Age at the time of first blood donation and donation pattern of blood donors in Australia

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Table of contents

Summary

Regular blood donation is essential to ensure the availability of blood and its products. Blood and its components are vital for the treatment of medical emergencies and chronic diseases, such as massive bleeding, trauma, and cancers. In Australia, and globally, advances in medical treatment have continuously increased the demand for blood and blood products. Currently, Australia is relying on imported plasma to meet its plasma demands. Thus, improving our understanding of the relationship between demographic and other variables with blood donation patterns can help blood collection agencies to refine policies to meet the changing demand of blood and its products.

This thesis aims to improve our understanding of blood donation patterns in Australia, particularly the relationship between the age at first blood donation and donation pattern. I started by identifying major demographic factors associated with return to donate in high-income countries (HICs), including Australia, and low- and middle-income countries (LMICs). The systematic review included LMICs to fill the knowledge gap as previous systematic reviews focused only on HICs. Results from studies conducted in HICs and LMICs were compared to identify if the same factor had different effects in each setting. I then explored the donation pattern of blood donors in Australia with a cohort study using data from the Australian Red Cross Blood Service. The study factor of this thesis is the donor's age at first donation. Analyses were adjusted for several factors identified to be associated with prospective donation pattern among first-time donors in the systematic review.

The systematic review identified the demographic factors and other factors that are associated with return behaviour in blood donors – first-time and repeat donors – across the globe. Shorter inter-donation interval, positive past donation history, a feeling of satisfaction, initial intention to return, and a convenient location to donate were associated with positive return behaviour in both settings. Adverse events, anxiety, and deferrals from donation reduced the likelihood of return in both settings. Sex and level of education showed varying effects on return behaviour in studies conducted in HICs and LMICs. Comparatively more studies reported older age as a predictor for return in HICs while younger donors were more likely to return in LMICs. Although the systematic review was not limited to studies specifically looking at age at first donation or studies conducted on first-time donors, I found the factors affecting return in both first-time and repeat donors were similar.

The cohort study used donation data that was collected from 1 January 2007 to 31 March 2019. This study showed that donors who started donating at less than 30 years of age donated less frequently in the future than donors who started at 30 years or older. Donors who started to donate for the first time at middle age were shown to actively donating for a longer period of time. Additionally, women donated less frequently compared to men, but their return rate for at least one donation was higher compared to men.

Overall, the results of this thesis suggest that the recruitment of middle-aged donors is more effective in meeting the short- to mid-term demand for blood products in Australia. The cohort study could not detect whether young donors would continue to donate blood after reaching middle age due to the relatively short period of follow up.

Further studies need to be conducted to better understand the factors contributing to the lower donation rate of younger donors in Australia. Future research could explore the motivational factors and barriers to blood donation in the Australian population, as well as measuring the incidence and impacts of adverse events and deferrals on future donations. A cohort study, with a much longer period of follow-up, will enable us to answer whether young donors will donate more often after reaching middle age. Efforts to identify barriers to donation in the Australian population especially in young donors will inform donor recruitment policies to target this population better.

Statement of Originality

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the thesis contains no material previously published by another person except where due reference is made in the thesis itself

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List of terms and abbreviations

AEs: Adverse events

Age at first donation: the age of a donor when blood was successfully donated for the first time.

Date of first donation: the date when a donor first successfully donated blood.

Deferrals: a situation where a donor is ineligible to donate based on the criteria applied to protect the health and safety of both the donors and transfusion recipient.

Donation career: the time interval between the first donation to the last observed donation (in years)

Donation yield: the total number of donations made during the follow-up period by a donor.

Donor pool/donor panel: a group of people who remain active as blood donors and are not categorized as lapsed.

HICs: High-income countries

First inter-donation interval: the time interval between the second whole blood donation to the first whole blood donation (in days).

Lapsed donors: donors who have not given blood in the last 24 months.

LMICs: Low- and middle-income countries

Mandatory deferral period: interval directly following a donation attempt during which a donor is prohibited from making blood donations.

RBC: Red blood cells

Repeat donations: subsequent donations after the first donation.

Return rate: the percentages of returning donors compared to the total number of donors

Returning donors: donors who returned to donate at least once.

VVRs: Vasovagal reactions

Chapter 1: Introduction

1.1 Blood donation

Blood donation is the process of collecting, testing, preparing, and storing blood products (1). It is vital as it ensures the availability of blood and blood products to enable the treatment of many medical conditions. Whole blood drawn from donors is processed into separate components which have different clinical uses. Red blood cells (RBCs) are used for the treatment of severe chronic anaemia, pregnancy-related complications, massive trauma, transplant surgery, cardiovascular surgery, and therapy for solid and haematological malignancies (2). Fresh frozen plasma infusion can be used for reversal of anticoagulant effects and platelets are used to prevent haemorrhage in patients with low platelets or platelet function defects (3). A specific component derived from plasma called immunoglobulins used to treat autoimmune conditions such as myasthenia gravis, Guillain-Barre syndrome, immune-thrombocytopenia and many others (4).

According to the World Health Organization (WHO) in 2015 (2), there were around 117.4 million blood donations collected worldwide. This donated blood was used differently in high-income countries (HICs) and low- and middle-income countries (LMICs). Up to 75% of blood transfusion recipients in HICs were for older people aged over 65 years (2, 5). Donated blood in HICs is primarily used for the treatment of massive trauma, therapy for malignancies, supportive care in cardiovascular surgery, and transplant surgery (5). Conversely, in LMICs, up to 52% of blood transfusions were given to children under 5 years of age for the treatment of childhood anaemia (2).

Ensuring a sufficient number of blood donors to maintain an adequate supply of safe blood and blood products to meet healthcare needs is the highest priority for blood collection agencies worldwide (6). As the population ages, it will impact both the supply and demand of blood products. Ageing donors will stop donating at a point in their lives due to medical conditions or age limit on eligibility criteria (7). Growing demand for blood products is caused by several factors including an increasing number of older patient groups with malignancies and chronic disease, therapeutic advances in haemato-oncology such as allogeneic stem cell transplantation, and increasing numbers of major surgical procedures (8). A study from Finland showed those aged 70 – 80 years of age had an eightfold higher RBC consumption than those 20-40 years old (9). Moreover, donated blood has a short shelf-life (10). Therefore, increasing blood donor recruitment and retention is important to ensure the continued availability of blood products to balance the demands for it.

Aside from securing an adequate supply of blood, it is critical to ensure the safety of blood products supplied. The WHO has made the screening of several blood-borne infections mandatory. The screening includes tests for human immunodeficiency virus (HIV), hepatitis B, hepatitis C, and syphilis. Out of the 173 countries which report to the WHO, 19 countries reported the inability to screen one or more of these infections (2). In Australia, blood products are also screened for cytomegalovirus (CMV), human T-cell lymphotropic virus (HTLV) I and II (11). Donated blood and blood products that test positive for blood-borne infections are discarded. For this reason, recruitment of safe donors is important as it will lead to less wastage of donated blood and less costs incurred (12).

Research from the WHO has identified voluntary donors to be the safest donors. Voluntary donors donate blood of their own free will without receiving any form of payments aside from small tokens, refreshments and reimbursements of direct travel costs (12). They are shown to be motivated by altruism and the desire to help others without reason to withhold health information (12). Voluntary donors who donate regularly are shown to have the lowest prevalence of blood-borne infections (2).

1.1.1 Blood donation in Australia

The Australian Red Cross Blood Service is the sole organisation responsible for collecting, testing, processing and distributing all blood in Australia. It has 83 fixed donor centres and 38 mobile units that visit over 1000 sites annually (13).

In Australia, it is predicted that 1 in 3 Australians will need blood in their lifetime but only 3% of the population donated blood each year (14). Although there were 89,534 new donors in 2017, there have been no significant changes in the number of new donors since 2008 (15). The increase in life expectancy and the increasing number of elderly people, the highest consumers of blood products, in Australia is expected to increase the demand for blood products in the future (5). A report from the Australian Institute for Health and Welfare in 2013 showed that 48% of red blood cells and 43% of plasma transfusions were given to older patients aged 65 – 84 years (5).

In general, the demand for red blood cells in Australia has decreased from 801,295 units in 2011-12 to 763,542 units in 2012-13 and then to 630,000 units in 2017-18 (5, 16). This decline is the result of several programs that aimed to improve the appropriate use of blood

products and reduce wastage. These programs include health provider training, improved data collection and implementation of the Patient Blood Management Guidelines (16).

Despite the decrease in the demand for red blood cells, demands for plasma donations increased to 500,000 in the year 2016-2017 (15). This has caused an increase in the spending of plasma-derived and recombinant blood products by $43.8 million to a total of $542.8 million (8.7% increase) from 2016-2017 to 2017-2018 (16). It is predicted that the demands for plasma will continue to increase by 11% each year (17).

Currently, Australia is importing selected plasma-derived and recombinant blood products to augment domestic supply. Australia imports these products through 5 companies (Bioverativ Australia Pty Ltd, CSL Behring (Australia) Pty Ltd, Novo Nordisk Pharmaceuticals Pty Ltd, Pfizer Australia Pty Limited, and Shire Australia Pty Limited) (16). In 2017-2018, the spending on imported blood products reached $136.78 million (16).

1.1.2 Blood donation procedures

To be able to successfully donate blood, donors are required to be aged between 18 to 70 years, weigh more than 50 kg and be physically fit and healthy at the time of donation. Donors also need to complete a confidential donor questionnaire to check their eligibility to give blood. If the potential donor passes a series of checks: a short interview, a health check, a haemoglobin check and blood pressure test, the donor will be able to donate (15).

Prospective donors who do not satisfy these tests are then be deferred for a period of time according to the type of deferral given. The interval between donations varies based on the type of the previous donation. In Australia, there is no difference in the mandatory interval between two donations in men and women. The interval between each whole blood donation is 12 weeks, whereas the interval between apheresis (plasma or platelet) donations is 2 weeks.

1.1.3 Problem statement and justification of research

There are several factors affecting the supply and demand for blood and its products in Australia. Firstly, the number of elderly individuals aged 65 and older in Australia is increasing. It increased from 2.2 million in 1997 to 3.79 million in 2017 and is projected to keep increasing to almost 6.5 million in 2037 (18). The increasing number of elderly

people will increase the demand for blood products for the treatment of diseases, as mentioned above (5).

Secondly, there is an increasing demand for plasma in Australia for the treatment of many conditions such as burns, autoimmune diseases, and bleeding problems (19). Due to insufficient plasma donations, Australia has to import plasma from overseas (16, 19, 20). Thirdly, the increasing age of the donors will cause some donors to stop donating due to old age or medical conditions (7). Lastly, the number of new donors has stagnated since 2006 (15, 21).

To ensure the sustained availability of blood and its products in Australia, effective strategies to recruit new donors that are more likely to be retained in the donor panel and actively retain existing donors need to be implemented. Recruitment of donors who are more likely to return and donate repeatedly for a longer period of time is ideal as it helps to build a reliable donor pool. It would also be a cost-effective approach in donor recruitment as relatively fewer resources are required to keep individuals as active donors. Therefore, it is important to identify factors that are associated with repeat donation to enable improvements to the existing recruitment strategies.

Several factors have been found to be associated with donor return and donation rates globally (22, 23). Demographic factors, such as older age, male gender, and having a higher level of education (college or high school equivalent) were shown to be associated with increased blood donation. (24-27). However, the direction of the association is not always consistent in all settings. Other factors such as anxiety, negative donor experiences ranging from discomfort to adverse events, and deferrals are shown to be deterrent factors to donating blood (28). Many of these studies that examined return behaviour reported a lack of data coverage and length of follow up as one of the limitations (26, 27). They could not capture donors who may have continued donating blood after moving to another location.

The majority of studies on donors' demographics were conducted in countries with a higher level of income such as the U.S (25, 29), Canada (30) and the Netherlands (31) and fewer studies have been conducted in low- and middle-income countries (LMICs) (32, 33). Examining the barriers and promoting factors to blood donation in LMICs and HICs would enable a comparison of the effects of a specific factor to donation behaviour in both groups. Furthermore, results of this comparison might be used to design a policy that

targets a specific population, for example, prospective donors from other ethnicities or from lower socioeconomic class in high-income countries.

Age at first donation has been shown to affect donation patterns differently in a limited number of studies conducted overseas. Studies from the U.S conducted by Schlumpf (23) and Lattimore (29) reported donors older than 30 and 45, respectively, donated more frequently compared to their younger counterparts. On the other hand, studies from the Netherlands by Wiersum–Osselton (31) and Brazil by de Almeida (33) reported donors aged 24 years and less were shown to have a higher likelihood of making a repeat donation compared to older donors.

Studies mentioned in the previous paragraphs were all conducted outside of Australia. Currently, only a single study from Australia has examined the association of age to return behaviour (34). However, the study has not specifically examined the effect on long-term donation patterns. The cohort study in this thesis will provide a better understanding of donation behaviour in Australia, particularly in relation to the age at first donation and inform the Australian Red Cross Blood Service to better recruit and retain donors. Furthermore, this research will use nationwide long-term data that enables us to capture the donation history of donors who have moved to another location within the country and follow-up the return behaviour for more than a decade.

1.2 Aims and objectives of the research

This research aims to improve understanding of blood donation patterns in Australia. The primary objective of this research is to determine the relationship between age at first donation and the donation pattern in blood donors in Australia.

Specifically, this research's objectives are to:

- Systematically review the association between several demographic factors and its association with return behaviour in blood donation in both high-income countries (HICs) and low-and middle-income countries (LMICs)
- Explore the donation pattern of new donors in Australia
- Measure the association between age at the time of the first donation with the donation pattern using nationwide blood donation in Australia.

1.3 Methodology

The author conducted two separate studies to answer the research questions. Firstly, a systematic review was conducted to examine various factors affecting return behaviour in countries based on their economic status according to the World Bank classification (35). This review compared the effects of identified factors in both HICs and LMICs.

A cohort study was then performed using blood donation data, which was collected by the Australian Red Cross Blood Service, while controlling for factors found in the systematic review. This study used donation data collected from all blood centres in Australia from 2007 to 2019.

1.4 Structure of the thesis

This thesis consists of 5 chapters: an introduction, a systematic review, a cohort study, and a combined discussion and conclusions section. A summary of the outline of this thesis is presented in figure 1. The first introductory chapter briefly touches upon an introduction of the blood collection process, procedures, and its status in Australia. The second chapter is a systematic review examining the effects of various factors to return behaviour in blood donors in HICs and LMICs. The third chapter contains a retrospective cohort that measures the association between age at the first donation and the donation pattern. Chapter 4 discusses the findings from the previous two chapters and chapter 5 is the conclusion of this thesis.

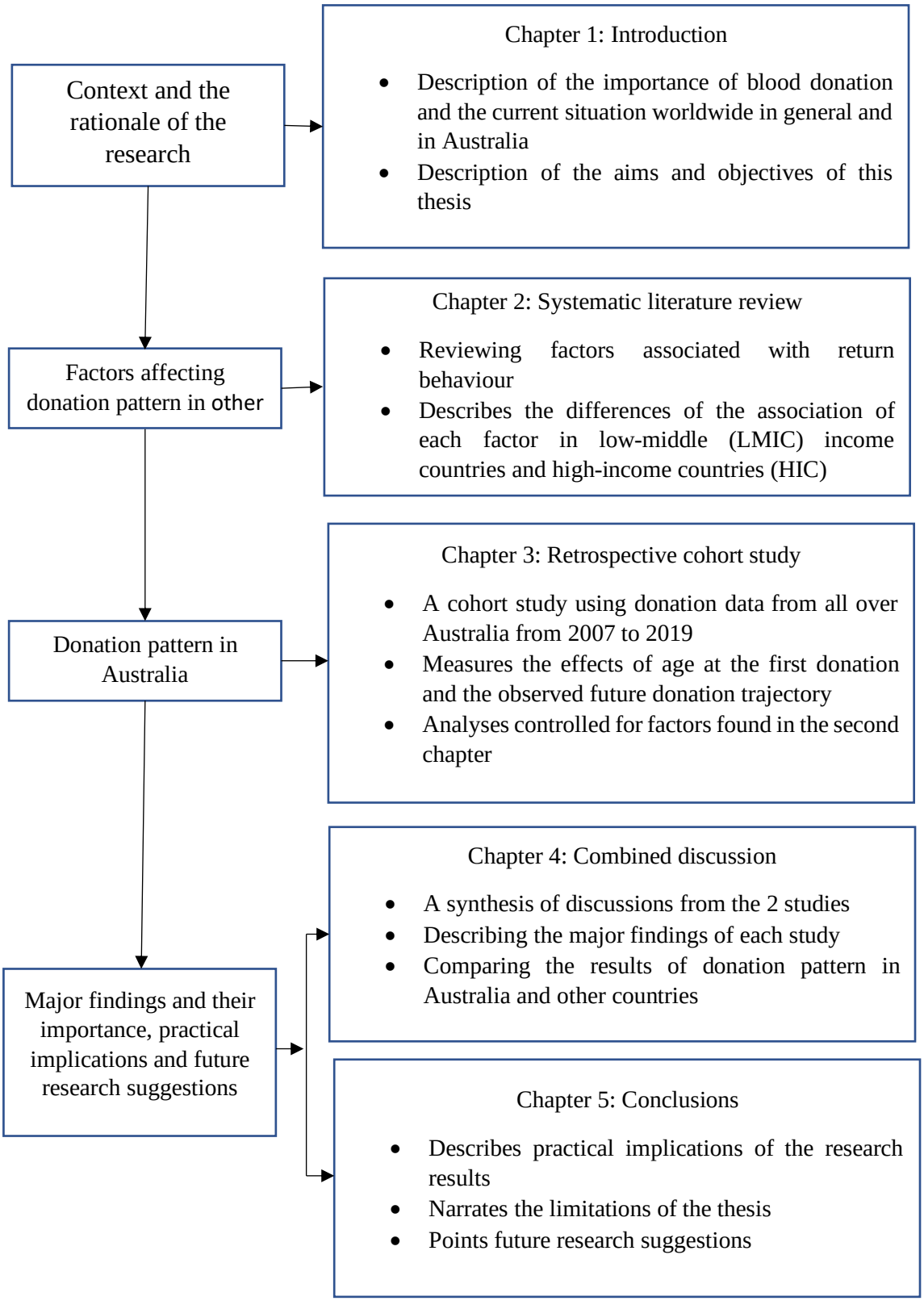

Figure 1 Thesis outline

Chapter 2: Factors associated with Return Behaviour in Blood Donors- do the association differ by income level of countries? - A Systematic Review

Manuscript in preparation for submission to Transfusion by Agus Priyono, Surendra Karki, Amalie Dyda

2.1 Abstract

Introduction: Blood transfusion contributes to saving millions of lives each year in both routine and emergency situations. Repeat blood donors make the largest contribution to the blood supply in Australia. Several studies have reported factors associated with donor return behaviour. However, the demographics and motivations associated with return to donation have been shown to differ across countries. In this systematic review, I aimed to synthesize the evidence on factors associated with return behaviour according to the country's economic status.

