EDQM Blood Conference
Innovation in Blood Establishment Processes

14-15 January 2025
Strasbourg, France

Session A3:
Donor protection
(8:30 – 10:00)

Moderators: **Johanna Castrén**, Finnish Red Cross Blood Service, Finland
Rada M. Grubovic Rastvorceva, SoHO Standards Section, EDQM

Speakers: **Hans Van Remoortel**, Belgian Red Cross-Flanders, Belgium
Katja van den Hurk, Donor Health, Sanquin Research & Amsterdam UMC, Dept of Public and Occupational Health & Amsterdam Public Health Research Institute, the Netherlands
Joanne Pink, Australian Red Cross Lifeblood, Australia
Amber Meulenbeld, Donor Health, Sanquin Research & Amsterdam UMC, Dept of Public and Occupational Health, the Netherlands

Please note:
- *Food and drink are not permitted in the conference rooms*
- *Photography & filming during the presentations are strictly forbidden*
- *Photos and videos may only be taken by Council of Europe staff members*
- *The session will be recorded for internal purposes only*

edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

How would we decide on a good plasmapheresis frequency?

Results and recommendations from the SUPPLY project

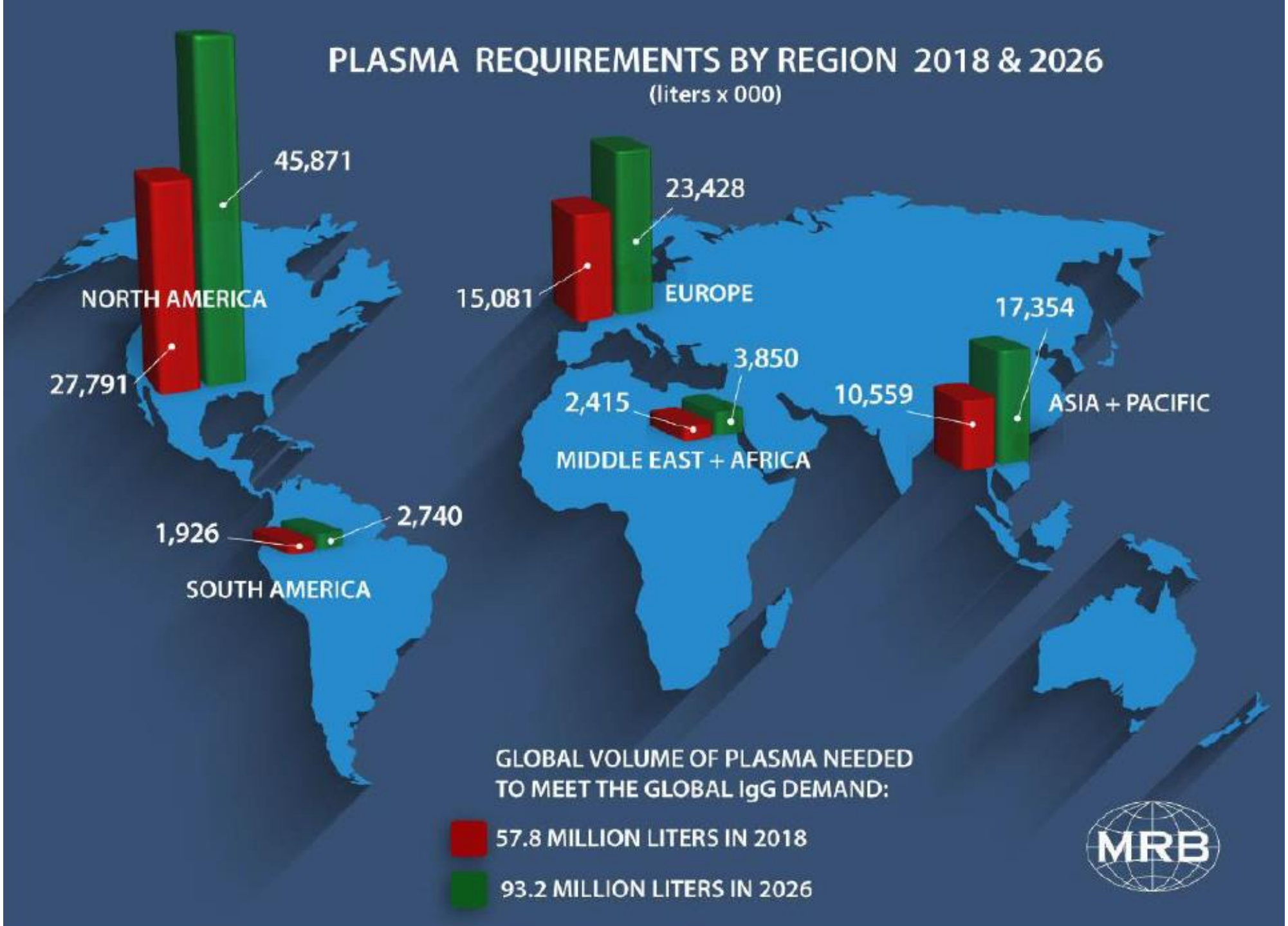
Prof. Dr. Hans Van Remoortel

Centre for Evidence-Based Practice – Belgian Red Cross

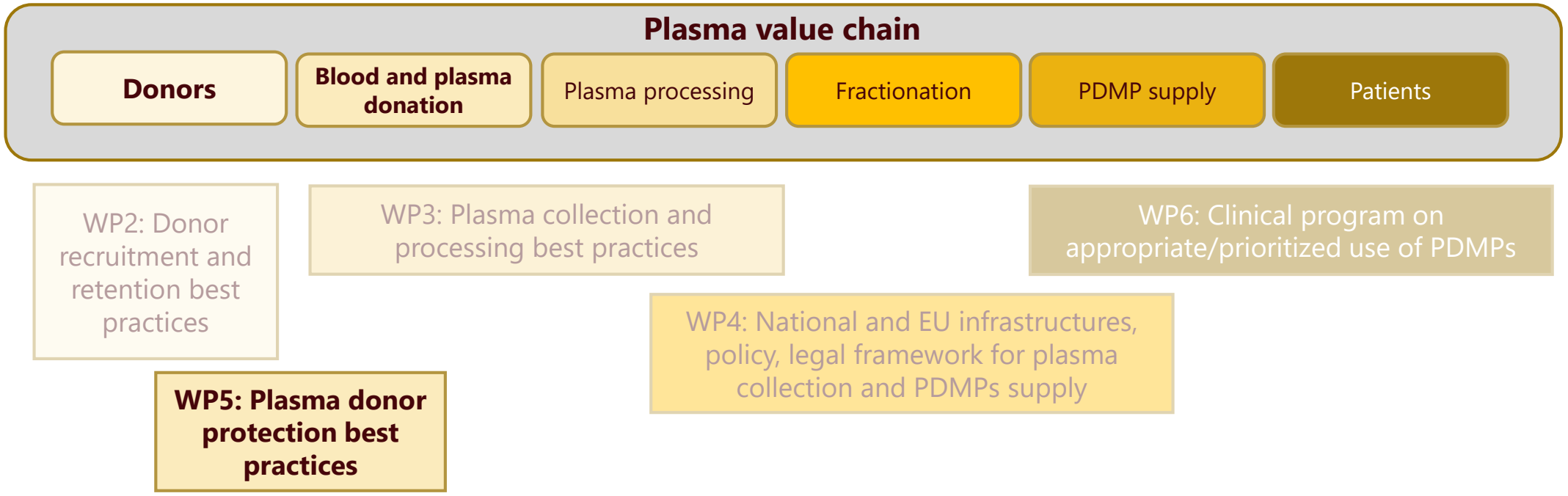
Leuven Institute of Healthcare Policy – KU Leuven

Disclosure

I have no conflicts of interest to declare


PLASMA REQUIREMENTS BY REGION 2018 & 2026
(liters x 000)
45,871
NORTH AMERICA
27,791
23,428
15,081
EUROPE
3,850
2,415
MIDDLE EAST + AFRICA
17,354
10,559
ASIA + PACIFIC
2,740
1,926
SOUTH AMERICA
GLOBAL VOLUME OF PLASMA NEEDED
TO MEET THE GLOBAL IgG DEMAND:
57.8 MILLION LITERS IN 2018
93.2 MILLION LITERS IN 2026
MRB

SUPPLY project
Strengthening voluntary non-remunerated plasma collection capacity in Europe



SUPPLY eba EUROPEAN BLOOD ALLIANCE

Country	Allowed donation frequency per donor
Belgium	Every 2 weeks Max 24x per year
France	Every 2 weeks Max 24x per year
Netherlands	Every 2 weeks Max 26x per year
Germany	2 days between donations Max 60x per year
Austria	1 per 72 hours Max 50x per year
Hungary	1 per 72 hours Max 45x per year
USA	Twice per week Max 104x per year

Aim

- To identify the **best available scientific evidence** that investigated the **impact** of plasmapheresis **frequency** on the safety or **health of donors**

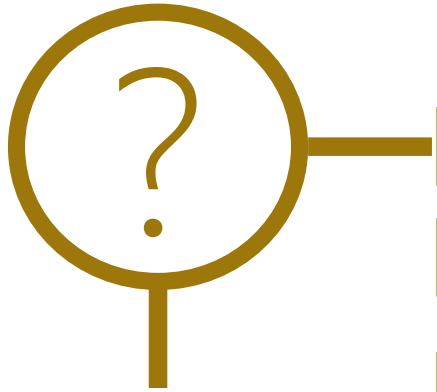
- To formulate **recommendations** towards a **safe** plasmapheresis frequency

SUPPLY | Co-funded by the European Union

Systematic review methodology

1. Draft research question
2. Develop search strategy
3. Select articles
4. Data extraction & synthesis
5. Quality assessment
6. Formulate conclusions

Step 1: Research question + eligibility criteria



What is the impact of plasmapheresis frequency on the safety or health of donors?

