies. Patients who have their venesections at Lifeblood make a significant contribution to the Australian blood supply that venesections at other institutions do not.

Table 2. Reasons to be investigated for HHC

Reasons	n (%)
High iron	2315 (53.2)
Family member diagnosed	1220 (28)
Incidental findings	1048 (24.1)
Symptoms	830 (19.1)
Abnormal liver function tests	245 (5.6)
Cardiac	38 (0.9)
Diabetes	35 (0.8)

HHC, hereditary haemochromatosis.

Table 3. Sources of information about haemochromatosis

Forms of information	n (%)
My doctor	3172 (72.9)
Internet	2727 (62.7)
Support groups	276 (6.3)
Social media communities	140 (3.2)
Social circles (family, friends, etc)	50 (1.2)
Research/academic publications	40 (0.9)
Self-knowledge	36 (0.8)
Haemochromatosis Australia	22 (0.5)
Do not access information	293 (6.7)

Medicare data[7] demonstrate that approximately two-thirds of therapeutic venesection in Australia occurs outside Lifeblood (Note: Lifeblood does not bill Medicare for services). The proportion of therapeutic venesections occurring outside Lifeblood centres varies between states and territories. There is scope to further analyse why this variation exists and introduce strategies and targeted communications to both referrers and patients to reduce barriers to Lifeblood referral. There might also be state-based differences in the propensity to test for and therefore diagnose HHC, and further targeted GP education might be considered.

Table 4. Main reasons for missing a donation appointment

Reasons	n (%)
Never miss an appointment	2348 (53.98)
Other commitments (work/social/travel)[A]	370 (8.5)
Health reasons (injury/surgery)[A]	335 (7.7)
Hard to get an appointment	232 (5.3)
Distance	211 (4.9)
Bad experience donating	159 (3.7)
Iron levels[A]	162 (3.7)
Donate elsewhere	140 (3.2)
Needle fear	119 (2.7)
I forgot[A]	87 (2.0)
Doctor's advice[A]	79 (1.8)
Referral issues[A]	54 (1.2)
COVID-19[A]	42 (1.0)

[A]Re-coded from 'Other'.

Those undergoing therapeutic venesection at Lifeblood report a positive experience with 62.5% reporting they attended Lifeblood due to their blood being used. It is therefore important to ensure communications to this cohort reinforce this benefit and potentially improve their compliance overall, as well as increasing donations that Lifeblood can use to meet the national demand. Additionally, donating at Lifeblood can reduce the burden placed on other healthcare providers and it might be easier and more convenient to get an appointment. Although, there are some notable costs to donating at Lifeblood, such as the length of time in a centre, the learnings from this study are being used by Lifeblood to improve the donation experience. For example, HHC donors now have the ability to manage their own appointments via the Lifeblood donor app or online via the donor portal rather than having to telephone the Lifeblood contact centre. Further work is needed to ensure the changes made result in improved treatment compliance and donor satisfaction.

Ensuring donors with HHC are monitored and managed appropriately is primarily the responsibility of their referring doctors. However, Lifeblood is in a unique position to provide education for this group of donors. This includes advice regarding the services available from HA, which can provide support and advice to people with haemochromatosis such as how to access their electronic ferritin monitoring tool, the My Iron Manager app.[8] Table 1 has information regarding the blood group distribution in therapeutic donors. Lifeblood provides additional specific information to donors with rare blood groups to ensure they are aware of the added importance of their donations.

There is ongoing debate in the literature regarding population screening for HHC, either through ferritin testing or genetic screening.[1,9] Lifeblood has recently introduced ferritin screening in first-time whole blood donors. This initiative is designed to reduce the impact of blood donation on potential donors who have low iron stores. An additional benefit to this screening program is that it will uncover donors with high ferritin who might go on to be diagnosed with haemochromatosis.

Finally, work is well advanced in the development of a haemochromatosis patient registry. This register is being developed by a partnership that includes HA, Lifeblood, Queensland Institute of Medical Research, Edith Cowan University, Queensland University of Technology and Hunter Medical Research Institute. The register, to be known as the National Haemochromatosis Patient Register, is expected to provide treatment, testing and outcome information, and will enable data-driven research in this area.

This study had some limitations. First, the survey was designed specifically for Lifeblood donors, and while including modifications of validated measures (eg MARS-10[5]), the instrument was unvalidated and unpiloted prior to administration. In terms of respondents, there were some differences between the survey responders and non-responders with regard to age, sex and donation history. Interpreting our findings in relation to the entire therapeutic cohort must therefore be approached cautiously. In particular, compliance is likely to be higher in those who completed the survey. Further, there might be an observed social desirability bias

with responders over-reporting compliance when this might not be the case. Future work could be conducted to investigate true compliance with treatment schedules. Additionally, this study has not sought the views of therapeutic donors who donate at non-Lifeblood facilities.

Conclusion

This study provides considerable insights into how well people undergoing therapeutic venesection at Lifeblood understand their condition, their self-reported compliance and their experience and relationship with Lifeblood. Potential improvements in compliance with prescribed venesection schedules and enhanced information provision will benefit therapeutic donors considerably. Information regarding plasma donation, where this can be performed safely, in addition to maintenance therapeutic donations, is expected to encourage therapeutic donors to contribute to the plasma supply. Additionally, advice regarding HA and the support and self-management tools it can offer will allow haemochromatosis patients to manage their condition in a more informed way.

Findings from this study are currently being used by Lifeblood to help improve the donation experience for these donors, including the ability to make and manage their own appointments through Lifeblood's donor App, and the ability to donate other donation types, such as plasma, once they have finished their scheduled treatments. It is hoped that these changes will help improve compliance with their venesection schedule as well as increase feelings of being part of the Lifeblood donor community.

Finally, we hope by targeted education and communication we can encourage GPs and specialists who treat HHC to refer to Lifeblood where the blood we take to help the donor's condition can also be used to help the Australian community. Future research focusing on non-Lifeblood HHC donors and potential referring doctors could help identify barriers to donating at Lifeblood. Overcoming these barriers could lead to less wastage of valuable blood donations.

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Competing interests: None.

Funding: None.

Provenance and peer review: Not commissioned, externally peer reviewed.

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Acknowledgements

Australian governments fund Australian Red Cross Lifeblood for the provision of blood, blood products and services to the Australian community. The authors wish to acknowledge Perfecto Diaz and Glen Shuttleworth for extracting data, supporting the management of the REDCap database and running campaigns to contact donors. The authors would like to thank the staff on the therapeutic helpdesk at Lifeblood who responded to additional donor enquiries that were not related to the study. The authors would also like to thank all the donors who completed the survey or provided emails with stories of their condition and the experiences donating at Lifeblood.

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