Methods: I systematically searched the literature using the databases ProQuest, PubMed, and Ovid Medline for studies published from January 2000 to April 2019. Only studies examining return behaviour written in English were included. PRISMA guidelines were used to screen and report identified studies. Factors likely to impact return behaviour, such as age, sex and level of education, were studied across the globe using the World Bank's categorisation of the country's economy (high income vs low/middle income).

Results: A total of 66 studies met the inclusion criteria. Short inter-donation interval, positive past donation history, a feeling of satisfaction, intention to return and a convenient location were associated with positive return behaviour. Adverse events, anxiety and deferrals reduced the likelihood of return. Older donors tended to return more than younger donors in high-income countries while younger donors were more likely to return in low- and middle-income countries. In all settings, male donors returned more often, although the reasons for this finding varied. There is a mixed effect of level of education on return behaviour.

Conclusion: Return behaviour is associated with age, sex and level of education but showed a different effect in high-income countries (HICs) and low- and middle-income countries (LMICs).

2.2 Introduction

Blood transfusion contributes to saving millions of lives each year in both routine and emergency situations. Ensuring a sufficient number of blood donors to maintain an adequate supply of safe blood and blood products to meet healthcare needs is the highest priority for blood collection agencies worldwide (6). Blood donations from 1% of the population is considered the minimum level needed to meet a nations basic requirements for transfusion, as defined by the World Health Organization (WHO) (33). The World Health Organization reported large differences in donation rates among countries globally

ranging from 32.1 donations per 1000 population in high-income countries, 14.9 donations per 1000 population in upper-middle-income countries, 7.8 in lower-middle-income countries, and 4.6 in low-income countries (36).

As one of the HICs, Australia has met the minimum donor requirement set by the WHO (3% of the Australian population donate blood) (37). However, the increasing need for plasma products for the treatment of many medical conditions could not be satisfied by the local supply (15). Current trends indicate that the total number of donors in Australia has had no significant changes from 2008 to 2017 (38, 39). An increasing number of the older population will pose a challenge to blood service as the need for red blood cells (RBC) increased (9). All these factors combined with the expected decrease in blood donors as they age, there is a need to increase the donation rate to balance the supply and demand for blood products.

Retention of regular blood donors offers more advantages over newly recruited donors due to lower marketing cost and frequent donors tend to have a healthier lifestyle (40), which resulted in less deferral and safer blood products. Several studies have examined factors associated with those who return to donate or those who lapse from donation. Identifying these factors can inform blood services to improve policies for donor retention

Several factors found to be positively associated with donor return are good experience in the previous donation, having a convenient place, and age more than 25 years (23). Donors who had donated before were shown to have a higher return compared to first-time donors (23). Having an adverse reaction was shown to reduce the likelihood of return in donors (41) as well as having received a deferral (42). A deferral is a situation where a donor is ineligible to donate (43).

Previous reviews investigating factors associated with those who return to donate have focused on a specific group of blood donors and are limited within high-income countries in men (44), in first-time donors (28) or in high-income countries only (45). Investigating factors associated with return behaviour in LMICs will improve our understanding of blood donation behaviour in a specific group, such as those with a low socioeconomic background or different cultural background. This will allow a more targeted approach to groups with similar characteristics. In this systematic review, I aimed to synthesize findings from all published studies and assess the differences in the observed associations

between various donor characteristics and donor return by income level of the countries using country's income level based on the World Bank classification (35).

2.3 Methods

This systematic review was conducted and reported according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines (46).

2.3.1 Eligibility criteria

The following inclusion criteria were applied: Studies with full text available, published in English, and published from January 2000 to April 2019. I included studies which examined the association between any donor characteristics and return behaviour in either first-time or repeat blood donor's donation in relation to whole blood, plasma, or platelet donation.

2.3.2 Information sources and search of the literature

Electronic searches were conducted in ProQuest, PubMed, and Ovid Medline. Search terms used were: "ti* (Blood don*) AND (Return OR Regular OR Repeat OR Retention) AND (Factors OR Age OR Demography OR Incentive OR Pattern)". Several filters were applied, such as publication date, full text only, and publication in English. The mentioned strategy was used in all 3 databases. I also manually searched all reference lists within articles included after the initial screen. I scanned titles, abstracts and full-text articles to determine their suitability for inclusion. I (AP) reviewed full-text articles for data extraction and further confirmed by Surendra (SK). When there was a disagreement, both authors discussed to reach a decision.

2.3.3 Data extraction

I extracted the following data from each publication: author, publication year, study design, study location, study population size, factors investigated, study outcome, sample status (first-time donors, repeat donors, or both), and type of donation (whole blood, apheresis or both).

2.3.4 Quality assessment and risk of bias

All case-control and cohort studies included in this review were assessed with the Newcastle-Ottawa Scale for quality assessment (47). I also used the modified Newcastle-Ottawa Scale (NOS) adapted from Modesti and colleagues (48) to assess the quality of cross-sectional studies.

2.4 Results

Study selection

In total, I identified 1203 articles through the database search. After removing duplicates, titles and abstracts of 745 articles were screened, of which 679 were excluded. A total of 66 publications were included in this systematic review. (See Figure 2)

Study characteristics

Of the included studies, there were 32 cohort studies, 2 case-control, 23 cross-sectional studies, and 9 intervention studies. The majority of studies came from HICs (n=53), with 13 studies from LMICs. These studies predominantly focused on donors who donated whole blood (n=39) and 26 studies included any donor, while 1 study specifically studied plasma donors. Based on the type of donors included in the studies, 14 studies included only first-time donors, 1 study involved repeat only donors, 37 studies included any type of donor, and 14 studies did not specifically mention the donors' status.

Study quality

Thirty-three studies were assessed using the NOS. I followed a study by Islam and colleagues that used a cut-off point of 7 to categorize the quality of a study using the Newcastle-Ottawa Scale (49). In this study, I considered a study with a score of ≥7 a high-quality study. Of all 33 studies assessed, 2 studies received a score of 6 and 32 studies received a score of 7 or higher. Twenty-three cross-sectional studies were assessed using modified NOS, of which 3 publications had a score of 6 or less and 20 studies had a score of ≥7. The quality score of each individual study is shown in Appendix 1. I did not assess the risk of publication bias or selective reporting bias, as I did not conduct a meta-analysis.

Study results

Tabulation of study characteristics is shown in Appendix 1. I identified several factors associated with return behaviour. The factors identified in this review were age, sex, level of education, history of past donation, inter-donation interval, incentives, intention, satisfaction, donation sites, history of deferrals, history of adverse events, and anxiety. The effects of each factor are shown in Table 1. Several intervention studies were also identified that examined return behaviour and are included and will be discussed in this review

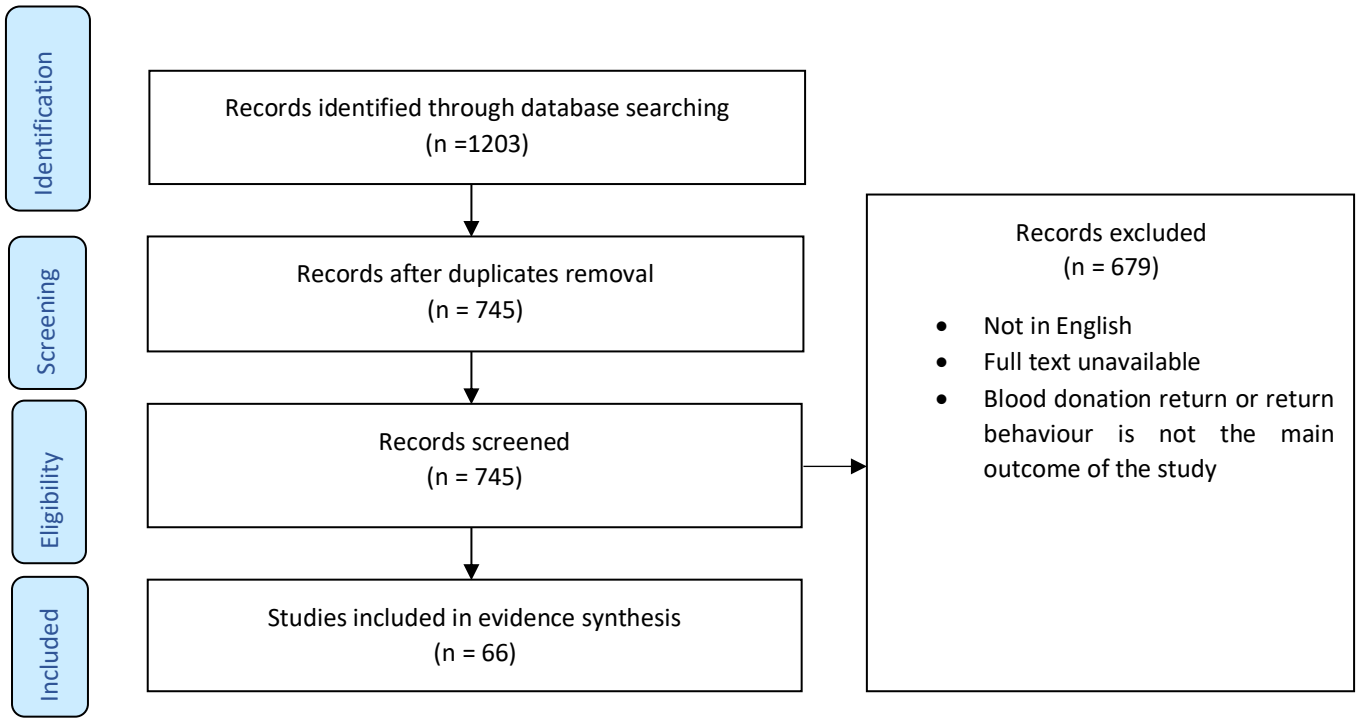

Figure 2 Study flow diagram

Age

There are 19 studies from HICs and 7 studies from LMICs looking at the association of age with donation pattern. Eighteen of the 19 (23-25, 29, 30, 34, 41, 42, 50-59) studies from HICs reported older age as a strong predictor of return (Adjusted Odds Ratio (aOR) ≥40 vs <40 1.23 (55), aOR 65+ vs <24 2.80 (29), all $p<0.05$). Five (32, 33, 60-62) out of 7 (31-33, 60-63) studies in LMICs that looked at age, reported younger donors returned more. Studies reported an interesting pattern of return rate based on the age group. The effect of age follows predominantly a U-shaped curve pattern where the youngest donors had a high donation yield decreasing until age 30 (50, 54). The return rate then increased until around 69 years and then declined again (30). Some studies used different age categories, for example, Lattimore and colleagues used 17-24, 25-34, 35-44, 45-54, 55-64, and 65+ (29) while Mousavi and colleagues used 18-29 and 30-65 (53). Overall, the majority of studies supporting older age as a positive factor consistently showed that donors aged > 40 returned more compared to their younger counterparts (41, 55, 59). Older people have also been shown to have a higher mean donation frequency (4.91 in 60 to 69 years vs 1.63 in 16 to 19 years)(55). Conversely, Notari and colleagues reported higher odds of returning within 25 months in young donors (aOR for 16, 18, 19, 20-24, 25-29, 30-39, 40-49, 50-59, and 60+, compared to 17, were 1.80, 0.51, 0.39, 0.41, 0.50, 0.58, 0.69, 0.80, and 0.93, respectively) (54)

Table 1 Summary of findings

Donor characteristics	Number of studies		Studies showing positive associations to return behaviour		Studies showing negative associations to return behaviour		Studies showing no impact or no difference	
	HICs	LMICs	HICs	LMICs	HICs	LMICs	HICs	LMICs
Age (>30 or >40 years of age)	19	7	18 studies (23-25, 29, 30, 34, 41, 42, 50-59)	1 study (64)	1 study (31)	5 studies (32, 33, 60-62)	-	1 study (63)
Sex (male)	16	11	16 studies (25, 27, 29-31, 34, 50, 52, 53, 55, 56, 65-69)	7 studies (32, 33, 63, 70-73)	-	2 studies (60, 61)	-	2 studies (62, 64)
Education (Higher)	4	6	2 studies (24, 25)	3 studies (64, 71, 72)	2 studies (65, 68)	2 studies (60, 61)	-	1 study (63)
Positive past donation history	7	4	7 studies (23, 24, 30, 50, 57, 67, 74)	4 studies (32, 60, 61, 63)	-	-	-	-
Short inter-donation interval	2	3	2 studies (26, 53)	1 study (32, 33, 63)	-	-	-	-
Incentives	4	1	4 studies (75-78)	1 study (73)	-	-	-	-
Intention to donate	5	1	5 studies (23, 52, 74, 79, 80)	1 study (72)	-	-	-	-
Convenience	3	-	3 studies (23, 81, 82)	-	-	-	-	-
Fixed location	4	1	4 studies (24, 51, 52, 83)	1 study (60)	-	-	-	-
Satisfaction (self-reported)	2	-	2 studies (65, 76)	-	-	-	-	-
Intervention	8	-	8 studies (40, 69, 84-89)	-	-	-	-	-
Experiencing adverse event(s) (AEs) or observation of AEs by donor	9	1	-	-	9 studies (31, 34, 41, 54, 67, 80, 81, 90, 91)	1 study (92)	-	-
Past deferral	7	1	-	-	7 studies (24, 34, 42, 57, 65, 93, 94)	1 study (92)	-	-
Anxiety	3	-	-	-	3 studies (68, 79, 91)	-	-	-

Sex

Sixteen studies from HICs (25, 27, 29-31, 34, 50, 52, 53, 55, 56, 65-69) and 7 studies from LMICs (32, 33, 63, 70-73) showed males had a higher rate of return compared to females (aOR ranging from 1.11 to 1.35 from several studies). This association was observed when the analyses were performed separately in first-time and repeat donor group (34). In contrast, female donors were found to have a higher return rate in China (male aOR 0.88 – 0.89) (60, 61). One study from a HIC reported that the difference in sex was only significant in those aged under 45 years with a similar return rate of both sexes above 45 years of age (27).

Level of education

There are 4 studies from HICs and 6 studies from LMICs that studied the association between level of education and return behaviour. Two out of 4 studies from the HICs group (24, 25) found return rate was higher in donors with a higher level of education, while the other 2 (65, 68) reported the return rate was higher in donors with a lower level of education. Three studies from LMICs (64, 71, 72) showed donors with a higher level of education returned more, while the opposite was found in 2 studies in LMICs (60, 61).

Murphy and colleagues reported the highest return in those who had completed college or higher compared to those with lower education (aOR ≤ high school diploma vs >high school diploma 0.39) (25). On the contrary, Ringwald and colleagues reported those with higher education had higher odds of not returning (aOR college or higher vs grade 12 or less 2.18. 95% CI 1.34-3.55) (68).