Population	Healthy adults who donated plasma via plasmapheresis
Intervention	Higher frequency of plasmapheresis
Comparator	Lower frequency of plasmapheresis, placebo, no plasmapheresis
Outcome	Primary: Adverse events (ISBT grading tool) Secondary: Cardiovascular health, protein levels
Design	Controlled experimental/observational studies
Search date	4th of December 2023

Step 2: Comprehensive search of the literature
Step 3: selection of articles

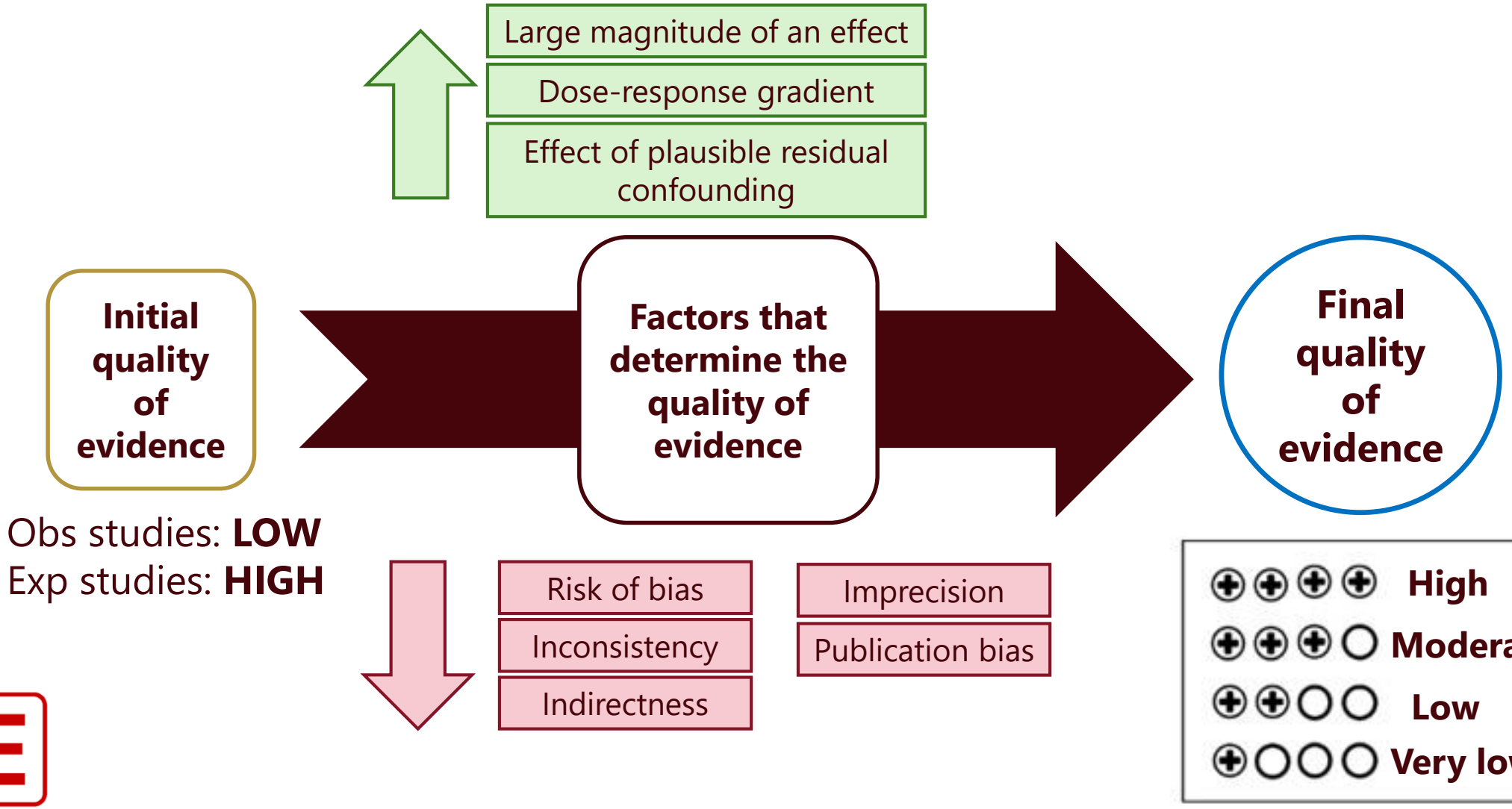
What is the impact of plasma donation frequency on safety or health of donors?

1,351 references screened based on title and abstract

37 full texts screenings

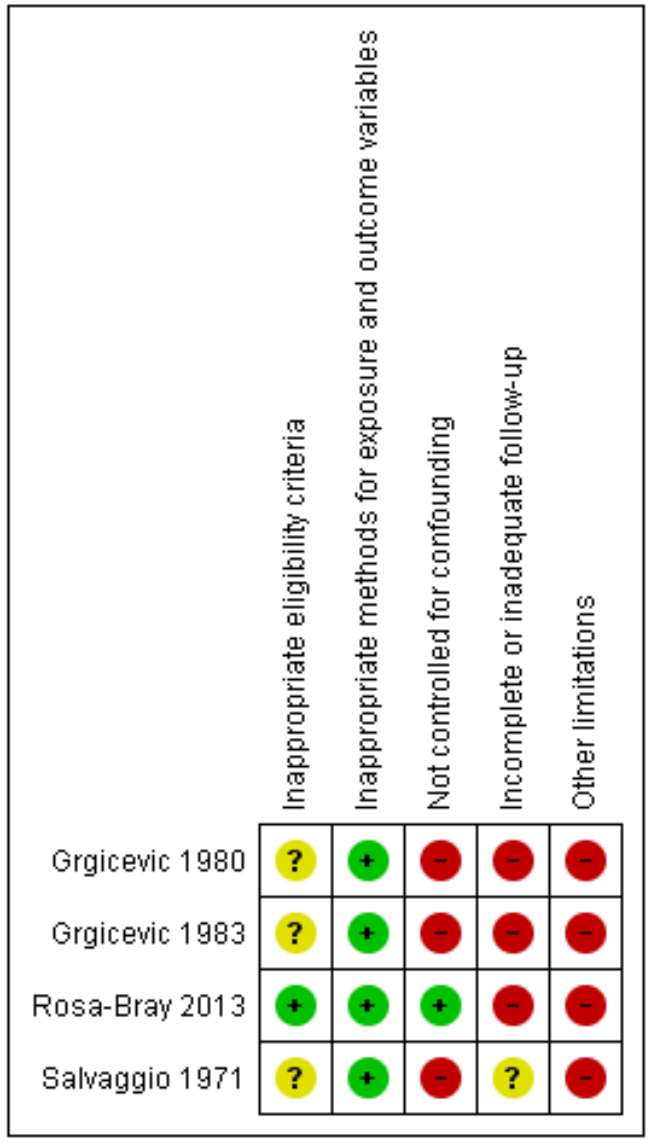
4 cohort studies (obs)
1 non-RCT (exp)
2 RCTs (exp)

Step 4: Data-extraction & synthesis
Step 5: Quality assessment



GRADE

Quality assessment of 4 observational studies



Initial certainty of evidence: **LOW**

Downgrading with 1 level due to

- methodological limitations
- imprecision of results (due to limited sample sizes)

Final certainty of evidence:

VERY LOW

Certainty of evidence	Definition
HIGH	We are very confident that the true effect lies close to that of the estimate of the effect Further research is **very unlikely to change our confidence** in the estimate of effect
MODERATE	We are moderately confident in the estimate of effect: the true effect is likely to be close to the estimate of effect, but possibility to be substantially different. Further research is **likely to have an important impact on our confidence** in the estimate of effect
LOW	Our confidence in the effect is limited: the true effect may be substantially different from the estimate of the effect. Further research is **very likely to have an important impact on our confidence** in the estimate of effect and is likely to change the estimate.
VERY LOW	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect. Any estimate of effect is very uncertain

Non-randomized controlled trial

Transfusion Medicine, 1993, **3**, 59–65

Protein levels and plasmapheresis intensity

T. S. Ciszewski, S. Ralston, D. Acteson, S. Wasi and S. J. Strong *The Canadian Red Cross Society, Blood Transfusion Service, Sudbury Centre and National Reference Laboratory, Ontario, Canada*

Donor recruitment

91 currently active donors

Duration: 6 months
Volume: max. 600 mL

High frequency: weekly (n=31)

Regular frequency: bi-weekly (n=30)

Control: regular whole blood donors (n=30)

Enrollment

Baseline

Monthly during 6 months

Outcomes

Total protein, IgG, IgA, IgM

Ciszewski 1993

Key results

- Concentrations of **TSP and IgG were significantly reduced** in the weekly plasmapheresis group but remained **within the normal ranges**

- **No** statistically significant **difference** from the initial concentrations was observed in **IgG, IgA and IgM levels** among any of the groups studied

- Mean **total protein** levels **dropped** during the first 3 months in the **weekly plasmapheresis group**, and returned to baseline levels 6 months after the end of the study.

ORIGINAL ARTICLE

Vox Sanguinis ISBT International Society of Blood Transfusion

Effects of plasmapheresis frequency on health status and exercise performance in men: A randomized controlled trial

Alexandre Mortier[1] | Jina Khoudary[2] | Sophie van Dooslaer de Ten Ryen[1] | Camille Lannoy[1] | Nicolas Benoit[1] | Nancy Antoine[1] | Sylvie Copine[1] | Hans Van Remoortel[3,4] | Philippe Vandekerckhove[2,4] | Veerle Compernolle[2,5] | Louise Deldicque[1,6]

Duration: 3 months
Volume: max. 650 mL

Donor recruitment

Randomization of 63 repeat male donors

Very high frequency: 2x/w (n=16)

High frequency: 3x/month (n=16)

Low frequency: 1x/month (n=16)

Placebo: sensation of donation (n=15)

Belgian Red Cross

Enrollment

UCL Université catholique de Louvain

Outcomes

d0 d42 d84

1   

Immunoglobulins, albumin, hemoglobin,...

2   

Physiological + exercise-related parameters (cardiovascular health)

3 adverse events adverse events

Mortier 2024

Adverse events

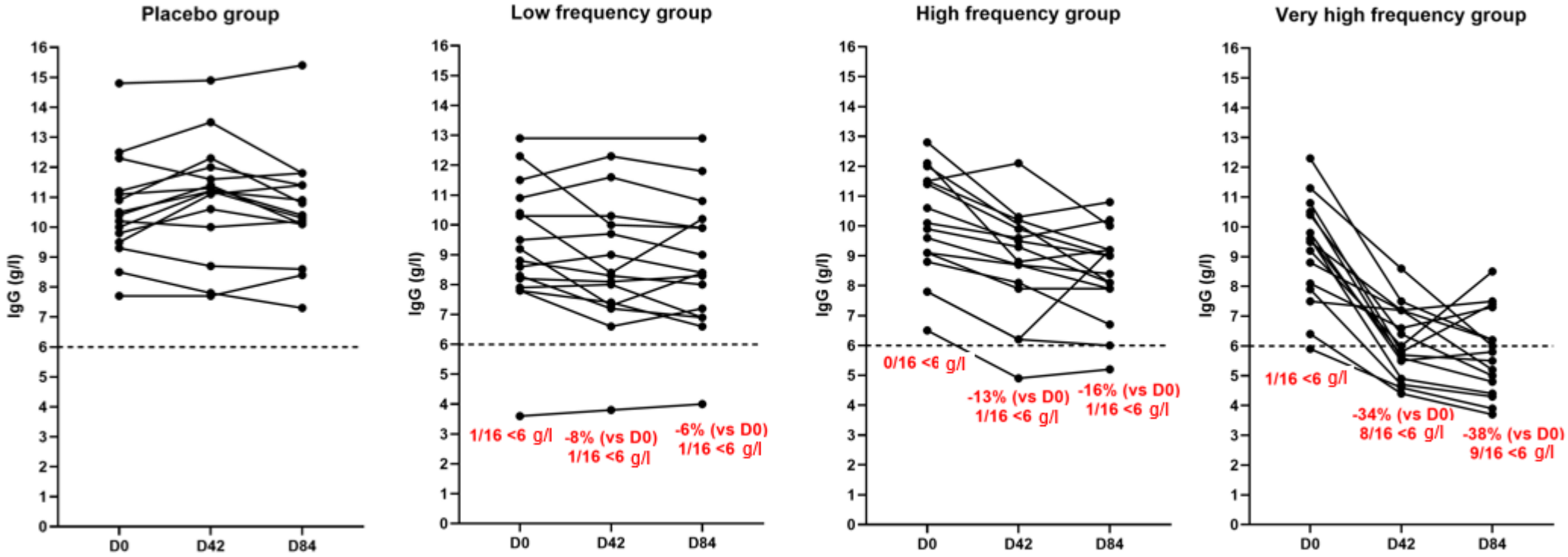
Few (minor) adverse events were reported in (very) high frequency plasmapheresis.
No other (major) events were reported.

Cardiovascular health

(Very) high frequency plasmapheresis may result in little to no difference in cardiovascular health markers

Protein levels

IgG levels decreased 38% with 2 donations/week
IgG levels decreased 16% with 3 donations/month



Mortier 2024

Haugen *et al. Trials* (2024) 25:175
https://doi.org/10.1186/s13063-024-08035-7

Trials

STUDY PROTOCOL Open Access

The effect of donation frequency on donor health in blood donors donating plasma by plasmapheresis: study protocol for a randomized controlled trial

Morten Haugen[1,2*], Karin Magnussen[1], Tonje Eiane Aarsland[3,4], Lise Sofie Haug Nissen-Meyer[5] and Tor A. Strand[6]

Donor recruitment

Randomization of 120 repeated male donors

Duration: 4 months
Volume: 650 mL

High frequency: 3x/2w (n=40)

Regular frequency: bi-weekly (n=40)

Control: whole blood donation (500mL) every 3 months (n=40)

Innlandet Hospital Trust

Enrollment

Baseline

Bi-weekly during 4 months

Bi-weekly during 1 follow-up month

Outcomes

1

Immunoglobulins, total protein, plasma proteins

2

Lipid profile (cardiovascular health)

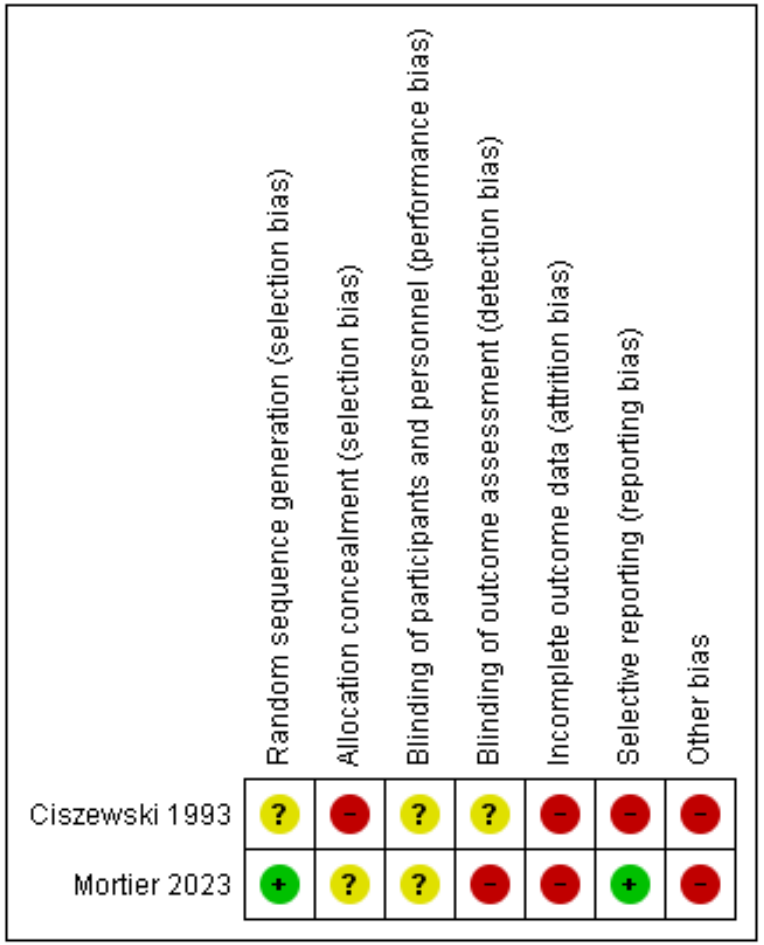
Haugen 2024

Key intermediate results (50% sampled)

- Concentrations of **TSP, IgG, Hb and ferritin were significantly reduced** in both high-frequency (3x every 2 weeks) and regular-frequency (1x every 2 weeks) plasma donors after 16 weeks
  - The degree of reduction increased with higher donation frequency

- The **recovery** of most of these plasma proteins to baseline levels **took more than 4 weeks** after donations