Positive past donation history and short inter-donation interval

Donors who have donated more in the past were found to have a higher return rate. Seven studies from HICs (23, 24, 30, 50, 57, 67, 74) and 4 studies from LMICs (32, 60, 61, 63) showed this result consistently. A study in China found repeat donor status was a predictor for making a repeat donation compared to first-time donors (aOR of return after 3 donations vs no previous donation history 11.01. 95% CI 10.20-12.08) (60). The number of donations in the first year of donating is also a strong predictor of return behaviour in both first-time and repeat donor groups. In first-time donors, a higher number of donations in the first year resulted in more donations in the subsequent years (32, 63). In repeat donors, the number of previous donations was strongly associated with the return rate in the future (41, 61).

Donation frequency is positively correlated with a short inter-donation interval, both first inter-donation interval and the subsequent intervals during the first year of donating. This result was shown in 2 studies from HIC (26, 53) and 3 studies from LMIC (32, 33, 63). One

study reported long interval between the time of the acceptance to the first donation significantly reduced the likelihood of returning for first-time donors (aOR short interval (29 days) 3.7. 95% CI 2.2 – 6.1) (53)

Intention to donate, convenience, self-reported satisfaction and location

Five studies from HICs and 1 study from an LMIC (23, 52, 72, 74, 79, 80) reported the donors' intention to make a return donation correlated positively with return behaviour. This factor was shown to predict return better in occasional donors (donors with less than 5 previous donations) compared to donors who had donated more (80).

Three studies from HICs reported convenience is positively associated with return behaviour (23, 81, 82). Several examples of the inconveniences reported no convenient place (too far) (82) and inconvenient opening times (81). Having a fixed location of donation site was also positively correlated with return behaviour in 4 studies from HIC (24, 51, 52, 83) and 1 study from an LMIC (60). Convenience and fixed location are shown to increase return rate in both first-time (82) and repeat donors (23). Fixed sites with regular operation hours offer more chance of donating while mobile sites only appear infrequently thus limiting the opportunity to donate (23). In China, although a higher rate of return was shown in "mobile" donation sites, these sites were placed in a fixed location (60). Donors' high satisfaction (self-reported) was found to be positively correlated with return as found by Nguyen and colleagues (76)

Intervention

Several intervention studies performed in HICs have shown to increase retention of blood donors. These interventions are post-donation message (40), pre-donation contacting (84, 87), motivational interviews (69, 85, 88) and applied tension (repeated isometric muscle tension) (86, 89). Applied tension increased retention of donors by reducing the likelihood of adverse events (86). Donor contacting, either through calling (87) or messaging (40), increased return in new donors and donors with less than 10 previous donations.

Incentives

The effect of incentives depends on the target group and the types of incentives given. In general 4 studies in HICs (75-78) and 1 study in an LMIC (73) showed a positive association between incentives and return to donation. Incentives increased the return rate in younger populations and those with higher education, while it decreased intention to return in older donors and returning donors (75).

Blood credits (a credit given to donors, or their designates, to be applied toward the fee they need to pay if they receive blood in the future), cholesterol screening and prostate-specific antigen (PSA) screening were the types of incentives shown to increase donations (75). Young donors were more likely to be attracted by compensatory incentives such as tickets to events, discounts or lottery tickets (77). Compensatory incentives do not always increase donation as one study found that 9% of the participants reported that they would be discouraged to return if offered compensatory incentives (75). Incentives are shown to attract first-time donors more (77) and the effect is only sustained for the first 2 years (78).

Adverse events (AEs), observations of adverse events and history of deferrals

Both experiencing adverse events and observations of adverse events were associated with lower return rate among donors in 9 studies from HICs (31, 34, 41, 54, 67, 80, 81, 90, 91) and 1 study from an LMIC (92). Different types of adverse events were found to have different effects on each gender, except for vasovagal reactions which have been shown to decrease return in both genders (91). Subjective distress is associated with decreased return in women, while the effect of the feeling of fatigue is more marked in decreasing return in men (91). Major adverse events are related with longer return interval and lower return rate when compared to minor or no adverse event (41, 54). In one study from a HIC, donors who experienced adverse events were less likely to return compared to donors without adverse reactions (OR minor reactions 0.65, OR major reaction 0.35) (54).

History of past deferrals

Being deferred in the past reduced return rate both in first-time and regular donors. Seven studies from HICs (24, 34, 42, 57, 65, 93, 94) and 1 study from a LMIC (92) confirmed this. One study reported a higher deferral rate in younger women (17 % vs 10% in young men) explaining lower donor proportion in this age group (27). Another study reported, donor deferrals were highest in young blood donors, but increased again in elderly blood donors beyond 71 years (95)

Donation related anxiety

Donation related anxiety is positively associated with lapse from donation, as was shown by 3 studies from HICs (68, 79, 91). These donors had a low return rate and were also more likely to experience more pain and adverse events (68). The effect of anxiety on donor return is more prominent in women (68). I did not find any study looking at the association of anxiety and return behaviour in LMICs.

2.5 Discussion

In this paper, I reviewed studies examining donor characteristics associated with return blood donation behaviour in HICs and LMICs. The majority of studies from HICs and LMICs showed that being male, older and having a higher education were positively associated with higher return behaviour. Positive past donation history, short inter-donation interval, intention, incentives, convenience, satisfaction, fixed donation sites and several interventions are positively associated with return in all studies from both HICs and LMICs. History of deferrals, history of adverse events, and observation of adverse events are negatively associated with return behaviour in both HICs and LMICs.

A previous systematic review conducted only on studies from HICs (45) found similar results to this systematic review. The majority of studies in this systematic review found that males have a higher return rate, especially those below 45 years of age. This might be explained by studies conducted in high-income countries showing a higher rate of adverse vasovagal reactions in females (90), higher deferral rates for females (27), pregnancy, and lactation (27, 50). In low – middle-income countries, a lower participation rate of females has been found to be associated with lower levels of education, and the need for permission from their husband (32).

Several studies found a U-shaped curve pattern in return rates among age groups. This pattern shows a higher return rate in the youngest group compared to the 20-29 years, which then increased progressively as the age group increased (50, 54). The higher return rate in the youngest group could be related to blood donation facilitated by universities or schools (34) making it a convenient place to donate. The decline in return rate in those aged 20-29 years could be attributed to younger donors moving to different areas to further their education or getting a new job (78), declining birth rate in some European countries which lowered adolescents donors recruitment (66), pregnancy and childbearing (27) and a higher rate of adverse events. The higher rate of adverse events in younger donors, especially those aged 16 and 17, may also eventually discourage some younger donors to return regularly (54).

It is hypothesized that recruiting donors older than 30 years would result in the most donations as they are considered as the most stable donor group (96). I found many papers reported a higher return rate and high donation yield in those aged 40 years and up. The higher rate of return in middle-aged and older donors may be due to a lower rate of adverse

events and a lower rate of deferrals compared to younger donors (92, 95). However, for donors above 65 years, the rate of return may decline due to medical reasons and increased recovery time after an adverse event (95).

Although results from most studies from HICs and LMICs showed that return was associated with being male and being older, the pattern of return based on age and gender is different in some studies performed in LMICs. In China, a higher return was observed in female and younger donors (61). It is hypothesized that "one blood policy" in China, where donors or their relatives can use the same amount of blood for free as they have donated, is the cause of this phenomenon (61). A study in Iran showed increasing age was associated with a reduced likelihood of making a repeat donation (32). Difficulty in accessing donation sites, having lower education and unawareness of the importance of blood donation are cited to be the cause (32).

The association between level of education and return rate was not similar in all studies. The previous review also found that the level of education has different effects on donor return (45). More studies reported that higher level of education is associated with higher return rate, especially in LMICs (64, 71, 72). In some studies, lower level of education is associated with higher return (60, 61). A study by Nguyen and colleagues (76) found that donors with a higher level of education showed less satisfaction with the donation process and they may have a different perception of the value of their time or might be accustomed to higher quality service. However, those with a higher level of education might donate more blood as they are more likely to be aware of the importance of blood donation and have greater access to health information (71).

Donors who gave blood frequently in the past are more likely to give blood in the next 6 month (74). Past donation history may play a role in building a donation habit (97). Having a positive past donation history was also shown to increase return of donors who had received a temporary deferral (24). This means that efforts to increase repeat donations might be beneficial in the long run as well as reduce the likelihood of lapsing due to receiving deferrals.

Incentives have different effects depending on the target group and the types of incentives given. Younger donors and first-time donors are more attracted to incentives compared to older, frequent donors. Specific types of incentives are only attractive to a specific population, for example, Prostate-Specific Antigen (PSA) screening is used to target the

older male population. Incentives, however, was proven to not affect donors' long-term commitment to donate suggesting that incentives are better used to increase donor recruitment (78). There are several concerns regarding the effects of incentives on donation pattern. Firstly, Incentives may decrease donation in centres without incentives program (78). Additionally, incentives may detrimentally affect the safety of blood supply due to at-risk donors concealing risky behaviours at screening to obtain the incentive (75). Lastly, current donors and returning donors who primarily donate due to altruistic reasons might be discouraged from donating when offered incentives, which was a result of a study from a HIC (75).

Donation site is one of the determining factors for return to donate. A study showed that repeat donors prefer to donate at a fixed location that is operating at a fixed time (23). A mobile collection site provides minimal opportunity to donate frequently due to coming once or twice a year (75). However, mobile collection sites in China appear to be more preferred and yielded more donation. This is thought to be caused by mobile collection sites appearing at a fixed location and at fixed times, mimicking a fixed site (60). There is no difference between HICs and LMICs when looking at the association of location with return behaviour.

Bagot and colleagues found that history of deferral was the major deterrent of return among all three factors (history of deferrals, anxiety, adverse events) in first-time donors (28). A higher rate of lapsing was found to be associated with the longer the duration of a deferral although it is hypothesized that duration alone is not a critical factor in predicting return (24). Similarly, the severity of an event also positively correlated with the lapse rate (67). A study concluded that the effect of deferrals and anxiety diminishes over time (28).

The majority of the papers reviewed in this study come from HICs where factors associated with return behaviour might be similar. One of the limitations of this paper is I did not include emotional and motivational factors that may affect return behaviour. I did not find any intervention studies to increase donor retention in LMICs. Interventions proven to be successful in HIC might not have the same effect in LMICs.

2.6 Conclusion

Donor return behaviour is affected by many factors. Some of the factors studied in this paper were shown to be associated with return rate in both HICs and LMICs. These factors are positive past donation history, short inter-donation interval, incentives, positive

satisfaction, intention to donate, experience adverse event(s) and receiving deferral(s). Age, sex and level of education were shown to have a different effect on return rate in both HICs and LMICs. This may be caused by a specific local factor in each study, for example, a policy in China that increases donation in women and those with a lower level of education. Blood establishments need to follow the local contextual factors affecting return behaviour to optimise their donor retention efforts.

Chapter 3: Age at first donation and future donation pattern of blood donors in Australia – a cohort study

Manuscript in preparation for submission to Transfusion by Agus Priyono, Surendra Karki, Amalie Dyda

3.1 Abstract

Introduction: Improving blood donor recruitment and retention is important to ensure the supply of blood products for the healthcare needs of the Australian population. Identifying characteristics of donors more likely to return and repeatedly donate can help to optimise donor recruitment and retention efforts.

Methods: I analysed donation data from three cohorts of blood donors who initiated donation in 2007, 2010, and 2013. Outcomes such as the proportion of donors returning to donate, the average length of donation career, total number of donations, and donation rates, were compared between groups based on their age at the first donation. I used Poisson regression to compare donor return and Negative-binomial regression to estimate the rate ratio of donation.

Results: A total of 330, 797 individuals comprised the three cohorts of donors. Compared to donors who started donating at 20-24 years, the likelihood of return to donate either whole blood or apheresis donation in all cohorts increased consistently as the age at first donation increased. Similarly, across all cohorts, the whole blood donation rate and plasmapheresis donation rate increased as the age at donation increased above 20-24 years. Donation rate was highest for donors >=60 years for whole blood and 50-59 for plasmapheresis donation. This pattern was consistent when stratified by sex. The likelihood of return and donation rate in the younger donor was slightly higher compared to those aged 20-24 years, but the pattern was not consistent across all cohorts. More females returned at least once, but males returned more frequently among all donors who returned at least once.

Conclusions: To meet the short- to mid-term sufficiency of blood supply, recruitment of middle-aged donors appears to be more effective. Studies with longer follow-up period are needed to examine whether young donors returned more when they reach middle age.

3.2 Introduction

Improving blood donor recruitment and retention strategies is crucial to ensure the enduring supply of blood and blood products for the healthcare needs of the Australian population. There were 99,969 new donors in Australia in 2017, and there has been no significant change in the total number of donors since 2008 (14, 39). Recently, the demand for whole blood donors has plateaued, but there has been an increasing demand for plasma and plasma-derived products (15). This has caused an increase in the spending of plasma-

derived and recombinant blood products by $43.8 million to a total of $542.8 million (8.7% increase) from 2016-2017 to 2017-2018 (16).

Repeat blood donors that remain in the donor panel for longer and make consistent donations are the backbone of donor panel to meet the ever-increasing demand of blood and blood products. Blood Collection agencies aim to optimise their donor recruitment strategies such that a new donor converts into a consistently donating repeat donor. Thus, understanding of the factors that are associated with a higher rate of return to donate and a more consistent donation can help to target specific segments of the population in recruitment strategies that are more likely to be retained ultimately increasing the number of loyal and long-term donors.

It has been hypothesised that recruiting younger donors can be beneficial for Blood Collection agencies as these agencies get the opportunity to educate young people about blood donation earlier in their lives and influence their behaviour in relation to return to donate. Younger donors have more lifetime opportunity to donate given they return to donate and meet all other eligibility for donation (98). In line with the above hypothesis, several countries including Australia introduced policies in the past where younger donors could start to donate from the age of 16 years (99). However, the minimum age for blood donation in Australia was increased to 18 in January 2018 as studies showed a higher rate of iron-deficiency in donors under 18 years of age (99, 100).

The results of previous studies are inconsistent as to whether there are benefits of targeting younger blood donors in recruitment efforts. Ownby et al. reported donors aged < 30 were less likely to return to make more donations compared to older donors (96), whereas Notari et al. found that the young donors had a higher likelihood of making a repeat donation (54).

Several studies have suggested that older donors have a higher rate of donation because they are stable donors (101), are highly committed to donation (8), and are less likely to experience donation-related adverse events (95). However, donors who start to donate later in life do not have the equivalent amount of life-time opportunity to donate as a relatively younger donor would have.

I did not find any studies looking at the relationship between age and blood donation in Australia. One of the limitations of studies conducted in other countries is a lack of data coverage. For example, in Norway and the U.S, the lack of centralised donor data

management made the researcher unable to capture donors who might have continued donating in another blood centre or area (54, 101).

This study will examine the donation trajectory of Australian blood donors. Thus, using routinely collected donor and donation-related data at the Australian Red Cross Blood Service (called Blood Service hereafter), I examined if starting to donate at a certain age group leads to varying donation pattern in the future while adjusting for other common confounders of donor return including the experience of adverse events in the first donation. The use of nationwide data will allow this study to capture the donation history of donors, even when they have moved to another location. In this study, I compared the likelihood of return to donate and the donation rate by age at first donation using three cohorts of donors who started to donate in 2007, 2010, and 2013.

3.3 Methods

3.3.1 Data sources and study subjects

I conducted a retrospective cohort study using de-identified blood donor's data routinely collected by Blood Service. In Australia, The Blood Service is the sole authority for the collection, processing and distribution of blood and blood products. It maintains a complete national database of donors and donation-related information, which are stored in the 'National Blood Management System' (NBMS). De-identified donor information extracted from the NBMS included donors' medical information, donation history, and adverse events (applicable only to the 2013-cohort).

I categorised three cohorts of voluntary blood donors who successfully donated blood for the first time in 2007 (2007-cohort), 2010 (2010-cohort) and 2013 (2013-cohort). I decided to examine the same outcomes in three different cohorts to measure if the donation pattern differed among donors who started to donate in different period of time.

I excluded donors who donated for therapeutic and autologous purposes, as well as donors who attended but did not make successful donations and where blood was taken for sampling purposes only. Eligible participants' donation history from their first donation to 31 March 2019 was used in this study.

3.3.2 Study definitions

Age at first donation is the main study variable. Within each cohort, I categorised age at first donation into age-groups of 16, 17, 18, 19, 20-24, 25-29, 30-39, 40-49, 50-59, ≥ 60

years. The separation of younger age groups (<20 years old) was performed due to the large number of study participants aged <20 years. This also allows for more detailed analysis in the younger age groups, as well as allowing for a direct comparison to an international study (54).

Return to donate, length of donation career, donation yield (total number of successful donations made in donation career), and donation rate are outcomes of interest. I defined a donor as 'returned donor' if the donor made a successful repeat donation at least once after the first-ever donation. For returning donors, I calculated the 'length of donor career' as the time period between the date of the first successful donation and the date of the latest recorded donation within the follow-up period. I defined the location of donation as metro if the donation site was located in the metro area and non-metro for other sites.