Quality assessment of experimental studies



Initial certainty of evidence: **HIGH**

Downgrading with 2 levels due to

- methodological limitations
- imprecision of results (due to limited sample sizes)

Final certainty of evidence:

LOW

Certainty of evidence	Definition
HIGH	We are very confident that the true effect lies close to that of the estimate of the effect Further research is **very unlikely to change our confidence** in the estimate of effect
MODERATE	We are moderately confident in the estimate of effect: the true effect is likely to be close to the estimate of effect, but possibility to be substantially different. Further research is **likely to have an important impact on our confidence** in the estimate of effect
LOW	Our confidence in the effect is limited: the true effect may be substantially different from the estimate of the effect. Further research is **very likely to have an important impact on our confidence** in the estimate of effect and is likely to change the estimate.
VERY LOW	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect. Any estimate of effect is very uncertain

SUPPLY WP5.2 recommendations

1. Adherence to the Blood Guide (21st edition 2023) until further evidence is acquired

•However: a maximum of two plasma donations per month, pending sufficient evidence confirming the safety of higher donation frequencies. This recommendation is based on expert opinion and reflects the view of a majority of WP5 members*

•*Alternative recommendation, supported by two WP5 members: a maximum of two plasma donations per month, unless a donor health and IgG management system is established by the respective blood establishment

2. IgG levels should be monitored. Evidence of optimal IgG algorithms and test intervals are lacking

3. Urgent initiation of prospective studies to examine the health consequences of plasma donation at varying frequencies

Recommendations are based on the use of the precautionary principle, placing donor safety first while awaiting further evidence.

SUPPLY | Co-funded by the European Union

WP5 SUPPLY members

Belgian Red Cross

- Tine D'aes
- Natalie Schroyens
- Veerle Compernolle

Evidence-based by CEBaP

AARHUS UNIVERSITY HOSPITAL

- Christian Erikstrup
- Susan Mikkelsen

Sanquin

- Katja van den Hurk
- Marloes Spekman

- Elodie Pouchol
- Pascale Richard

EFS
ÉTABLISSEMENT FRANÇAIS DU SANG

- Torsten Tonn
- Thomas Burkhardt

German Red Cross

- Pierre Tiberghien
- Peter O'Leary
- Petar Kos
- Gaia Mori

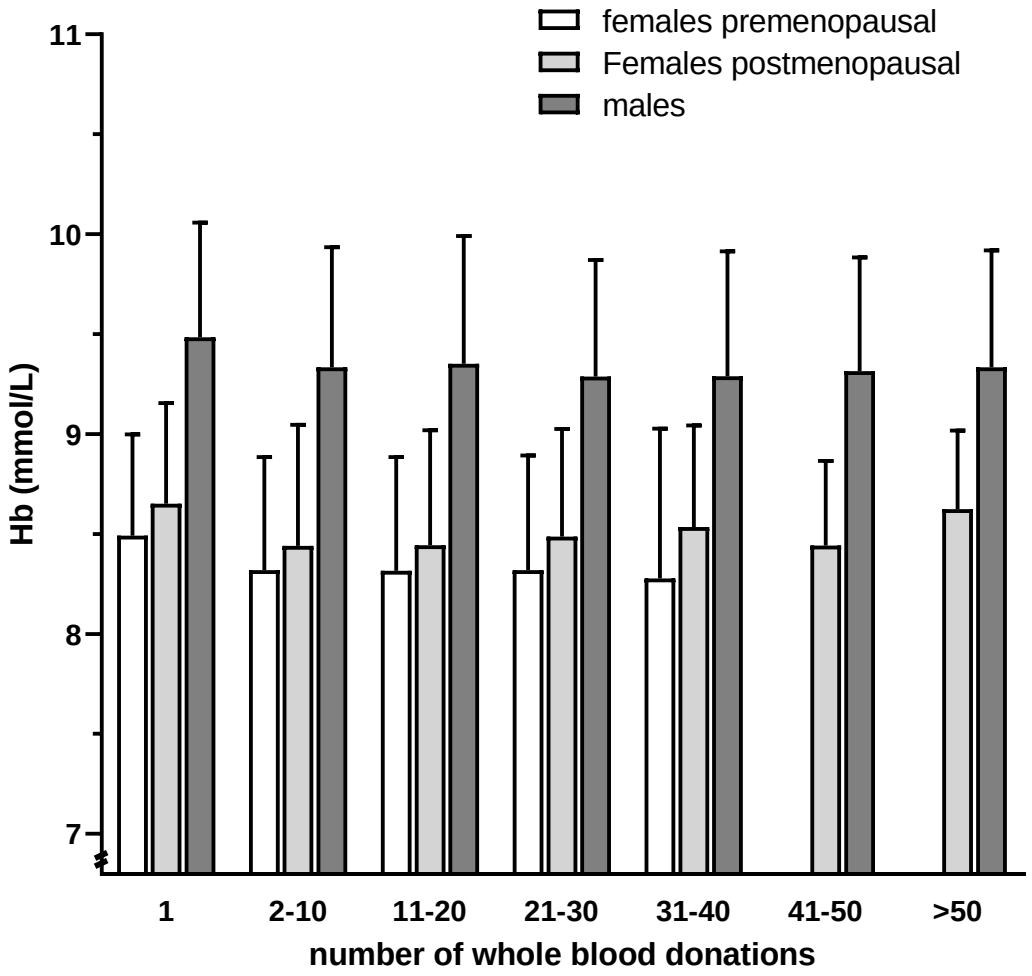
eba
European Blood Alliance

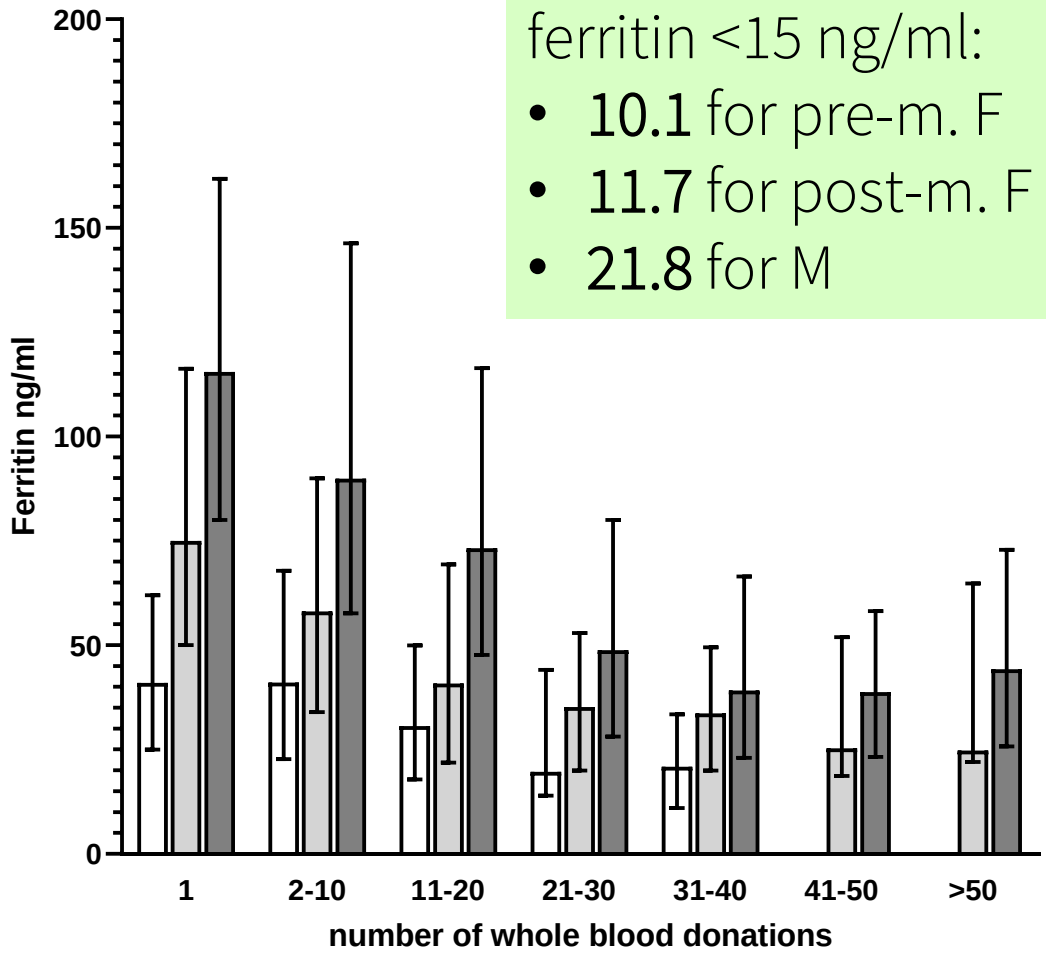
Whole blood donor iron management across Europe: *experiences and challenges in four blood establishments*

Katja van den Hurk, Mikko Arvas, David Roberts, Johanna Castrén, Christian Erikstrup
Epidemiologist, Head of Donor Studies, Principal Investigator on Donor Health,
Sanquin Research, Amsterdam UMC Public & Occupational Health

For Life.