I used donor's sex, location of donation, blood groups, history of experiencing adverse event(s) related to the first donation as covariates in the analyses

Due to changes in the adverse events reporting and documentation resulting in loss of information on adverse event prior to 2011, I decided to use adverse events data in the analysis only for the 2013-cohort.

This research has received approval from the Australian Red Cross Blood Service Human Research Ethics Committee (Reference number: 04032019).

3.3.3 Statistical methods

I calculated the percentage of returning donors in each age group with 95% confidence intervals. I also calculated the average length of donation career and the average number of donation (donation yield) for whole blood donation with 95% confidence intervals.

I used Poisson regression models to examine the association between age at first donation and the likelihood of making a repeat donation at least once (return vs no return). A Poisson regression model is an alternative method to estimate the risk ratio for a binary response variable when more appropriate log-binomial modelling has convergence issues (102). In this thesis, Poisson regression was used because the log-binomial model did not converge with the data used for analysis.

To examine the ratio of donation rates between age groups, I used negative binomial regression models. This method was chosen over Poisson due to overdispersion of the data. Analyses were performed separately for whole blood and plasma donations to see any difference in the pattern of these two donations. These separated analyses were intended to see which age group donated whole blood and plasma more frequently as these 2 types of donations have different length of mandatory deferral period (12 weeks for whole blood and 2 weeks for plasma donation). I examined the association in unadjusted model and in multiple regression models adjusted for sex, location of donation, blood group, history of experiencing adverse event related to the first donation (only included for 2013-cohort). I conducted overall and sex-stratified analyses.

Due to changes in regulations in 2014, that allowed donors aged 16 and 17 to donate only once a year (103), I excluded these two groups in the final analysis for the 2013-cohort.

I considered a p-value of <0.05 statistically significant, and where appropriate provided the point estimates of effect measures with 95% confidence intervals. I conducted all statistical analyses using Stata version 16 (Stata 16.0, StataCorp LLC, College Station, Texas)

3.4 Results

3.4.1 Characteristics of study participants

I had 120,469, 114,497, and 95,381 first-time blood donors in the 2007, 2010 and 2013 cohorts (hereafter called as 2007-cohort, 2010-cohort, and 2013-cohort), respectively. Average donor's age at baseline was similar in all cohorts (31.3 years (standard deviation (sd)-13.66), 30.9 years (sd-13.89) and 30.8 years (sd-13.58) for 2007-, 2010-, and 2013-cohort, respectively. The percentage of females was slightly higher than males in all cohorts (55.07% in 2007, 54.14% in 2010 and 54.54 in 2013). Detailed participants' characteristics for each cohort are presented in Table 2.

In all cohorts, the proportion of younger donors (<20 years old) was higher than the other age groups. Donors aged less than 20 years made up 27%, 30%, and 28% of total donors in 2007-, 2010-, and 2013-cohort, respectively. Donors who started donating at ≥60 years of age made up 3.8 % of the total cohort.

Table 2 Characteristics of study participants

Characteristics	2007-cohort		2010-cohort		2013-cohort	
	N	%	N	%	N	%
Age groups						
16	13,178	10.94	15,442	13.49	11,422	11.92
17	7,677	6.37	8,485	7.41	6,922	7.22
18	6,415	5.33	5,574	4.87	4,670	4.87
19	5,216	4.33	4,507	3.94	3,827	3.99
20 - 24	20,773	17.24	18,181	15.88	16,068	16.77
25 - 29	15,108	12.54	14,753	12.89	13,212	13.79
30 - 39	20,061	16.65	18,179	15.88	16,388	17.1
40 - 49	16,383	13.6	14,270	12.46	11,489	11.99
50 - 59	11,352	9.42	10,523	9.19	7,991	8.34
≥60	4,306	3.57	4,583	4	3,842	4.01
Total	120,469	100	114,497	100	95,831	100
Mean age (standard deviation)	31.33 (13.66)		30.94 (13.89)		30.82 (13.58)	
Sex						
Male	54,121	44.93	52,505	45.86	43,569	45.46
Female	66,348	55.07	61,992	54.14	52,262	54.54
Location						
Metro	77,641	64.45	71,389	62.35	61,556	64.23
Non-metro	42,828	35.55	43,103	37.65	34,274	35.77
Blood Group						
Other groups	111,610	92.65	105,841	92.44	88,018	91.85
O-negative	8,859	7.35	8,656	7.56	7,813	8.15
Duration of follow up (years)	12		9		6	

Average length of observation (years) Mean (standard deviation)	3.6 (4.0)	2.8 (3.1)	2.0 (2.2)	
Experienced adverse event(s) in their first donation				
No	N/A	N/A	81,996	85.56
Yes	N/A	N/A	13,835	14.44
First whole blood inter-donation interval in returning donor (days)				
Mean (standard deviation)	427.81 (676.47)	332.40 (505.67)	316.55 (381.20)	
Number of donations made in the follow-up period				
All types	851,462	738,660	534,363	
Whole blood	631,307	513,277	348,349	
Plasmapheresis	204,870	212,554	177,217	
Plateletpheresis	15,285	12,829	8,797	
The proportion of returning donor in 2 years				
Percentages	62.8%	65.5%	61.3%	

3.4.2 Proportion of returning donors

Figure 3 shows the percentage of donors in all three cohorts who returned to make a successful donation at least once over the follow-up period. Although there was a slightly

higher return in donors younger than 20-24 years age group, the return percentage was comparatively higher in donors aged 30 or older where it increased consistently as the age increased (Figure 3). In all cohorts, donors who started to donate at 17-years returned the least. Donors who first donated at 60+-years returned highest (>80% in all three cohorts).

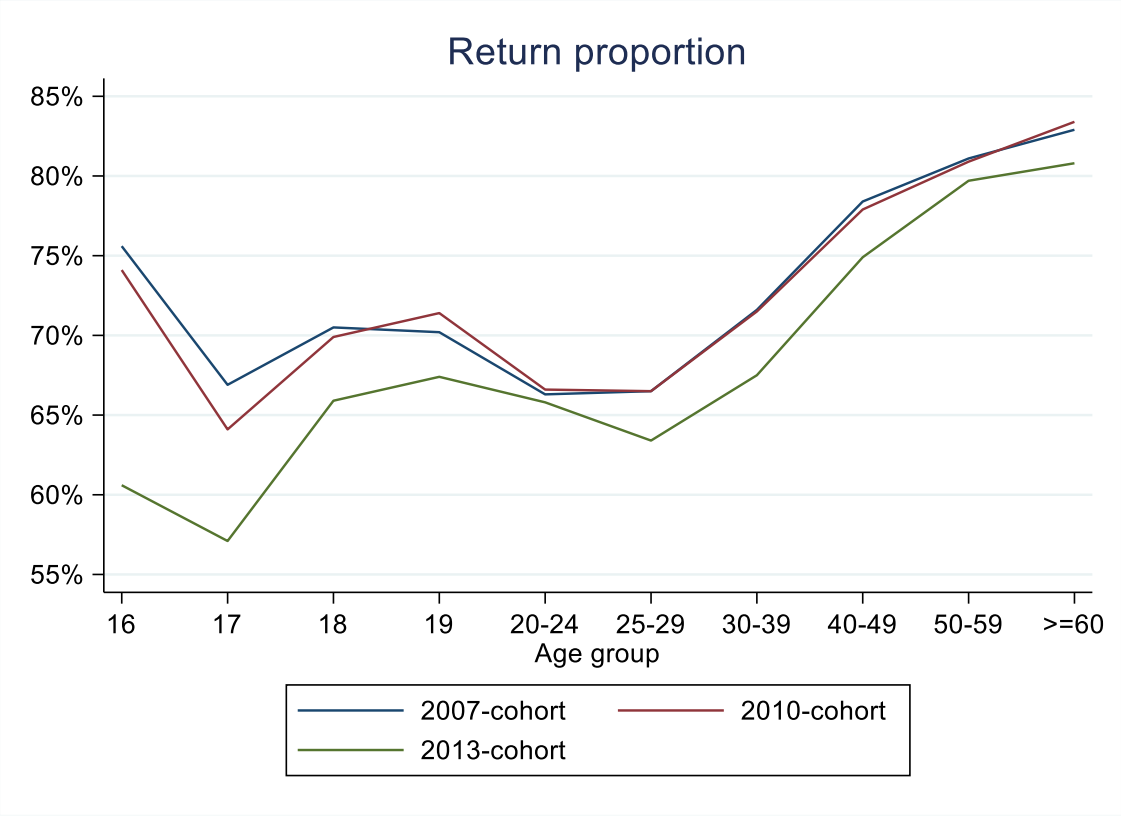

Figure 3 Return proportion by age group

Figure 4 shows the proportion of donors returning to donate by age at first donation for each cohort during their respective follow-up period. The three oldest age groups had the highest return proportion and a higher proportion of them returned earlier in all cohorts. For all cohorts, the majority of returning donors returned within the first 2 years of starting donation. After 2 years, the return proportion relatively plateaued until the end of the follow-up.

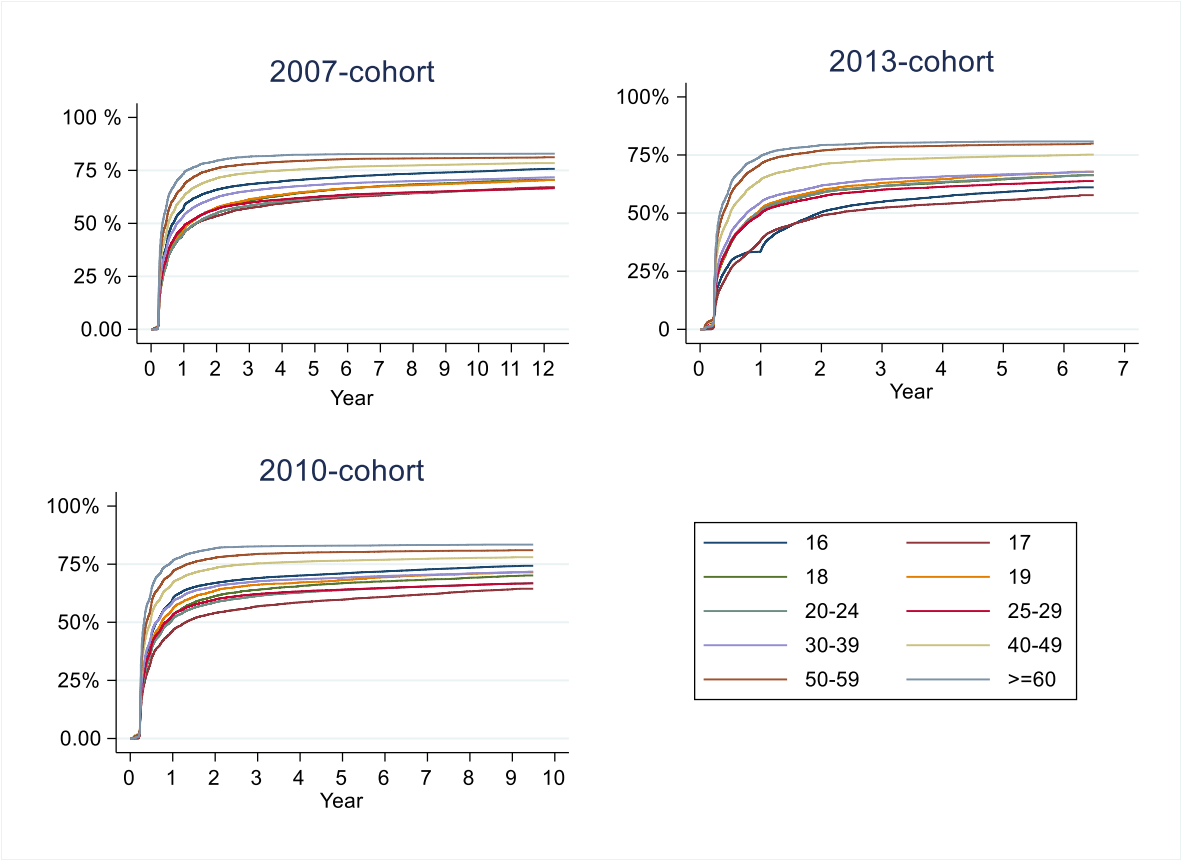

Figure 4 Time taken to return by age at first donation

Poisson regression models adjusted for sex, blood group, and location of donation showed that overall, the middle-aged (40-50 years old) and older donors (<50 years old) are consistently more likely to return to donate. For donors aged 30 and older, as the age at first donation increased donor return also increased consistently in all cohorts (highest in ≥60 years age group, 2007 Relative Risk (RR) 1.23, 2010 RR 1.24, 2013 RR 1.21, all $p<0.05$). Young donors age 18 and 19 had a higher likelihood of making a repeat donation in cohort-2007 and cohort-2010 but was not significantly different in 2013 cohort compared to the reference group. The 17-years donors had similar return to the reference group in 2007-cohort whereas in 2010- and 2013-cohort they had significantly lower return. The 16-years donor return was 1.12 and 1.11 times higher compared to 20-24 years group in 2007- and 2010-cohort but it was significantly lower in 2013-cohort (RR: 0.91).

The overall model showed that female donors were more likely to return in the 2007- and 2010-cohorts (2017 RR 1.02, 2010 RR 1.02, all $p<0.05$), but the difference was not significant for the 2013-cohort. s. When I restricted the regression model to donors aged ≥18-years, I did not find any significant difference in the likelihood of return by sex (Female 2007 RR 1.01 (95% CI 0.99-

1.02), 2010 RR 0.99 (95% CI 0.98-1.01), 2013 RR 0.99 (95% CI 0.97-1.00). Sex-stratified return proportion can be found in Appendix 2.

Table 3 Adjusted relative risk of return by age at first donation

Variables	2007 Cohort			2010 cohort			2013 cohort		
Age groups	RR	95% CI		RR	95% CI		RR	95% CI	
16	1.12	1.09	1.15	1.11	1.08	1.13	0.91	0.88	0.94
17	1.00	0.97	1.03	0.96	0.93	0.99	0.86	0.83	0.89
18	1.06	1.02	1.09	1.05	1.01	1.09	1.00	0.96	1.04
19	1.06	1.02	1.10	1.07	1.03	1.11	1.02	0.98	1.07
20-24	1.00	(reference)		1.00	(reference)		1.00	(reference)	
25-29	1.00	0.98	1.03	1.00	0.98	1.03	0.97	0.94	0.99
30-39	1.07	1.05	1.10	1.07	1.05	1.10	1.02	1.00	1.05
40-49	1.17	1.14	1.20	1.16	1.13	1.19	1.13	1.10	1.16
50-59	1.21	1.18	1.24	1.21	1.17	1.24	1.20	1.16	1.23
≥60	1.23	1.19	1.28	1.24	1.20	1.29	1.21	1.16	1.26
sex									
Male	1.00	(reference)		1.00	(reference)		1.00	(reference)	
Female	1.02	1.01	1.03	1.02	1.00	1.03	1.01	0.99	1.02
Blood groups									
Other groups	1.00	(reference)		1.00	(reference)		1.00	(reference)	
O negative	1.11	1.08	1.13	1.14	1.11	1.17	1.15	1.12	1.18
Location									
non-metro	1.00	(reference)		1.00	(reference)		1.00	(reference)	
Metro	0.94	0.93	0.96	0.97	0.96	0.98	0.94	0.93	0.96

Note: the multiple regression model included sex, blood groups, metro location.

3.4.3 Donation career until follow-up

Figure 5 showed that donors aged 25-29 years had the shortest donation career in the 2007-cohort and 2010-cohort, whereas the donation career was shortest for those aged 17 years

donor in 2013-cohort. In all three cohorts, donors who first gave their donations at 40-59 stayed active as a donor the longest compared to the other groups.

The group that had the longest donation career in each cohort are 40-49 years (4.0 years, sd 4.1 (2007-cohort)), 50-59 years (3.2 years, sd 3.1 (2010-cohort) and 2.5 years, sd 2.2(2013-cohort). The 25-29 years group had the shortest donation career in 2007 (3.1 years, sd 3.9) and 2010 (2.4 years, sd 3.0), while the 17-year-old group had shortest donation career in 2013-cohort (1.7 years, sd 2.1).

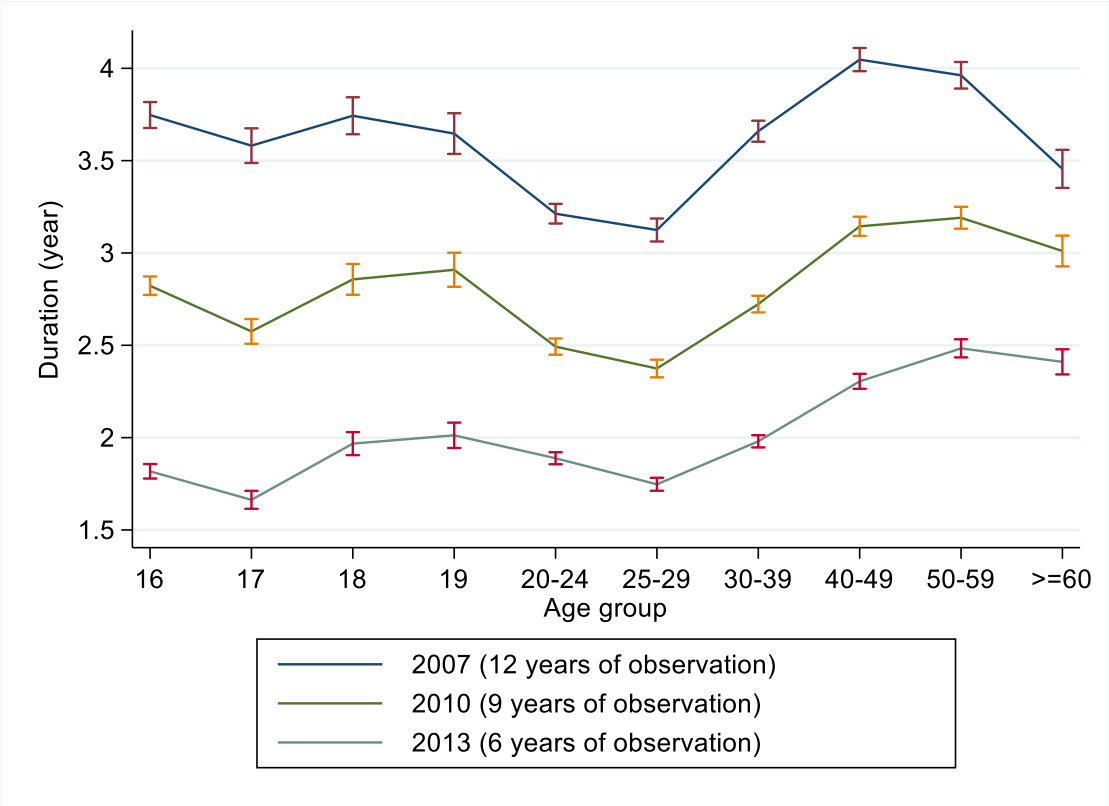

Figure 5 Donor's donation career by each age group

3.4.4 Donation yield for whole blood donations

In all cohorts, the whole blood donation yield was similar up to age 25-29, and thereafter increased consistently as the age at first donation increased. Donors aged ≥60 years donated the most frequent throughout the follow-up period [8.9 times (sd 9.1), 7.9 times (sd, 7.5) and 6.4 times (sd, 5.6) in 2007-, 2010-, and 2013-cohort, respectively] (Figure 6). Figure 6 suggested that this pattern was similar in all cohorts when the yield was examined for males and females separately. Figure 6 also shows a widening gap in whole blood yield between the two genders for donors aged 25 or older. This gap was also found in sex-stratified results for plasma donation except for the oldest group (see Appendix 3)

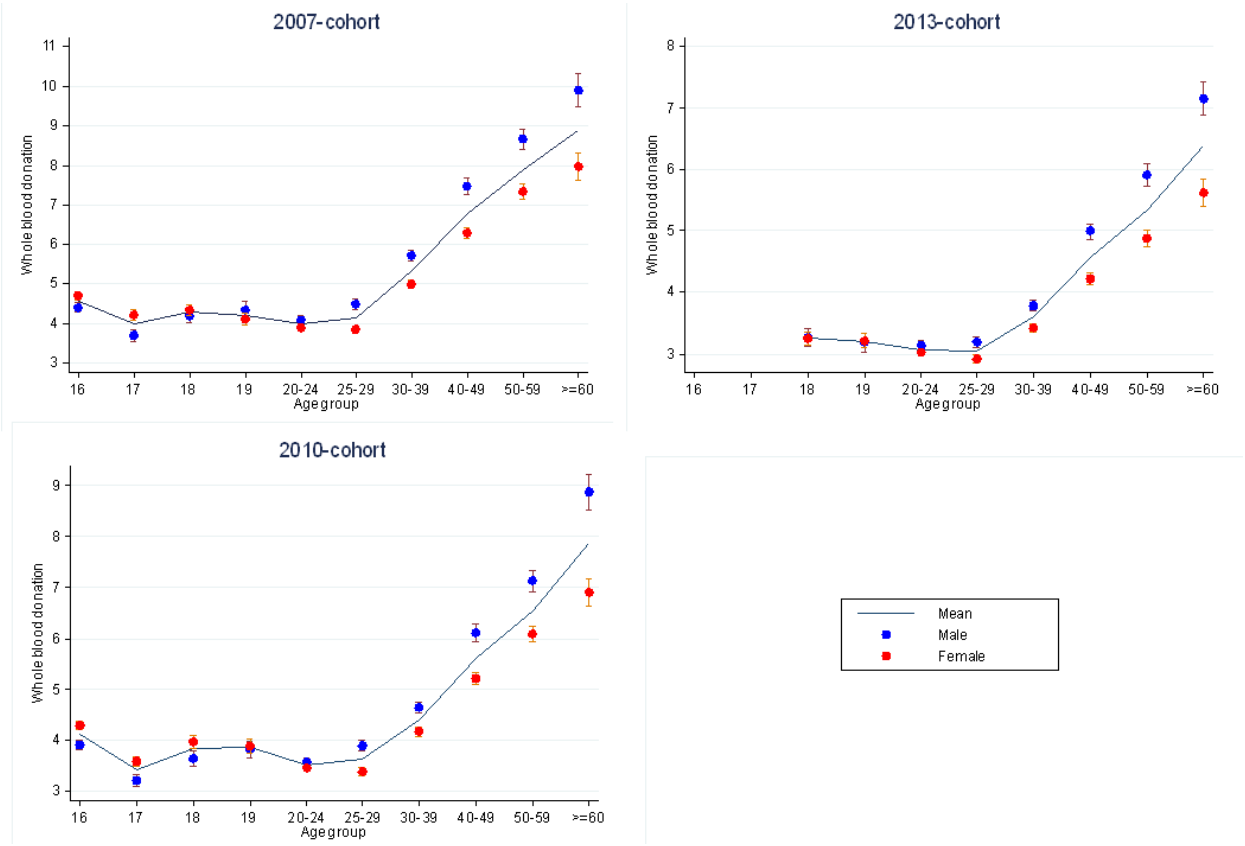

Figure 6 Whole blood donation yield

3.4.5 The ratio of whole blood donation rates between each group

In the 2007-cohort, compared to the reference group of donors aged 20-24, donors who started donating at 16, 18, 19 had a higher rate of donation (RR 16-year 1.15, RR 18-year 1.08, RR 19-year 1.06, all $p>0.05$) whereas the rate of donation increased consistently as the age at first donation increased onwards from 24-29 years group (Table 4,). The rate of donation was highest in donors aged ≥60 years (RR 2.16, 95% CI 2.09 – 2.22).

Overall, the trend in the donation rate was similar in all cohorts suggesting that the rate of donation was similar for a follow-up period of 6-12 years. Also, the rate in males and females had a similar trend except for some minor variations (see Table 4). Analyses showed that the donation rate in males was higher compared to females in all cohorts (RR 2007-cohort 1.09, RR 2010-cohort 1.06, RR 2013-cohort 1.11, all $p<0.05$)

Table 4 Age-wise donation rate for whole blood donations

Whole blood	2007 Cohort											
	Overall						Sex- Stratified, adjusted					
	Unadjusted			Adjusted			Male			Female		
Age group	RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI	
16	1.15	1.12	1.17	1.11	1.09	1.14	1.05	1.01	1.08	1.17	1.14	1.20
17	1.00	0.97	1.02	0.98	0.95	1.00	0.89	0.86	0.93	1.05	1.02	1.09
18	1.08	1.05	1.10	1.08	1.05	1.10	1.03	0.99	1.07	1.11	1.07	1.15
19	1.06	1.03	1.09	1.05	1.02	1.09	1.05	1.00	1.10	1.05	1.02	1.09
20 - 24	1.00	(reference)		1.00	(reference)		1.00	(reference)		1.00	(reference)	
25 - 29	1.04	1.02	1.06	1.04	1.02	1.06	1.10	1.07	1.14	0.99	0.96	1.01
30 - 39	1.34	1.32	1.37	1.31	1.29	1.33	1.38	1.34	1.42	1.25	1.22	1.28
40 - 49	1.71	1.68	1.74	1.66	1.63	1.70	1.79	1.73	1.84	1.57	1.53	1.61
50 - 59	1.99	1.95	2.03	1.93	1.89	1.97	2.07	2.00	2.14	1.83	1.78	1.88
≥60	2.24	2.17	2.30	2.16	2.09	2.22	2.36	2.26	2.47	1.98	1.91	2.06
Sex												
Female		N/A		1.00	(reference)			N/A			N/A	
Male		N/A		1.09	1.08	1.10		N/A			N/A	
	2010 Cohort											
Age group												
16	1.17	1.15	1.20	1.16	1.14	1.18	1.08	1.04	1.11	1.22	1.19	1.26
17	0.97	0.95	1.00	0.97	0.95	0.99	0.90	0.86	0.93	1.03	1.00	1.06
18	1.09	1.06	1.12	1.09	1.06	1.12	1.01	0.97	1.06	1.15	1.11	1.19
19	1.10	1.07	1.13	1.10	1.07	1.13	1.06	1.01	1.11	1.12	1.08	1.17
20 - 24	1.00	(reference)		1.00	(reference)		1.00	(reference)		1.00	(reference)	
25 - 29	1.03	1.01	1.05	1.03	1.01	1.05	1.10	1.07	1.13	0.98	0.95	1.00
30 - 39	1.25	1.23	1.28	1.24	1.21	1.26	1.29	1.25	1.33	1.19	1.16	1.22
40 - 49	1.60	1.57	1.63	1.57	1.54	1.60	1.70	1.65	1.75	1.48	1.44	1.51
50 - 59	1.87	1.83	1.91	1.83	1.79	1.87	1.96	1.90	2.03	1.73	1.68	1.77
≥60	2.25	2.18	2.31	2.19	2.14	2.26	2.45	2.35	2.55	1.96	1.89	2.03
Sex												
Female		N/A		1.00	(reference)			N/A			N/A	
Male		N/A		1.07	1.06	1.08		N/A			N/A	

	2013 Cohort											
	Overall						Sex- Stratified, adjusted					
	Unadjusted			Fully adjusted			Male			Female		
Age group	RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI	
16		N/A			N/A			N/A			N/A	
17		N/A			N/A			N/A			N/A	
18	1.06	1.03	1.09	1.07	1.04	1.10	1.05	1.00	1.09	1.08	1.04	1.12
19	1.04	1.01	1.08	1.04	1.01	1.08	1.01	0.96	1.06	1.07	1.03	1.11
20 - 24	1.00	(reference)		1.00	(reference)		1.00	(reference)		1.00	(reference)	
25 - 29	0.99	0.97	1.01	0.98	0.96	1.00	1.02	0.99	1.06	0.96	0.93	0.98
30 - 39	1.17	1.15	1.19	1.13	1.11	1.16	1.20	1.16	1.23	1.09	1.06	1.12
40 - 49	1.49	1.46	1.52	1.42	1.39	1.45	1.56	1.51	1.61	1.33	1.29	1.36
50 - 59	1.74	1.70	1.78	1.65	1.61	1.69	1.83	1.77	1.89	1.52	1.48	1.56
≥60	2.08	2.02	2.14	1.94	1.89	2.00	2.20	2.11	2.29	1.74	1.67	1.81
Sex												
Female		N/A		1.00	(reference)			N/A			N/A	
Male		N/A		1.11	1.10	1.12		N/A			N/A	

Note: adjusted for sex, blood groups, metro location and history of experiencing adverse events in the first donation (limited to 2013 cohort)

3.4.6 The ratio of plasmapheresis donation rates between each group

A separate analysis of plasma donations showed that donors who started to donate at 50-59 years (RR 1.97, 2007-cohort; RR 1.76, 2013-cohort, all $p<0.05$) and those starting to donate at >=60 years (RR 2.54, 2013-cohort) had the highest plasma donation rate compared to the 20-24 years group. The 25-29 years group had the lowest donation rate in 2007 (RR 0.93) compared to the reference group (20-24 years), while the reference group had the lowest plasma donation in 2010 and 2013. Males significantly donated more plasma compared to females (RR 1.40, 2007-cohort; RR 1.35 2010-cohort, RR 1.41, 2013-cohort; all $p<0.05$)

In the sex-stratified analysis, both males and females under 30 years old (and males < 35 years old in the 2013-cohort) were shown to have no significant difference or minimal difference in the number of donations made with the 20-24 years group. In males,

the 50-59 (RR 1.99, 2007-cohort; RR 1.83, 2013-cohort) and the oldest group (RR 2.19, 2010-cohort) had the highest donation rate compared to the reference group (20-24 years old). In females, the oldest group donated plasma the most frequent compared to the other groups (RR 2.30, 2007-cohort; RR 3.05, 2010-cohort; RR 1.76, 2013-cohort; all $p<0.05$).

Table 5 Age-wise donation rate for plasmapheresis donations

Plasmapheresis	2007 Cohort											
	Overall						Sex- Stratified, adjusted					
	Unadjusted			Fully adjusted			Male			Female		
Age group	RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI	
16	1.14	1.07	1.22	1.14	1.07	1.22	1.15	1.04	1.27	1.12	1.02	1.23
17	1.12	1.03	1.21	1.12	1.03	1.21	1.05	0.94	1.18	1.17	1.05	1.30
18	1.10	1.02	1.20	1.09	1.00	1.18	1.12	1.00	1.25	1.06	0.95	1.18
19	1.00	0.92	1.09	1.01	0.93	1.10	0.96	0.85	1.09	1.06	0.94	1.20
20 - 24	1.00	(reference)		1.00	(reference)		1.00	(reference)		1.00	(reference)	
25 - 29	0.95	0.89	1.01	0.93	0.87	0.99	0.95	0.87	1.04	0.90	0.82	0.99
30 - 39	1.35	1.27	1.43	1.32	1.25	1.40	1.35	1.24	1.46	1.29	1.19	1.41
40 - 49	1.70	1.60	1.80	1.65	1.56	1.75	1.79	1.65	1.95	1.50	1.38	1.63
50 - 59	2.01	1.88	2.15	1.97	1.84	2.11	1.99	1.81	2.19	1.94	1.76	2.13
≥60	1.93	1.59	2.35	1.88	1.55	2.28	1.52	1.16	1.99	2.30	1.75	3.02
Sex												
Female		N/A		1.00	(reference)			N/A			N/A	
Male		N/A		1.40	1.36	1.45		N/A			N/A	
	2010 Cohort											
Age group												
16	1.00	0.94	1.06	1.00	0.95	1.06	1.02	0.94	1.12	0.98	0.91	1.07
17	0.96	0.89	1.03	0.97	0.90	1.04	0.91	0.82	1.01	1.03	0.93	1.14
18	1.10	1.02	1.19	1.11	1.03	1.20	1.13	1.02	1.26	1.10	0.99	1.21
19	1.09	1.01	1.18	1.11	1.02	1.20	1.16	1.03	1.30	1.06	0.95	1.18
20 - 24	1.00	(reference)		1.00	(reference)		1.00	(reference)		1.00	(reference)	
25 - 29	1.00	0.95	1.06	1.00	0.94	1.05	0.99	0.92	1.07	1.00	0.92	1.09
30 - 39	1.18	1.12	1.24	1.17	1.11	1.23	1.16	1.08	1.25	1.19	1.10	1.28
40 - 49	1.67	1.59	1.77	1.67	1.58	1.76	1.68	1.56	1.82	1.65	1.53	1.78
50 - 59	1.86	1.75	1.97	1.86	1.75	1.97	1.82	1.68	1.98	1.90	1.75	2.06
≥60	2.53	2.24	2.86	2.54	2.25	2.87	2.19	1.85	2.58	3.05	2.54	3.66

	2010 Cohort											
	Non-sex-stratified						Sex- Stratified, adjusted					
	Unadjusted			Fully adjusted			Male			Female		
	RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI	
Sex												
Female	N/A			1.00	(reference)		N/A			N/A		
Male	N/A			1.35	1.31	1.39	N/A			N/A		
	2013 Cohort											
Age group												
16	N/A			N/A			N/A			N/A		
17	N/A			N/A			N/A			N/A		
18	1.07	0.99	1.15	1.05	0.98	1.13	1.03	0.93	1.14	1.07	0.96	1.20
19	0.98	0.91	1.06	0.99	0.91	1.06	0.91	0.81	1.01	1.07	0.96	1.19
20 - 24	1.00	(reference)		1.00	(reference)		1.00	(reference)		1.00	(reference)	
25 - 29	1.00	0.95	1.05	0.97	0.93	1.03	0.99	0.92	1.07	0.95	0.88	1.02
30 - 39	1.11	1.05	1.16	1.08	1.03	1.13	1.06	0.99	1.14	1.11	1.03	1.19
40 - 49	1.50	1.43	1.58	1.47	1.40	1.55	1.50	1.40	1.62	1.44	1.34	1.54
50 - 59	1.81	1.71	1.91	1.76	1.67	1.86	1.83	1.69	1.98	1.69	1.56	1.82
≥60	1.78	1.61	1.96	1.73	1.57	1.91	1.71	1.50	1.95	1.76	1.53	2.02
Sex												
Female	N/A			1.00	(reference)		N/A			N/A		
Male	N/A			1.41	1.36	1.45	N/A			N/A		

Note: adjusted for sex, blood groups, metro location and history of experiencing adverse events in the first donation (limited to 2013 cohort)

3.5 Discussion

In this study, I found older donors returned more and donated more. Males donated more than females. The 20-24 years groups were shown to have the lowest proportion of return and lowest future donation rate in all cohorts. The return proportion and donation rate increased as the age at first donation increased from 25-29 years and beyond. Although younger donors aged 18, and 19 years had a slightly higher return and donation rate, it was not as high as the donors starting to donate aged 30 years and over. Although females had a higher likelihood of returning to donate at least once, the donation rate over the follow-up

period was higher for male donors suggesting that males donated more often if they returned at least once.