Ferritin and Hb before routine ferritin measurements





OR for Hb deferral if ferritin <15 ng/ml:

- **10.1** for pre-m. F
- **11.7** for post-m. F
- **21.8** for M

Prinsze F. et al, Transfusion 2021

EDQM Guide to the preparation, use and quality assurance of BLOOD COMPONENTS, 21st Edition, 2023

STANDARD

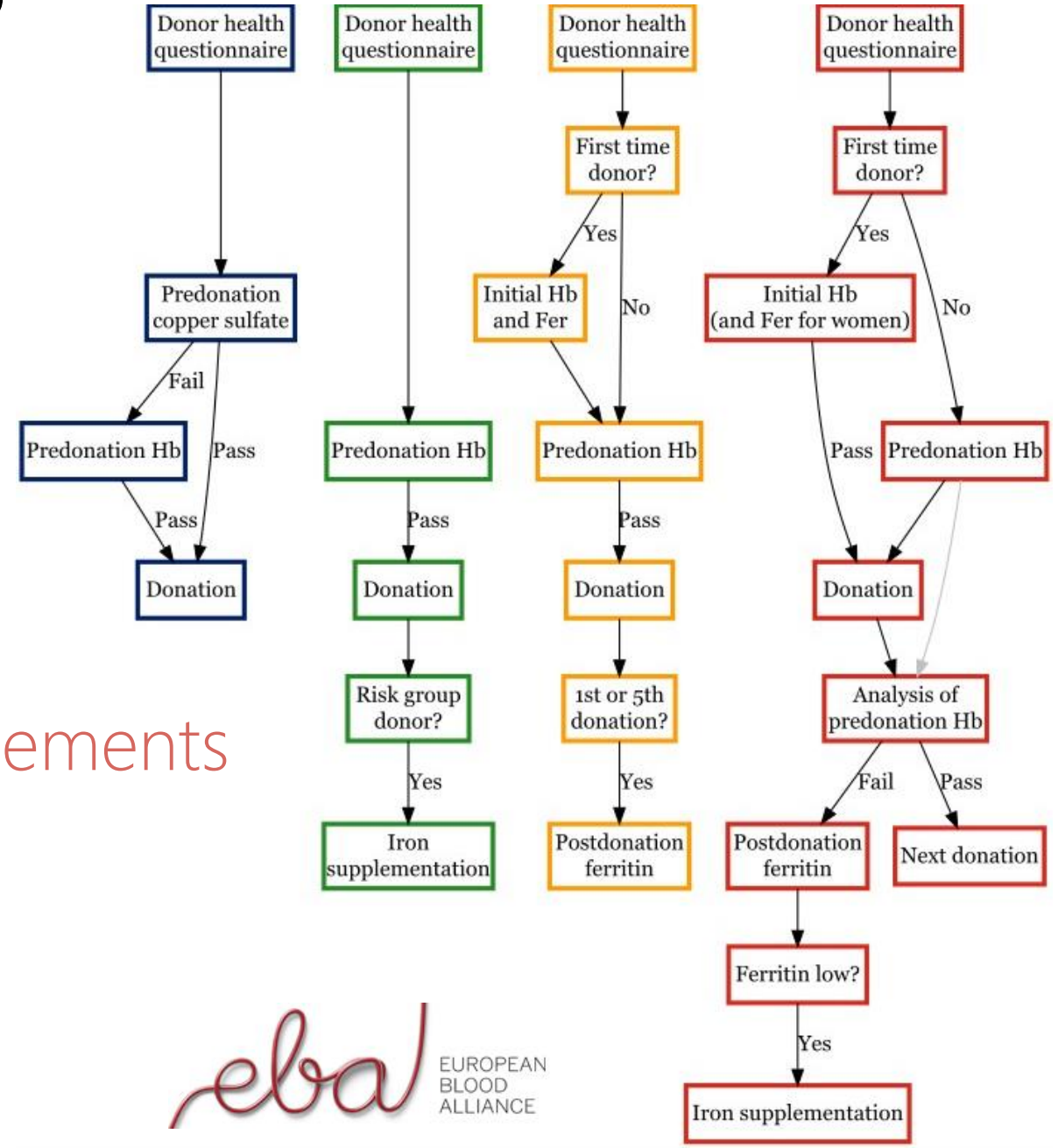
2.2.4.1. Blood establishments should have measures in place to minimise iron depletion in frequent blood donors.

Measures to prevent iron depletion and to protect donor health may include:

- Provision of materials for donor education, particularly in regard to the impact of blood donation on iron stores;
- Individual tailoring of donation frequency or the interval between donations and/or of the type of blood component donation based on sex, age, Hb values and iron status *(Evidence level C, E)*;
- Use of tests to assess iron status, such as ferritin, soluble transferrin receptor and red blood cell (RBC) indices;
- Iron supplementation taking into account the risk of delaying the diagnosis of unapparent underlying diseases and adverse effects of the iron preparations;

Iron management policies in:

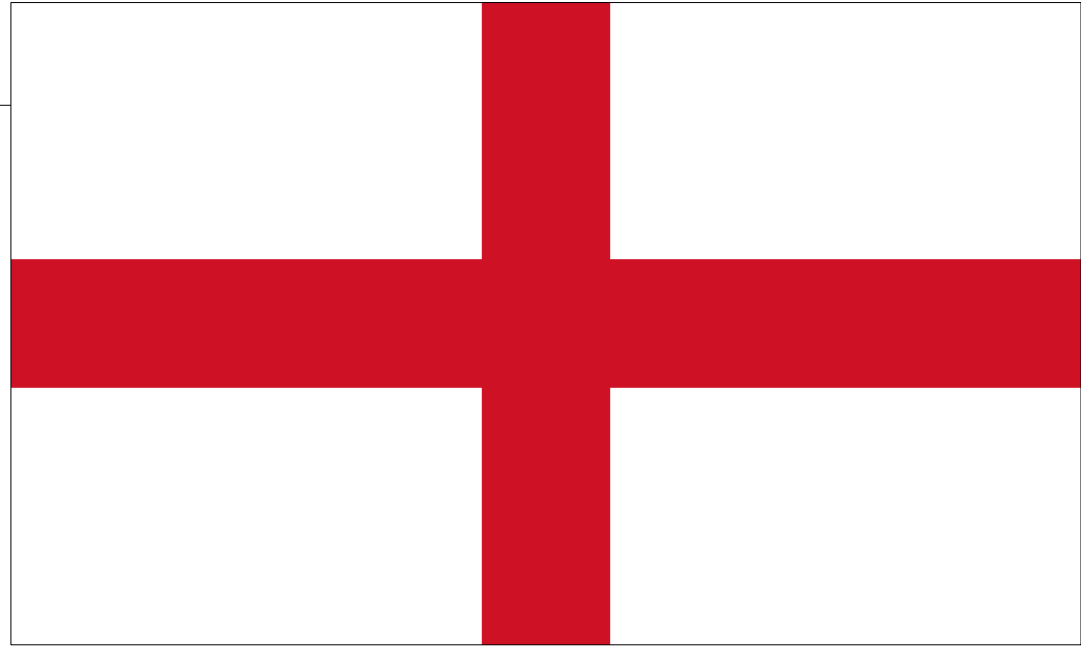
- England -
- Finland Supplements
- The Netherlands Ferritin
- Denmark Ferritin+supplements



Van den Hurk K. et al., Transfusion Medicine Reviews, 2024

EUROPEAN BLOOD ALLIANCE

Copper-sulphate + venous HemoCue Hb @ NHSBT - England



- 1.2 million donations by 750,000 donors annually
- Minimum donation intervals 12 (M) and 16 (F) weeks
- Copper sulphate test with capillary blood
- Venous HemoCue if it fails

Risk group based iron suplementation @FRCBS - Finland

	Women 18 - 25 years	Women 26 - 50 years	All donors donating every 4 month (or more frequently)
Iron	á 50 mg Ferrous(bi)-glycinate	á 50 mg Ferrous(bi)-glycinate	á 50 mg Ferrous(bi)-glycinate
Ascorbic acid	á 50 mg	á 50 mg	á 50 mg
Number of tablets	40	20	20
Total iron (mg)	2000	1000	1000

- Only after a donation (not by a deferral)
- Dietary supplement (not a pharmaceutical)