I observed that younger donors had a relatively lower return rate compared to older donors. A similar result was found in other studies reporting a lower return rate in young donors and progressive increase in return as donors' age increased (23, 29, 34, 55). Relatively lower return rate in younger donors is an issue that is observed in other studies and may be due to a combination of several factors. In 2009, a study conducted in the U.S by Notari and colleagues suggested that donation opportunity may be a contributing factor in young donors (54). To some extent, the lower return rate in the youngest groups may be explained by the period of moving out of high school to college (34, 54). In Australia, the high number of first-time young donors in the past resulted from the Blood Service blood drives in schools and universities across Australia (34), however, once they finish their years in schools and Universities they might not have the same convenience to donate blood. Another reason cited as a cause for the low return rate and successful donation in young donors is the higher number of lifestyle-related deferrals (101). These deferrals include having a new sex partner, having a new tattoo, and increased travel (104).

The middle-aged and older donors are found to be the most reliable donors in the donor panel. I observed that the return proportion increased as the age increased in these donors. Several other studies have reported similar results (29, 52, 57). Studies have identified several factors that may explain the observed association. Older donors have a higher likelihood of knowing someone who had received blood before (105). This awareness of the usefulness of giving blood may be one of the reasons for the higher return rate to donate blood. Another factor that may lead to a higher return in older donors is due to stronger motivation for wanting to save the life of others compared to young donors (105).

I found that the overall number of donations increased as the age at first donation increased to greater than 25 years. Several studies found a similar result (22, 58, 106). For example, Yazer and colleagues reported a proportionate increase in donation rate in donors as the age increased (58). Several studies have explained the relationship between the lower donation rate in younger donors compared to middle-aged and older donors. Several events occurring throughout the life course may prevent younger people from donating repeatedly. These events are childbirth, starting a job, travelling, and losing a job (107). Burgdorf and colleagues (108) reported such findings in younger women may be due to pregnancy and breastfeeding, and the two frequent deferrals in young females because of

anaemia and iron deficiency. This argument is further strengthened by Misje and colleagues (27) that found donation behaviour in women aged 45 years and above was similar to men whereas women below 45 were less likely to donate regularly compared to men. They found that pregnancy was the reason for 32% of women aged less than 45 to stop donating (27), a result similar to another study (109). Another study also reported pregnancy and having children almost doubles the odds of lapsing to donate in both men and women (107). Secondly, a change of residency was quoted as a reason for young donors to stop donating (101). This may be due to data issues in studies that use routine data, as not having a centralised donor database may not capture donation made in other states or provinces. This data, which was obtained from all blood collection sites in Australia, are less likely to be impacted by such issue did not find an increased donation rate in young donors which suggests there are other more important factors. Thirdly, convenience is an important factor that affects donation pattern (110), especially in young donors (82).

Younger people are more likely to get deferred (95) for lifestyle-related deferrals such as taking illegal drugs, having a new body piercing (101), getting a new tattoo and having a new sex partner (104). Getting a deferral has been shown to be associated with lower future return and donation rate in several studies (42, 94). Also, young donors are more likely to experience adverse events such as vasovagal reactions (VVRs) (92), which are shown to increase the risk of non-return and decrease future donations (67, 90, 111). They also have a higher likelihood of becoming iron-deficient compared to older donors (100), thus preventing them from donating. Due to a higher risk of iron deficiency in teenagers, the Australian Red Cross Blood Service has increased the minimum age to make a donation to 18 in 2018 (99).

Looking at the sex differences, females were found to have a higher percentage of returning at least once compared to males. This result is different from other studies as more studies have reported that return behaviour is found to be higher in males (27, 55, 56, 66). This might be explained by the use of different definition of return in those studies. For example, the use of return within the first 12 months in a study from Germany (66).

I also found that males had a higher overall number of donations if they returned to donate at least once, a similar result reported by Öhrner and colleagues (104). However, the Öhrner and colleague's study result may also be due to change in regulations in Stockholm that allow men to donate four times a year and only three times a year for women (104). In

Australia, there is no difference in time-period eligibility for the next donation between men and women. This suggests there are other barriers that prevent women from donating more often. The lower donation rate in females might be attributed to females having a higher deferral rate for anaemia (112), pregnancy and breastfeeding (27), and higher susceptibility to vasovagal reactions (112). Another factor reported that associated with low donation rate in females is anxiety (68).

Although Misje and colleagues found that there was no difference in donation behaviour in men and women older than 45 years among Norwegian blood donors (27), I did not find the same result. I found that starting from 30 years old, there is a significant difference in the number of whole blood and plasma donations made by men and women. There need to be studies exploring the specific barriers that reduce blood donation from older women.

The large size of the cohorts and the nation-wide coverage of data are key strengths of this study. This study used a large nationwide database of all type of donations in Australia. It allowed us to capture donors who had continued donating despite moving to another location. I also examined the study outcomes in multiple cohorts from different periods, which allowed to observe if donation pattern deviated for different time cohorts.

There are some limitations to this study. Firstly, although the length of observation period ranges from 6 to 12 years in the cohorts, it is insufficient to conclude which age group is more productive in blood donation in the long-term. For example, a donor who first donated at 18 years old in 2007 will only be 30 years old at the end of the observation period. This period is a time when young donors are focused on their work, studies and family responsibilities as these factors account for 40 - 49% of donor lapse (109). I could not examine whether donors, who started to donate at a younger age, would continue to donate when they reach middle age. Secondly, I did not have access to several factors that may impact the association between age at first donation and future donation patterns such as education level, socioeconomic status, family history of donation, and substance abuse. These factors have been proven to affect the donation pattern (61, 71, 108, 109), I did not exclude donors who are temporary residents in Australia as they may continue donating blood after leaving the country. Thirdly, log-binomial models could not be used to measure the relative risk of return in donors as the data did not converge. Log-binomial modelling is an appropriate model to estimate the relative risk for common outcomes as the use of adjusted odds ratio overestimate the importance of a risk factor (113). However, Poisson

regression has been shown to produce comparatively similar point estimates and standard errors as log-binomial modelling (102)

3.6 Conclusion

In summary, in all cohorts, I found younger donors had relatively lower return and donation rate compared to donors who started at middle-aged or later. Females returned more often for at least once, but males returned more in the overall follow-up. Within the follow-up period, donor starting to donate at middle-aged and older contributed most to the blood supply compared to younger donors. To meet the short- to mid-term sufficiency of blood supply, recruitment of middle-aged donors appears to be more effective. Due to the limited period of follow-up, I could not conclude that donors who started younger would yield less donation throughout their lives. Future studies should include longer follow-up time to see if young donors return when they reach middle age and enquire more about barriers for repeated donations in younger donors and older women

Chapter 4: Combined discussion

A separate discussion for findings from each of the studies is presented in chapter 2 and 3. In this chapter, I will provide a more general discussion about major demographic factors and their association with return behaviour. This chapter starts with a brief summary of the main findings from both the systematic review in chapter 2 and the cohort study in chapter 3. I will then continue to discuss the association of the major demographic factors with the future donation pattern. Donor's age at first donation and its association with future donation pattern is the focus of this thesis. The effects of sex, deferrals, and adverse events to donation pattern will also be discussed.

4.1 Main findings from the systematic review

The systematic review compared the association between several factors and return behaviour to donate blood in HICs and LMICs. Experiencing or having observed adverse events, anxiety and history of receiving deferrals were consistently shown to decrease return behaviour in both settings. Similarly, positive donation history, positive donation experience, having a convenient location and having short inter-donation interval, were consistently associated with increased return in both settings. While age and level of education had a different effect on return in both groups, and sex was shown to have inconsistent result only in the LMIC group.

This part of the discussion will focus on the effect of age and sex to return behaviour and donation pattern from studies performed in HICs. The majority of studies performed in HICs concluded that donors aged 30 years and older had higher odds of making a repeat donation compared to donors aged younger than 30 years (42, 53, 96). However, the rate of donation decrease as the donors' age increased to more than 60 years (24). All studies from HICs included in the systematic review concluded that men donated more frequently compared to women during the observation period.

4.2 Main results of the cohort study

The retrospective cohort study investigated the association between age at the first donation and the future donation patterns. It showed that those who started donating at a later age were more likely to have a greater number of donations over their lifetime donation career. They have a higher likelihood of making a repeat donation, donated whole blood and other blood products more frequently, and remain as a donor for a longer period of time when compared to younger donors.

I found no significant difference or minimal difference in the donations rates between donors aged less than 30 years. Teen donors did not have a significant difference or were shown to have a minimal (<10%) difference in the number of whole blood donations made when compared to the group with the lowest donation.

The cohort study showed a linear relationship between age and the number of blood donations for donors who started donating at 30 years and above. The groups shown to have donated the most frequently are the 60 years or older for whole blood donation and 50-59 years for plasma donation. In all cohorts, donors who started to donate blood at 50 years or older had donated whole blood almost twice as much as donors who started at 20-24 years of age.

Over the follow-up period, men donated more units of blood than women in all cohorts. Men donated 6 - 10% times more whole blood compared to women. The difference between the number of plasma donations by sex was more marked. Men donated 40% more plasma than women.

The pattern of whole blood and plasma donation based on age persisted when the analyses were stratified by sex. Both men and women showed a linear association from age 30 years to more than 60 years for whole blood donations and from 30-59 years for combined plasma and platelet donations. Those aged 50-59 years and donors aged 60 or more were the most productive plasma and whole blood donors, respectively, compared to the 20-24-year group.

4.3 The association between age at first donation and the donation pattern

The retrospective cohort study showed similar donation rates in all young donors aged < 30 years and a linear increase in the donation rate for donors aged ≥ 30. Several other studies from HICs found similar results. There are several factors thought to motivate individuals to donate blood. Donors often report altruism as the main motivation to donate blood (44, 114). Awareness of the need for blood and knowing someone who had received blood transfusion before have been found to be associated with making a blood donation (104, 105). Different age groups have different motivational factors and barriers associated with blood donation. These factors will be discussed in more detail in each age group separately.

The cohort study showed donors aged less than 30 years donated less frequently compared to donors who first gave blood at 30 years or older. There are several factors causing young donors to participate less in donating blood. Firstly, young donors may prioritise activities other than donating blood. The results of the cohort study showed young donors who started donating at 30 years or younger had a lower likelihood of returning and had a shorter donation career. Donors of this age are in a busy life period where they may start a family or a new job. Events, such as starting a family or getting a new job, were reported to decrease the likelihood of making a repeat blood donation (107). Young donors might not have time (53, 59) and feel donating is inconvenient (82) during this period. Efforts to minimise inconvenience, such as periodical blood drives in workplaces, and reducing waiting period may help to capture and retain young donors as a blood donor.

Secondly, young donors have a higher behavioural risk profile. They were found to have received more lifestyle-related deferrals such as getting a new tattoo, having a new sexual partner, having used recreational drugs, and having travelled to endemic-countries (29, 104). A study in the U.S also reported donors aged 18 to 24 years were the group with the highest transfusion-transmissible infections, such as HIV and hepatitis B infection (115). Deferrals prevent potential donors from donating and potential donors might think they are ineligible to donate blood indefinitely (94). Giving a clear explanation of the nature of their deferrals to donors and asking them to return as soon as they are eligible might increase participation in this group.

Lastly, the lack of awareness of the importance of blood donation might contribute to the low donation rate in young donors. A study from Canada reported young donors were less likely to know someone who had received a blood transfusion (105). They often donate blood because of social pressure from friends and family (114).

Factors causing the lower participation of young people in donating blood in Australia needs to be explored further. Due to the lack of data on deferrals and adverse events, this thesis could not determine whether these factors caused lower participation of young people. Studies that aimed to explore deterrent factors in donating blood in young Australian need to be conducted. The results of these new studies will help policymakers to formulate programs to capture more young donors.

Donors who began donating at 30 years and older were shown to donate more blood than those who started earlier in Australia. Other studies from HICs found similar results. Older

donors were found to donate more blood, returned more often and returned earlier compared to other groups (23, 25, 29, 50, 55, 59). A study from the U.K found increasing return rate and decreasing inter-donation interval as the donors' age increased starting from the age of 25 (29). Donors who returned earlier and returned more in the first year were more likely to make more donations in the future (26). Studies from other countries found several motivations and barriers specific to each age group. It will be discussed more in the following paragraphs.

I found increasing length and donation career and total donations made as the age of the first donation increased from the middle age. This finding might be explained by the availability of time, positive feelings after donating and increased awareness in older donors. The middle-age (45 – 60 years) period is when people usually have a steady job and may not have to care for their children as their children have grown up (81). Having more time to themselves might cause older donors to participate in activities such as donating blood.

Personal satisfaction is one of the motivating factors reported by older donors (114). This positive emotional feeling, often called a 'warm glow', may drive older donors to make subsequent blood donations (116). Donating blood makes older donors feel more positive about themselves. A study in Germany found older donors considered making a successful donation as a good parameter of health (95).

Older donors often have a greater awareness of the need for blood (105). They often reported knowing people who had been treated with blood products or experienced the death of a family member (107). The factors mentioned above - time availability, positive emotional feeling, and awareness – might be contributing reasons for older donors to make repeat blood donations. This continued donation may generate a habit that further explains the higher participation of older donors in blood donation.

The association of age and donation pattern in Australia is similar to other HICs. However, the barriers and motivational factors for donating blood in Australian donors might be different. This thesis did not explore motivational and barriers to donating blood in Australia. More research needs to be conducted to identify specific barriers and motivational factors to donating blood in a specific age group or a specific population in Australia.

4.4 The association between sex and the donation pattern

The results from the cohort study showed that men made more blood (RBCs, plasma and platelet) donation compared to women. This result matched the results from other studies showing higher donations made by men (52, 66, 114). Some countries allowed a different number of maximum donations between men and women, such as in Sweden and Italy, (104, 117) but Bani and colleagues predicted this was unlikely to be the cause of the gender-related differences in donation frequencies (117). This difference might be related to the differences in the motivational factors and barriers to donating blood between both genders, bodily changes in women and women affected more by deferral and adverse events. These factors will be discussed below with the results of studies from the U.S and Europe.

A survey in Canada reported altruism as the main motivational factor for both genders to donate blood (105). They also found different motivations for donating blood for both genders. Male donors were more likely to be motivated to donate blood by getting a remuneration, sense of achievement and recognition from others while females were more affected by the awareness of a need for blood products (105, 114).

There are several barriers to donating blood that affect both genders differently. A survey conducted in the U.S found men were more concerned with blood donation interfering with their free time while females were more affected by the expectation of trauma, fear of needles and blood and feeling unwell (118).

Aside from the differences in motivational factors and barriers to donate between the two genders, two European studies explain the differences in donation frequencies between men and women. Women experience a greater number of changes in their bodies than men over time such as pregnancy, menopause, and changes in body weight, which makes them ineligible to donate (117, 119). Having young children may also contribute to lower donation rates in women, as was shown in the Netherlands and Italy (107).

Lower donation rates for women is also associated with adverse events and deferrals. Adverse events affect women more than men. Studies from the U.S and Australia show that women have a lower return rate when both genders have experienced an adverse event (67, 111). In a study from the U.S, female sex was found to be associated with a higher chance of experiencing adverse events (120). Conversely, adverse events were not considered a major issue for young men to continue donating (104). Women were more likely to get

deferred than men in each age group (121). These deferrals are due to pregnancy and lactation, especially in those aged 45 or younger (27), and low haemoglobin especially in premenopausal women (121, 122).

In the cohort study, I found a similar proportion of return donation between men and women aged 30 years and older (see Appendix 2). However, for donors aged 30 years and older, men significantly donated more frequently than women. The difference in the donation yield by both genders increases as the age increased for donors aged 30 years and older (Figure 6). This means that more women returned at least once to donate blood, but they did not return as frequent as men.

The lower number of blood donations made by Australian women might be related to adverse events and deferrals. Although this study did not explore the incidence of deferrals and adverse events in women, Australian data on donors adverse events in 2013 showed higher adverse events rate in women compared to men across all age groups (123).

Efforts to reduce the incidence of adverse events in women might increase women participation in donating blood. More research to explore the gender differences in blood donation in Australia, including the effects of deferrals and adverse events, is needed to better understand the cause of lower participation of women in blood donation.

4.5 The association between adverse events (AEs) and the donation pattern

There are risks of experiencing adverse events from donating blood. These events include vasovagal reactions (VVRs), phlebotomy-related complications, and iron deficiency. Vasovagal reactions range from dizziness, pallor, weakness, hypotension, to syncope or loss of consciousness. It can occur during or shortly after blood donation at the transfusion site (immediate-type) or within 24 hours of visiting the transfusion site (delayed-type). Phlebotomy-related complications, such as sore arm, bruising and even permanent disability, can occur (124).

Iron deficiency is common among regular whole blood donors (124), but has not been found to be associated with regular plasma donors (125). Evidence shows that each donation causes a loss of 213 to 236 mg of iron leading to depletion of body iron stores (124). In Australia, a study in 2014 reported the incidence of iron deficiency was 6.3% and 26.4% in male and female whole blood donors, respectively (126). Iron loss can lead to many other symptoms such as fatigue, decreased physical and job performance, and

cognitive changes. It has also been found to cause restless leg syndrome (124). Iron deficiency anaemia is more common in women because of lower iron reserves and increased loss due to menstrual blood in women (124).

Additional risks are present for plasma donation. These risks are related to the longer duration of plasma donation and the use of anticoagulation in apheresis donation (124). Donors reported having experienced more painful arm due to the longer period of the needle in the arm (127). The incidence of venepuncture-related complications in apheresis donations has been reported to range between 0.5% to 6% (124). Plasma donation also poses a higher risk of hypovolaemia and vasovagal reactions due to the duration of the procedure and the higher volume of blood removed (124).

Citrate toxicity (citrate-induced symptoms) is an adverse event specific to plasmapheresis that is caused by the usage of anticoagulation. A review from Austria reported mild citrate-induced symptoms, such as perioral tingling, malaise, nausea and chills, occur in up to 80% of donors and are found more frequently in women (124). Other events with lower incidence (up to 0.4% of all procedures) include convulsions, chest tightness, hypertension and laryngeal spasm (124).

In 2016, the National Blood Authority reported the incidence of AEs in Australia in 2013-14 (123). It was found that 2.68% of all blood donations resulted in an adverse event. Immediate-type VVRs, such as dizziness or lightheadedness, were the most common type of AEs (18 % of all AEs). The rates of each adverse event were as follow : immediate-type VVRs (176 events per10,000 donations), delayed-type VVRs (27/ 10,000 donations), citrate reaction (31 per 10,000 donations), haematoma (13 per 10,000 donations), painful arm (11 per 10,000 donations), and nerve irritation or injury (4 per 10,000 donations).

Experiencing AEs has been shown consistently to reduce the likelihood of making subsequent donations in all donors and prolong return time in several countries such as the U.S, the Netherlands, and Australia (41, 67, 91, 111). A study by Newman and colleagues showed a reduction in return rates in donors experiencing any events (67). The return rate was found to be lower in donors experiencing major events compared to donors with minor or no reactions (aOR of return in major reactions 0.31, minor reactions aOR 0.59. Compared to donors with no reactions) (41). Although getting a small bruise following a donation might not be a big problem, a study reported that observations of AEs may decrease return and increase levels of perceived risk of blood donation (80). A recent study

from Australia showed longer return time in those experiencing events (median 161 days following syncope vs 39 days following an uncomplicated donation) (111).

The lower overall lifetime donations for young donors in the cohort study might be related to AEs. Younger donors are more prone to all types of AEs compared to older donors (120, 128), especially donors aged <20 years old (128). In 2013, Australian donors aged under 18 years had the highest rate of adverse events (71.1 events/ 1000 donations) compared to other age groups, followed by the 18-20 years group (40.3 events/ 1000 donations) (123). Moreover, a recent study from Australia showed young donors were less likely to make a repeat donation after experiencing an adverse event (129). The likelihood of making a repeat donation after experiencing an event increases as donors' age increased (41, 111, 120). The higher rate of adverse events and the lower likelihood of making a repeat donation after experiencing adverse events in young donors explain the lower donation rate in Australian young donors.

4.6 The association between deferrals and future donation pattern

A deferral is a situation where a donor is ineligible to donate based on the criteria applied to protect the health and safety of both the donors and transfusion recipient (43). Deferrals could be given temporarily for a limited time period or permanently based on the type of deferrals.

Deferrals have been shown to prolong return time, decrease return rate (42, 93), reduce donation frequency (93), and result in donor loss (94). For donors who returned to donate, deferred donors returned longer than non-deferred donors (median 13.2 weeks for deferred group vs 2.7 weeks in non-deferred groups) (93). Deferred donors also significantly donated less blood compared to non-deferred group (mean donation of 0.8 in deferred vs 1.7 donations in non-deferred groups in the 3-year follow–up) (93). Zou and colleagues estimated deferrals-associated loss of 647,828 donors in the U.S from 2001 to 2006 (94).

Some deferrals are more prevalent in specific age groups. Young donors (aged 18-29 years) have been found to be deferred for lifestyle-related reasons more frequently, while older donors are more likely to be deferred for conditions related to reduced health status (101). Some examples of lifestyle-related deferrals are using illegal drugs, having a body piercing, having a new sex partner, and travel-related deferrals. Health-related deferrals frequently mentioned in studies are low haemoglobin, low or high blood pressure, and cardiac diseases (95).

Deferrals reduced blood donation in several ways. Deferrals cause a negative emotional response in donors, which disrupts donors' perception of their capability, health status (37) and their confidence in their ability to donate blood (93). Deferrals also disturb the regularity of donation and reduce donors' expectation that a future donation will be accepted (37).

The lower donation rate in young donors in the cohort study may be influenced by deferrals. Young donors (< 20 years old) were shown to have a higher deferral rate compared to older donors (95, 121). Australian studies investigating the incidence of deferrals in each age group could not be found. Being younger (<30 years old) is also associated with a lower likelihood of making a repeat donation after receiving deferrals (24). An Australian study in 2011 confirmed this finding (93).

Although the cohort study could not conclude that deferrals prevented young Australian donors to donate blood, deferrals may be a significant factor in this finding. Age-stratified studies measuring the direct impact of deferrals on donation pattern in Australia are required.

4.7 Ways to improve donor retention

Identifying barriers to blood donation in specific populations will lead to group-specific interventions which may increase donation. Reducing the incidence of adverse events and the impact of deferrals might also increase donor retention. Several interventions have been shown to be effective in specific age groups and genders.

Gemelli and colleagues (40) studied the effects of a post-donation short messaging service (SMS) on whole blood donors and found higher odds of returning for donors receiving a reminder SMS. This effect was shown similarly in both sexes and in all age groups. Phone call reminders also had similar results in first-time donors (87). A similar study in Germany on first-time donors showed post-donation contact increased return only in males (84). As time constraints were a major issue for returning to donate, accessibility of donation centres and blood donation buses is essential. Strategies to integrate blood donation routines into a busy life can be developed with the aid of a mobile application, connecting donors to personalised data and invitations, and supporting dialogue with the blood donation centre (104).

I found lower overall donation rates in young donors and female donors. The discussion will focus more on ways to retain these groups as active blood donors. In females, some of the most recognized barriers to donating are higher deferral rates especially due to low haemoglobin levels and higher adverse events rate (117). Addressing these problems might increase retention in women (130).

Since young donors are more likely to report inconvenience as a reason to stop donating, providing them with a convenient place with extended hours might increase donation in this age group (82). Carey and colleagues found that the majority of donors aged 32 years or less in the U.S. donated in mobile collection sites and suggested mobile collection sites may increase the number of young donors (83). Japan included blood donation in the school curriculum in 2013 to increase blood donors among young donors (7). Having young donors recruit friends might be a feasible way to increase young donors pool (101), as young donors often reported having support from their peers as one of the motivational factors to donate blood (114). Social media may also be used to increase young donors (131). A study in the U.S suggested higher social media use in young people may be a way to give health information to young people (132). Older donors (65 and older) in the U.S reported preferring phone calls over messaging or electronic mails as a way of receiving contacts from the blood bank (133).

Reducing the incidence of AEs might reduce donor loss. Water loading (WL) and applied muscle tension (AMT) are some of the interventions proven to be beneficial in reducing the incidence of VVRs (134). Ingesting 500 ml of water 30 minutes before blood donation reduced the risk of dizziness and light-headedness in novice blood donors (135). This effect was also found in young donors (136). A study on healthy adults aged 18-70 years found both 500 ml of water and isotonic fluid had a similar effect in reducing VVRs (137). Muscle tension reduced syncopal-type reactions (137, 138) and increased donor return (86, 89). It is thought AMT reduced anxiety or physiological consequences of anxiety (138). Another approach suggested to decrease VVRs is to reduce blood collection volume from 500 ml to 400 ml (139).

To address iron deficiency and anaemia in frequent blood donors, several studies suggested ferritin measurement and oral iron supplementation to prevent blood donation induced iron deficiency (122, 140). Baart and colleagues suggested prolonging the minimum donation interval in donors found to have a relatively lower haemoglobin (141).

Several studies have suggested ways to increase donor retention after receiving deferrals. These efforts fall into two categories: giving clear information and contact following donation. Giving clear information to donors regarding the nature of their deferral, their eligibility, and when they may return is required (121). Information given could reduce the negative emotional experience and enhance the perceived benefits to donors such as donor's safety (37). Giving information to whole blood deferred donors about their eligibility to donate plasma was shown to be effective (142). This may help convert whole blood donors to plasma donors to satisfy the demand for plasma. This information also allows a donor to stay engaged with the blood centre and maintain their identity as a blood donor (143). A recent literature review on donor deferral showed contact following donation attempt increased return in previously deferred donors (143). Contacting donors as soon as they are eligible to donate again may help encourage donation. Katz and colleagues found a similar return among malaria-deferred donors who were contacted after being eligible and non-deferred repeat donors (144).

Another effort to minimize the negative effects of AEs and deferrals is to encourage donors to make a repeat donation. A positive donation history was shown to alleviate the negative effects of adverse events and deferrals on return donation. Two studies from Australia and the U.S have shown that repeat donors had a higher likelihood of making a repeat donation after experiencing an adverse event compared to first-time donors who had experienced an adverse event (67, 111). Another study from the U.S reported a higher return rate in donors with positive past donation history compared to first-time donors after receiving deferrals (42).

4.8 Limitations

This thesis has several limitations. Firstly, the relatively short period of follow-up of the cohort study could not capture young donors' donation pattern when they reach middle age. Young donors, when they reach middle age might show a similar donation pattern to donors who first gave blood at middle age due to having more time. Secondly, the cohort study did not control for other important confounders, such as deferrals and adverse events, for all cohorts due to limited data on these factors. Lastly, most of the reference studies are derived from studies conducted overseas as there were no prior relevant studies conducted in Australia.

Chapter 5: Conclusions and recommendations

5.1 Conclusions

This thesis aimed to improve our understanding of the pattern of blood donation in Australia particularly the association of the donors' age at first donation and the future donation pattern while adjusting for the effect of other important demographic factors.

Donation behaviour is affected by many factors. While having experienced donating blood, short inter-donation interval, receiving incentives, and donors' positive satisfaction were shown to positively associated with future donation in the systematic review, the opposite was found for adverse events and deferrals. Demographic factors affect donation pattern differently in different countries. In high-income countries, being older and being male were positively associated with more blood donation. However, studies from low-and-middle-income countries found younger age as a positive predictor of return.

In Australia, donors who started giving blood at the age of less than 30 years were shown to have a lower donation rate compared to donors aged 30 years or older. Although women had a higher likelihood of making a repeat donation, they donated whole blood and plasma less frequently compared to men during the follow-up period. The difference in the number of donations made between both genders increased as the donors' age increased.

The cohort study showed similar results to studies from other high-income countries. Demographic factors associated with an increased future donation in Australia are older age at the first donation and being male. Experiencing adverse events and receiving deferrals were negatively associated with return behaviour.

5.2 Recommendations

Based on the findings of this thesis, it appears that the recruitment of new donors aged 30 years and above is a sensible approach to meet the short- to mid-term need for blood and blood products. However, today's young donor will be tomorrow's adult donor. Hence, it is crucial to understand the reasons behind the lower return rate among younger donors and find innovative and effective strategies to attract and retain younger donors as well.

This thesis has provided a deeper understanding of the blood donation pattern in Australian new donors. It has also generated questions for future studies. Further studies, particularly qualitative studies, need to be conducted to better understand the specific blood donation patterns in different age groups. Understanding the motivations and barriers to donating blood in each group of donors, especially in a younger age group will help improve

recruitment and retention strategies. Lastly, a cohort study with a longer period of follow-up is required to examine if young donors will resume blood donation after reaching middle age.

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Appendices

Appendix 1 Studies included in the systematic review

SN	Title	Year Published	Study type	Donors (first time or repeat)	Donation type	Country	Research questions, aims or objectives of the study	Sample size	Quality scale	Reference
1.	Well-being and return rate of first-time whole blood donors	2019	I	First time	WB	Germany	Measure the association between well-being and return to donation in first-time donor	102 participants in the intervention group and 115 in the control group	N/A	(84)
2.	Determinants of blood donation status in Malaysia: profiling the non-donors, occasional donors and regular donors	2018	CS	Both	WB	Malaysia	Describe the sociodemographic and lifestyle-related factors associated with blood donation status of non-donors, occasional donors, and regular donors.	550	8	(71)
3.	The association between interval from acceptance to first-time donation missed first appointment and future donation behaviour	2018	CO	First time	Mixed	Norway	Are missed first appointment and interval to first-time donation related to future donation pattern in first-time donors?	807	9	(53)
4.	Motivational factors for blood donation, potential barriers, and knowledge about blood donation in first-time and repeat blood donors	2018	CS	Both	Mixed	Ghana	Factors motivating and inhibiting blood donation in first time and repeat donors	350	5	(73)

5.	Reasons to end the donor career: a quantitative study among stopped blood donors in the Netherlands	2018	CS	Not Specifically Stated	WB	The Netherlands	Describe reasons to stop donating blood	1865 stopped donors	9	(81)
6.	Evaluation of the impact of a personalized post-donation short messaging service on the retention of whole blood donors	2018	I	Not Specifically Stated	WB	Australia	Investigate whether receipt of a personalized post-donation SMS promoted donor retention	2605 donors and 1796 controls	N/A	(40)
7.	Psychosocial characteristics of blood donors influence their voluntary nonmedical lapse	2018	CO	Not Specifically Stated	Mixed	The Netherlands	Investigate whether psychosocial characteristics, measured before the first donation, similarly predict subsequent voluntary nonmedical lapse.	2964 donors	8	(79)
8.	Trends in age and red blood cell donation habits among several racial/ethnic minority groups in the United States	2017	CS	Both	WB	The United States	Describe donation patterns by donor status, age, and race/ethnicity in the United States	5,907,614 donors (1,428,986 first-time and 4,478,628 repeat donors)	7	(58)
9.	Motivational factors for blood donation in first-time donors and repeat donors: a cross-sectional study in West Pomerania	2017	CS	Both	WB	Germany	Analyse motivational factors for blood donation in different donor groups	2443 participants, 14·3% first-time and 85·3% repeat donors.	8	(114)
10.	Changes in the Whole Blood Donor Population in South-West	2017	CS	First time	WB	Germany	Compare first-time donor (FTD) characteristics and their return rates.	86,995 donors in 2010 to	9	(66)