Risk group based donation intervals @FRCBS - Finland

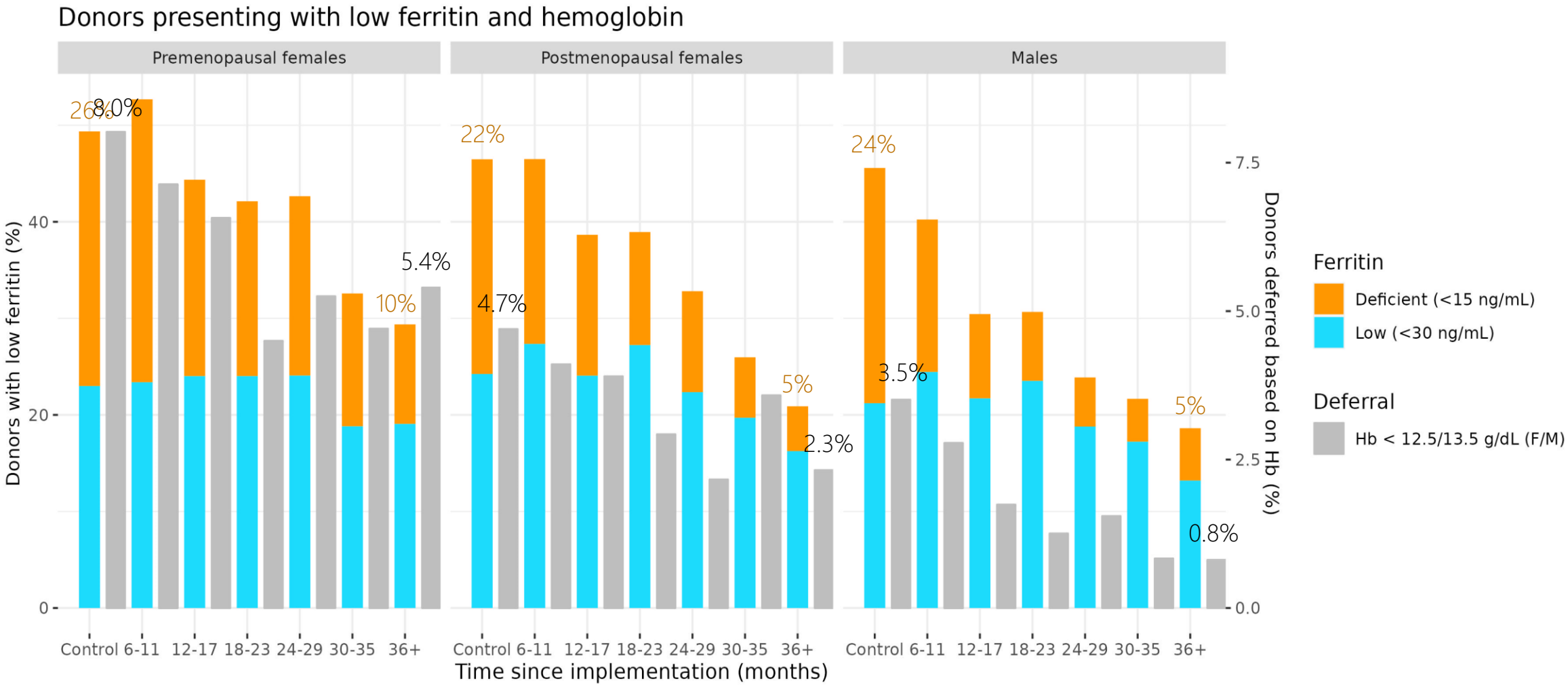
- 188,000 donations by ~ 118,000 donors annually

	Women 18-25 years	Women 26-70 years	Men
Suggested, instructed (supported by the staff and in all marketing/communication material)	Max. 1 / year	Max 2-3 / year	Max 3-4 / year
Allowed minimal interval	91 days	91 days	61 days

Finnish Red Cross Blood Service

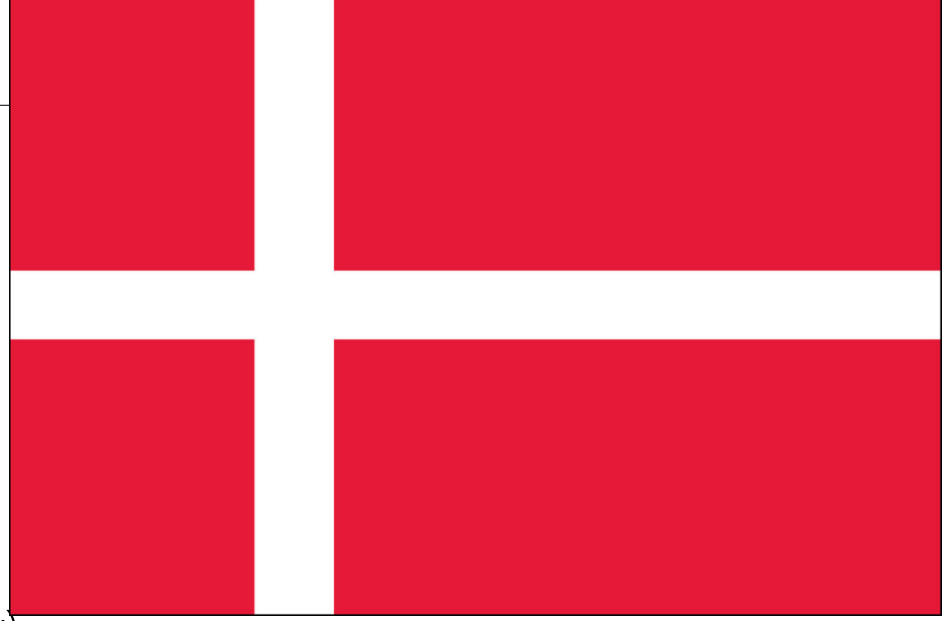
Hb & ferritin-guided intervals @Sanquin - the Netherlands

- 400,000 donations by ~280,000 donors annually
- Haemoglobin (Hb) must be > 13.5 (M) or 12.6 (F) g/dl
- Ferritin-guided donation intervals (since 2017):
  - Measured every 5th donation
  - Tested from sampling pouch <u>after donation</u>
  - Deferral:
    - < 15 ng/ml: 12 months
    - 15-30 ng/ml: 6 months
    - >30 ng/ml: -



Meulenbeld et al., The Lancet, 2024

Hb + ferritin and iron supplementation @Central Denmark Region - Denmark



- 200,000 donations by ~120,000 donors annually

National guidelines:
•Minimum donation intervals: 12 weeks for all donors.
•Hb measurement:
  - Measured pre-donation (HemoCue) or post-donation (Sysmex).
  - Mandatory pre-donation Hb measurement if previously low.

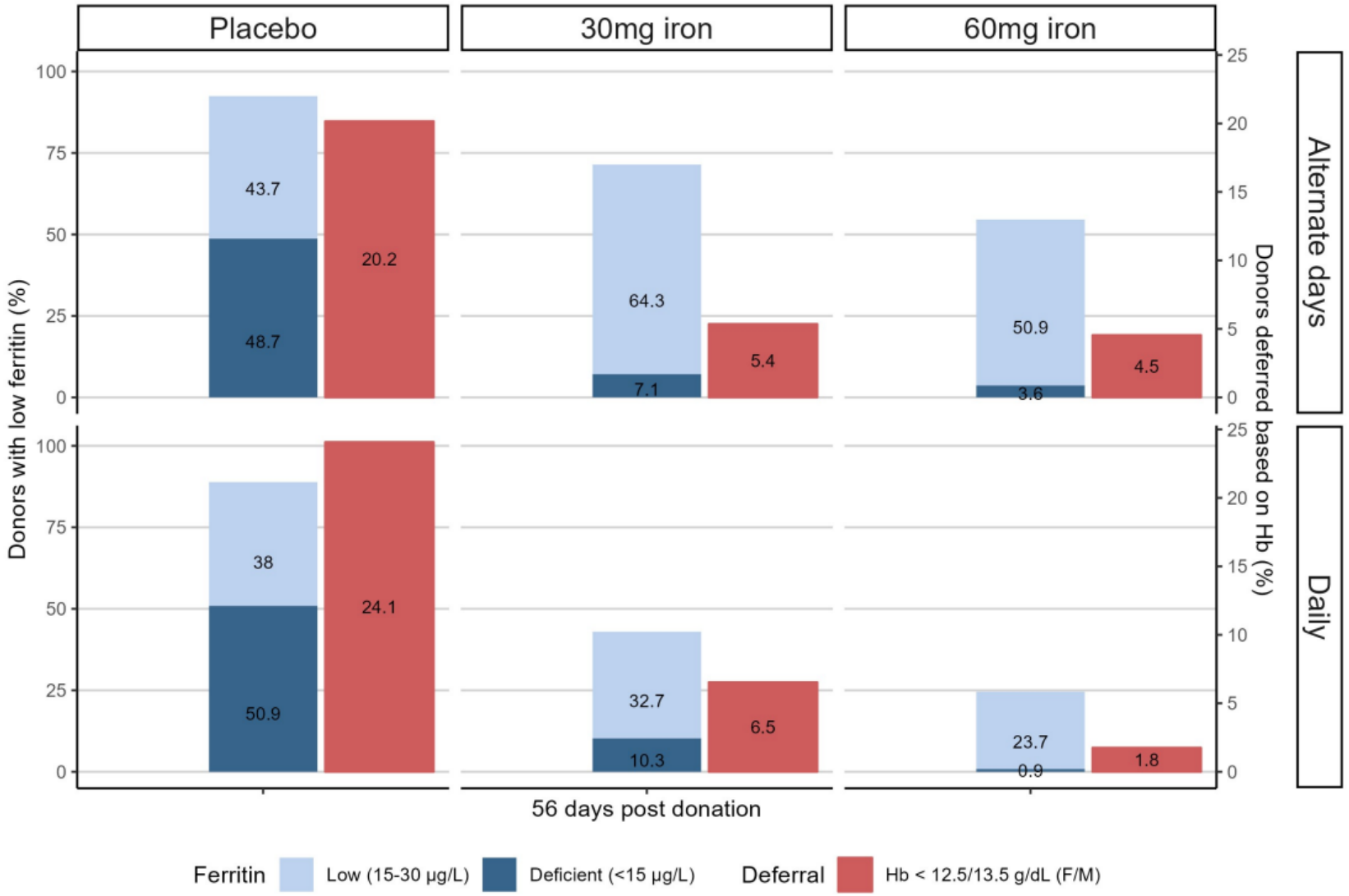
Ferritin and iron supplementation:
No national requirement for ferritin testing; regional discretion applies.