	Germany: 2010 versus 2016							66,163 donors in 2016		
11.	Frequent whole blood donors: understanding this population and predictors of lapse	2017	CO	Both	WB	Australia	Describe the demographic profile of Australian frequent whole blood donors and to determine predictors of a lapse within this group.	90,867 donors	9	(34)
12.	A motivational interview promotes retention of blood donors with high internal motivation	2017	I	Not Specifically Stated	WB	The United States	Determine the ability of a motivational interview to promote internal motivation for giving blood and future donation attempts	484 donors	N/A	(85)
13.	Who returns and becomes a regular blood donor? Analysis of a donor database in Fukushima, Japan	2017	CO	Both	WB	Japan	Investigate the characteristics of a Japanese frequent blood donor club members	2030 first-time and 2137 returning donors	9	(52)
14.	Analysis of the Factors Affecting the Interval between Blood Donations Using Log-Normal Hazard Model with Gamma Correlated Frailties	2016	CO	Both	Mixed	Iran	Determine the effective factors on the interval between the blood donations	424 donors	7	(64)
15.	Why Do Blood Donors Lapse or Reduce Their Donation's Frequency?	2016	CS	Both	WB	Canada	Determine reasons for lapse	1879 donors	7	(109)
16.	Increasing first-time blood donation of newly registered donors using	2016	I	First time	Mixed	The Netherlands	Intervention study aims to increase first-time return behaviour of newly registered	937 donors	N/A	(69)

	implementation intentions and explicit commitment techniques						donors using implementation intentions and explicit commitment techniques.			
17.	Blood donor to inactive donor transition in the Basel region between 1996 and 2011: a retrospective cohort study	2015	CO	First time	WB	Switzerland	Study the behaviour of first-time blood donors in the region of Basel, Switzerland, between 1996 and 2011 and describes factors associated with a transition from active to inactive donor in two successive first-time donor cohorts (1996–2002, 2003–2008).	17 430 donors	9	(56)
18.	Factors Associated with Repeat Blood Donation at the Northern Zone Blood Transfusion Centre in Tanzania	2015	CS	Not Specifically Stated	Mixed	Tanzania	Describe factors associated with repeat blood donation.	454 donors	8	(72)
19.	An analysis of first-time blood donors return behaviour using regression models	2015	CS	First Time	Mixed	Iran	Analyse blood donor return behaviour.	864 first-time donors	8	(32)
20.	Blood donors in England and North Wales: demography and patterns of donation	2015	CS	Both	WB	The U.K.	Present demographic characteristics of England and North Wales donors	348,740 donors with 2,854,460 donations .	N/A	(29)
21.	First-time whole blood donation: A critical step for donor safety and retention on first three donations	2015	CO	First time	WB	Belgium	Determine the impact of the donor's retention in relation to the occurrence of vasovagal reaction for the first three blood donations.	33,279 first-time donors	9	(90)

22.	Characteristics of donors who do or do not return to give blood and barriers to their return	2014	CO	Not Specifically Stated	WB	, The Netherlands	Factors associated with return behaviour in blood donors	4,901 donors	8	(57)
23.	Monetary compensation and blood donor return: results of a donor survey in southwest Germany	2014	CO	Both	WB	Germany	Return behaviour in compensated vs non-compensated first-time donors in Southwest Germany.	3,077 non-compensated and 738 compensated first-time donors	7	(78)
24.	Risk factors for complications in donors at first and repeat whole blood donation: a cohort study with assessment of the impact on donor return	2014	CO	Both	WB	The Netherlands	Assess the 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.	28.786 FT donors 522.958 repeat donations	7	(31)
25.	The influence of adverse reactions, subjective distress, and anxiety on the retention of first-time blood donors	2013	CO	First time	Mixed	The Netherlands	Investigate the effects of adverse events (i.e., needle reactions, fatigue, and vasovagal reactions) and feelings of distress and anxiety on retention of first-time blood donors.	1278 donors	7	(91)
26.	Long-term return behaviour of Chinese whole blood donors	2013	CO	Both	WB	China	Understanding donor return behaviour	54267 donors	9	(61)
27.	The effects of leg crossing and applied tension on blood donor return	2013	I	Not Specifically Stated	mixed	The United States	Does practising applied tension improve blood donor return?	133 standard applied tension 131 tension with legs crossed	N/A	(86)

								140 control		
28.	Donation return time at fixed and mobile donation sites	2012	CO	Not Specifically Stated	WB	The United States	The effects of fixed donation sites vs mobile sites on donation return pattern	4,990,619 donations	9	(83)
29.	Relationship between first-year blood donation, return rate for subsequent donation and demographic characteristics	2012	CO	First time	Mixed	Iran	The relationships between donor demographics, number of donation in the first year, and first inter-donation interval and return pattern in Iran	1,500 donors	9	(63)
30.	Vasovagal reactions in Chinese blood donors: impact on donor return	2012	CO	Both	WB	Hong Kong	Association between vasovagal reactions and donor retention in Hong Kong.	208 235 donations	8	(92)
31.	Epidemiological Profiles of Foreign-Born and US-Born Hispanic Blood Donors in a Major Metropolitan Area in the United States	2012	CS	Both	WB	The United States	Evaluate blood donation behaviours and demographics of foreign-born and US-born Hispanic donors between 2006 and 2009 in metropolitan Atlanta, GA, USA.	5,119 foreign-born and 11,841 US-Born Hispanics donors	9	(51)
32.	Internation intervals and patterns of return among blood donors in Brazil	2012	CO	Both	WB	Brazil	Donation frequency, inter-donation intervals, and their association with donor demographics, status, and type of donation were examined	306,770 allogeneic donations, 38.9% came from 95,127 first-time donors and 61.1%	9	(33)

								from 149,664 repeat donors		
33.	Adverse reactions and other factors that impact subsequent blood donation visits	2012	CO	Repeat	WB	The United States	Measure the impact of adverse reactions on donor return behaviour	665.501 donations	8	(41)
34.	Individual and contextual determinants of blood donation frequency with a focus on clinic accessibility: a case study of Toronto, Canada	2012	CS	Both	WB	Canada	Investigate the individual and contextual determinants of the decision to donate multiple times, with a focus on accessibility to clinics.	30,054 donors	9	(30)
35.	The impact of temporary deferral due to low haemoglobin: future return, time to return, and frequency of subsequent donation	2011	CO	Both	WB	Australia	The effects of a 6-month deferral due to low haemoglobin (Hb) on the subsequent donation patterns of Australian whole blood donors.	1,011 donors in the deferred group, and 68,675 donors in the comparison group.	9	(93)
36.	Analysis of Chinese donors' return behaviour	2011	CO	Both	WB	China	Comparison of demographic factors between first-time donors and repeat donors	241,552 donations from first time and repeat donors	9	(60)
37.	Donor return after temporary deferral	2011	CO	Both	WB	The United States	The consequences of temporary pre-donation deferral on donor return behaviour	505,623 deferrals	9	(24)
38.	Evaluation of the return rate of volunteer blood donors	2011	CO	First time	Mixed	Brazil	Estimate the return rate of first-time donors of the Ribeirão Preto Blood	115,553 donors	9	(62)

							Centre and other blood centres in its coverage region.			
39.	The effects of a phone call prompt on subsequent blood donation among first-time donors	2011	I	First time	Mixed	Canada	Examine the effect of phone call reminders to retain donors among first-time donors	Intervention group (n = 870) and the control (n = 734) group.	N/A	(87)
40.	Demographic Patterns of Blood Donors and Donations in a Large Metropolitan Area	2011	CS	Both	WB	The United States	Assess the demographic characteristics of donors over multiple years to better understand the effects of changing demographics on blood availability.	389 340 blood donations	9	(55)
41.	Demographic profile of blood donors at three major Brazilian blood centres: results from the International REDS-II study, 2007 to 2008	2010	CS	Both	Mixed	Brazil	Describe the demographic profile of blood donors in the three centres in Brazil.	615,379 blood donations from 410,423 donors.	9	(70)
42.	An adapted post-donation motivational interview enhances blood donor retention	2010	I	Not Specifically Stated	WB	The United States	Examine the effects of a post-donation adapted motivational interview (AMI) on blood donor attitudes and repeat donation behaviour	215 donors	N/A	(88)
43.	Vasovagal syncope and blood donor return: examination of the role of experience and affective expectancies	2010	CS	Both	Mixed	The United States	Examine the extent to which experience with blood donation and vasovagal sensations during blood donation uniquely predict the likelihood of donor return, even when controlling for affective expectancies.	446 donors	9	(118)

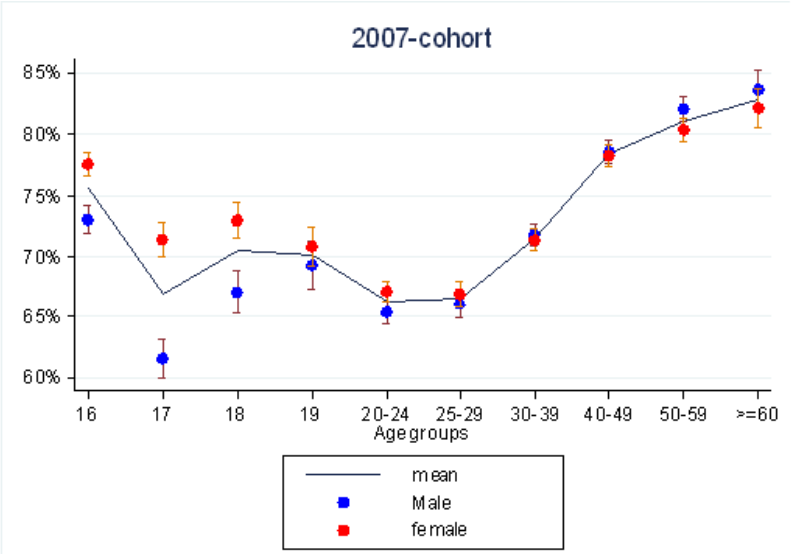
44.	Gender differences in presentation rates, deferrals and return behaviour among Norwegian blood donors	2010	CO	Not Specifically Stated	WB	Norway	Study gender-related causes of deferrals and cessation of donation in the blood donor population of Norway's largest blood bank.	17 812 donors	9	(27)
45.	Age-related donor returns patterns among first-time blood donors in the United States	2009	CO	First time	WB	The United States	Measure the effect of age of first donation on return behaviour	2.3 million FT donors	9	(54)
46.	Effects of applied muscle tension on the likelihood of blood donor return	2009	I	Not Specifically Stated	Mixed	the United States	The effects of muscle tension on return behaviour in men and women	1,059 donors	N/A	(89)
47.	Minority and foreign-born representation among US blood donors: demographics and donation frequency for 2006	2009	CS	Both	WB	The United States	Describing the demographic profiles of the U.S blood donors	1,288,998 donations	9	(25)
48.	Donor deferral and resulting donor loss at the American Red Cross Blood Services, 2001 through 2006	2008	CO	Both	Mixed	The United States	The effect of deferred donor on return rate in the United States	47,814,370 presentations with 12.8% deferred	9	(94)
49.	Factors influencing donor return	2008	CO	Both	WB	The United States	Determine factors impacting donor return behaviour	7,905 donors	8	(23)

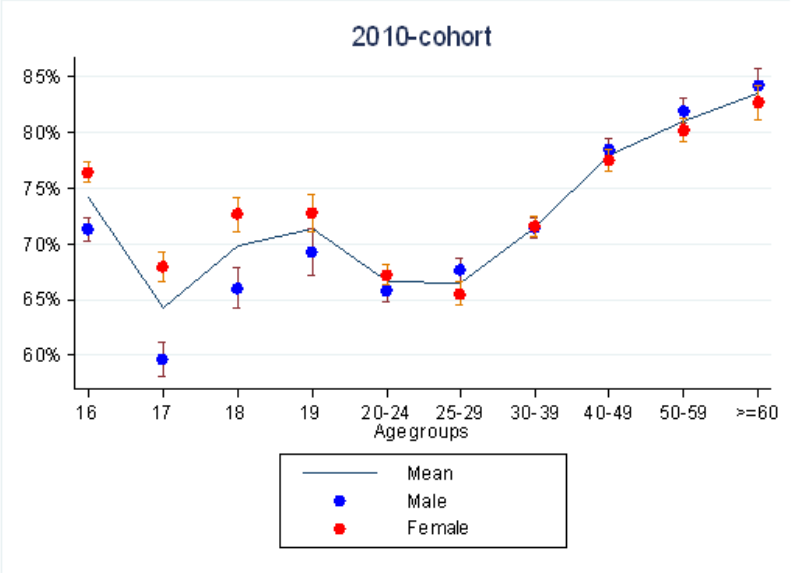
50.	Changing age distribution of the blood donor population in the United States	2008	CS	Both	Mixed	The United States	Describe changes over time in donor and donation patterns.	4,483,553, 4,749,679, 4,654,851, and 4,358,518 volunteer blood donors in 1996, 1999, 2002, and 2005, respectively.	9	(59)
51.	Blood donor satisfaction and intention of future donation	2008	CS	Both	Mixed	The United States	Evaluate correlations between overall satisfaction with the donation process and donor demographics and the effect of both on a donor's intent to return.	851 donors	6	(76)
52.	Recruiting and retaining young people as voluntary blood donors	2008	CO	First time	WB	Norway	Study the reasons for pre-donation deferral of young potential donors	2057 donors	8	(101)
53.	Why do some apheresis donors donate blood just once?	2007	CC	Not Specifically Stated	Apheresis	Germany	Factors affecting non-return in blood donors	188 respondents	6	(68)
54.	Determinants of return behaviour: a comparison of current and lapsed donors	2007	CC	Both	WB	Canada	Compare the demographic factors among current donors and lapsed donors	855 current donors and 656 lapsed donors	8	(65)
55.	Determinants of repeated blood donation among new and experienced blood donors	2007	CO	Both	Mixed	Canada	Identify factors predicting repeated blood donation among experienced and new donors.	2231 donors (2070 experienced and 161 new donors)	7	(74)
56.	The consequences of temporary deferral on future whole blood donation	2007	CO	Both	WB	The United States	Investigate blood donor return after deferral expiration.	6,222 temporary deferrals	9	(42)

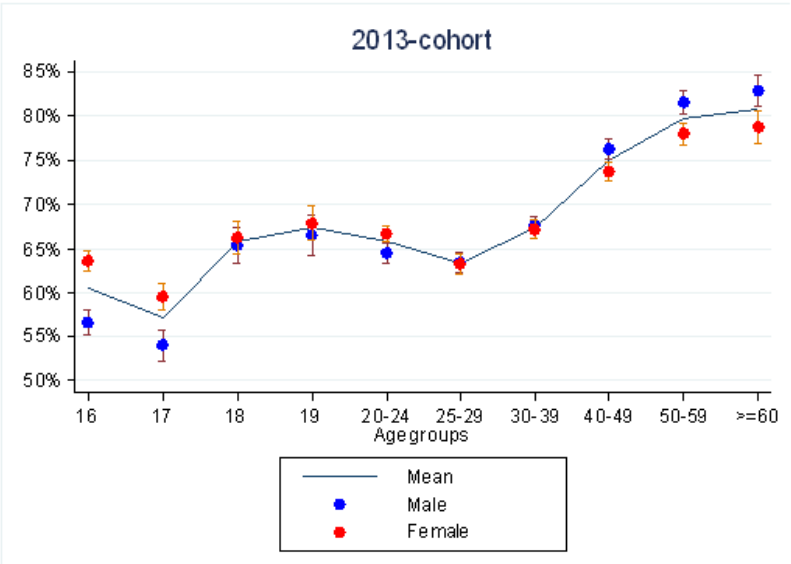
57.	Convenience, the bane of our existence, and other barriers to donating	2006	CS	Both	WB	The United States	Understanding the major deterrents to blood donation	4,142 donors (1705 first-time and 2437 repeat US donors)	7	(82)
58.	Eliciting repeat blood donations: tell early career donors why their blood type is special and more will give again	2006	I	Not Specifically Stated	Mixed	New Zealand	The impact of the intervention (sending a personalized letter to donors) to return behaviour	318 donors	N/A	(145)
59.	The effect of whole-blood donor adverse events on blood donor return rates	2006	CO	Both	WB	The United States	Measure the impact of adverse events on blood donor return rate	1000 donors	9	(67)
60.	First-year donation patterns predict long-term commitment for first-time donors	2005	CO	First time	WB	The United States	Comparing return rates in first-time donors based on their first-year donation frequency	179,409 donors	8	(26)
61.	Mild reactions to blood donation predict a decreased likelihood of donor return	2004	CS	Not Specifically Stated	Mixed	Canada	Measure the effect of mild reactions (e.g., faintness, dizziness, light-headedness) on donor retention	1052 donors	7	(146)
62.	Attitudes toward blood donation incentives in the United States: implications for donor recruitment	2003	CS	Both	Mixed	The United States	Measure the effectiveness of various donation incentive programs by demographics, first-time or repeat status, and collection site.	45,588 donors	6	(75)

63.	Predicting future blood donor returns: past behaviour, intentions, and observer effects	2002	CO	Both	Mixed	The UK	Explore the efficacy of 6 factors (e.g., intentions) to predict the number of future blood donations	630 donors	6	(80)
64.	The potential impact of incentives on future blood donation behaviour	2001	CS	Both	Mixed	The United States	Measure the impact of incentives on donor recruitment and return.	7,489 respondents	7	(77)
65.	Bruising following blood donation, its management and the response and subsequent return rates of affected donors	2000	CO	Both	Mixed	The UK	Determine the effect of bruising and its management on return rate	329 donors	9	(147)
66.	Predicting a donor's likelihood of donating within a preselected time interval	2000	CS	Both	Mixed	Germany	Compare the likelihood of return donation among first time and repeat donors within a specified time interval	760,000 donors	9	(50)

Appendix 2 Return proportion, sex-stratified







Appendix 3 Plasma yield, sex-stratified