Central Denmark Region (and similar in other regions apart from South Denmark):
Ferritin measured in first-time female donors and donors with low Hb (will change to every 10 donations)

- Hb below deferral limits: 4 months deferral (will change to 6 months)
- Hb <110 g/L (females) or <125 g/L (males): 6 months deferral
- Ferritin <22 ng/mL: 20 doses of 100 mg ferrous sulfate (will change to <30 ng/mL)
- Ferritin <15 ng/mL: 60 doses of 100 mg ferrous sulfate

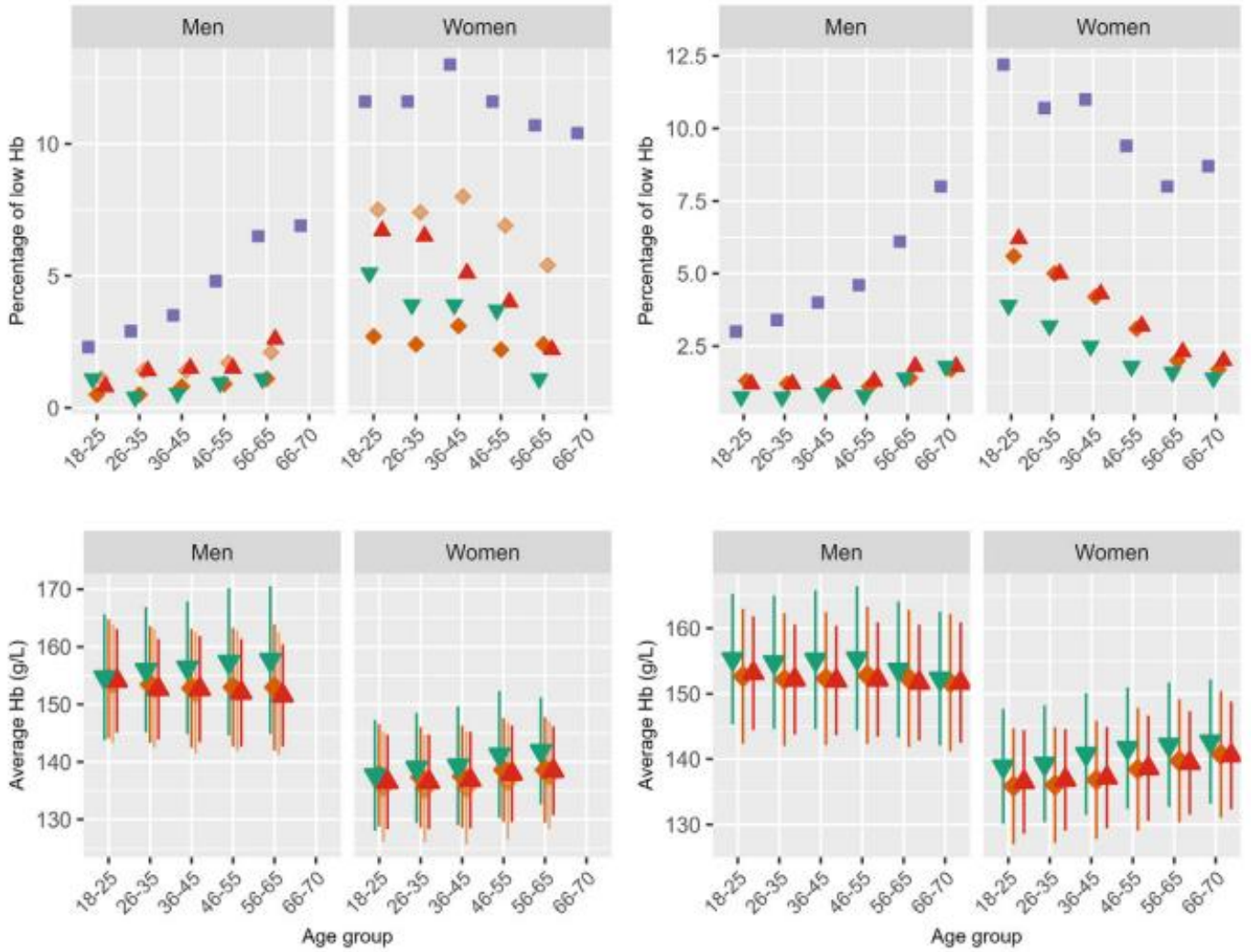
56 days of 60mg iron supplementation effective – FORTE RCT

- 830 donors with ferritin <30 ng/mL randomized to 6 trial arms.
- Significant reductions in low Hb and iron deficiency.
- No gastrointestinal discomfort.



Karregat et al., MedRXiv, 2025

Hb levels/deferrals

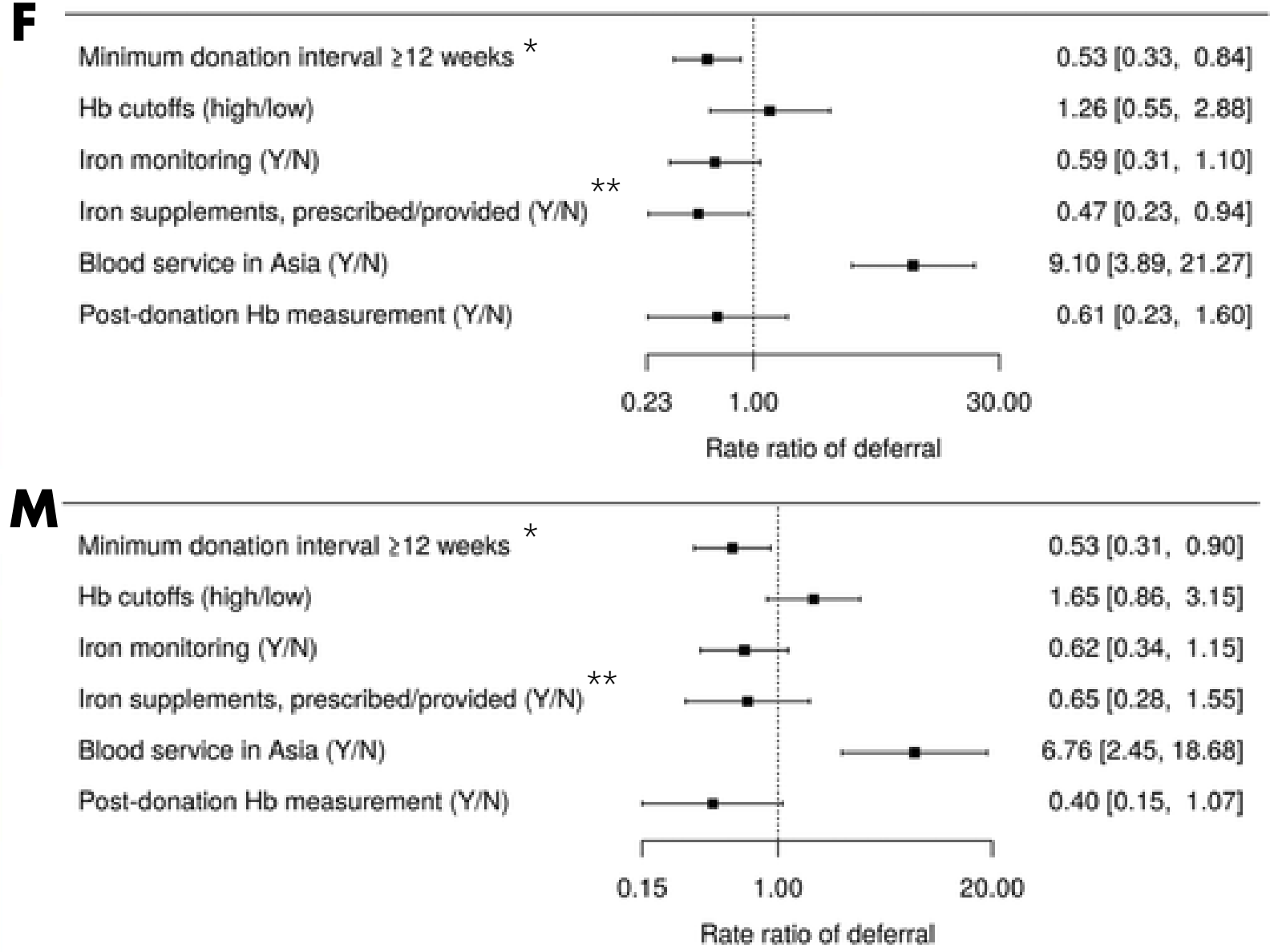


Country ENG FI NL DK

Van den Hurk K. et al., Transfusion Medicine Reviews, 2024

International policy comparison

RR for Hb deferral



*E. Di Angelantonio et al., The Lancet, 2017
*A. Meulenbeld et al., The Lancet 2024
**J. Kiss et al., JAMA, 2015
**J. Karregat et al., MedRXiv, 2025

BEST Collaborative

Zalpuri, et al., Transfusion, 2020

Overall conclusions

- Significant diversity in policies across countries
- Low-Hb deferrals and Hb levels quite comparable across countries
  - Exception: England, where no ferritin is measured *and* no supplements were provided

➢ Effective iron management strategies appear to be essential for maintaining adequate iron and Hb levels in whole blood donors

  ➢ Supported by evidence from RCTs

ECDHM

6th European Conference on Donor Health and Management

SUSTAINABILITY IN DONATIONS

Wijk aan Zee
The Netherlands
10-12 september 2025
www.ECDHM.org

Sanquin

eba EUROPEAN BLOOD ALLIANCE

Minimising iron loss in plateletpheresis is an important component of Lifeblood's donor iron health strategy

Dr Jo Pink

Additional authors: Dr Jo Speedy, Michael Halley-Frame, Dr Veronica Hoad

Australian Red Cross Lifeblood, Melbourne Australia

Australian Red Cross Lifeblood®

Conflicts of interest

- Nil conflicts of interest or disclosures

Australian Red Cross Lifeblood

Australian Red Cross Lifeblood

- 102 donor centres, mobiles and pop-up centres
- 592,000 active and registered donors
- In 2023/24 we supplied about 1.1 million blood components for direct transfusion and 869 tonne plasma for PDMPs

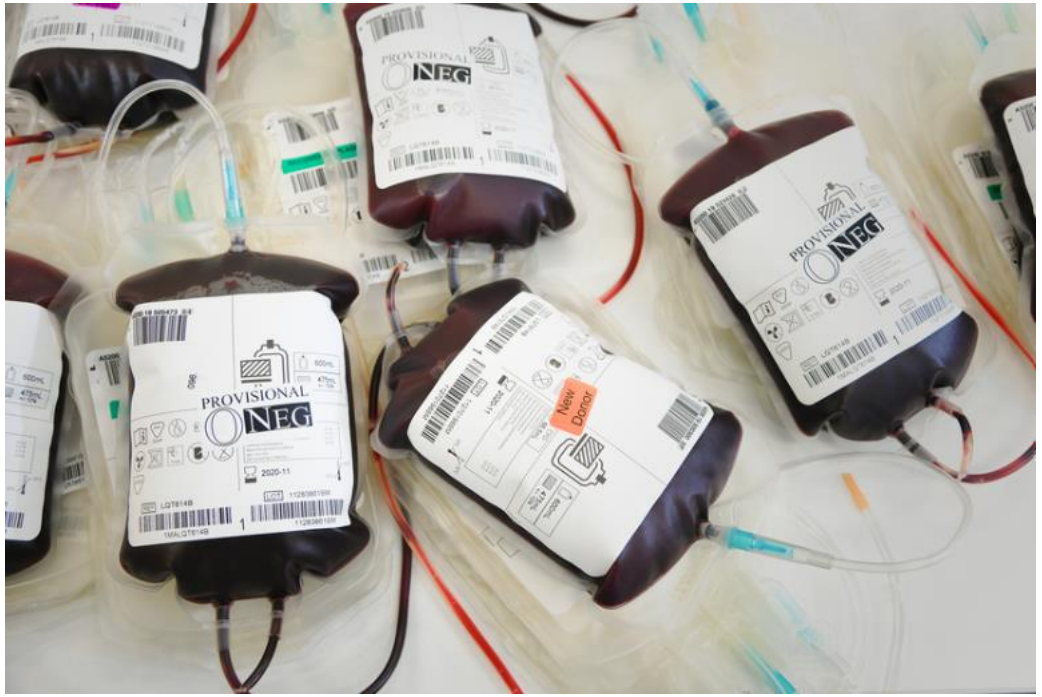
Overview

- Donor iron health strategy
- Plateletpheresis
  - Panel demographics
  - Iron deficiency
  - Lymphopenia
- Trial of plasma rinseback
- Longer-term strategies

Lifeblood iron strategy

Whole blood

- Minimum donation age of 18 years
- 12-week donation intervals
- Iron supp recommendation females 18-45 years



- Ferritin testing
  - ✓ First and then every 10 WB
  - ✓ >20g/L drop in Hb
  - ✓ Hb in buffer zone: Females 115 -119g/L, Males 125 -129g/L

Australian Red Cross Lifeblood

Ferritin result management

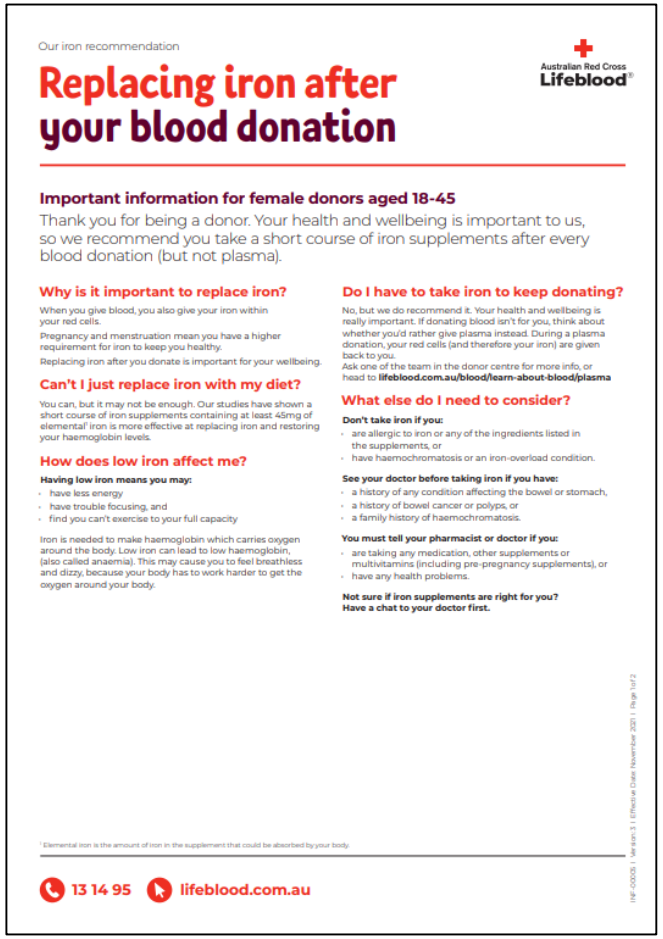
All donors with an abnormal result will continue to be referred to their doctor for investigation.

	FERRITIN [ug/L]		WHOLE BLOOD ELIGIBILITY	APHERESIS ELIGIBILITY
	Females	**Males**		
Low	<15	<30	**✗ 6 months**	□*
High#	401-999	501-999	□	□
Very High#	≥1,000	≥1,000	**✗ Until cleared**	**✗ Until cleared**

* Still required to meet the minimum acceptable Hb limit for apheresis

May be eligible for our Therapeutic Program if high ferritin secondary to haemochromatosis

Lifeblood iron strategy



Our iron recommendation

Australian Red Cross Lifeblood

Replacing iron after your blood donation

Important information for female donors aged 18-45

Thank you for being a donor. Your health and wellbeing is important to us, so we recommend you take a short course of iron supplements after every blood donation (but not plasma).

Why is it important to replace iron?

When you give blood, you also give your iron within your red cells.

Pregnancy and menstruation mean you have a higher requirement for iron to keep you healthy.

Replacing iron after you donate is important for your wellbeing.

Can't I just replace iron with my diet?

You can, but it may not be enough. Our studies have shown a short course of iron supplements containing at least 45mg of elemental[1] iron is more effective at replacing iron and restoring your haemoglobin levels.

How does low iron affect me?

Having low iron means you may:

- have less energy
- have trouble focusing, and
- find you can't exercise to your full capacity

Iron is needed to make haemoglobin which carries oxygen around the body. Low iron can lead to low haemoglobin, (also called anaemia). This may cause you to feel breathless and dizzy, because your body has to work harder to get the oxygen around your body.

Do I have to take iron to keep donating?

No, but we do recommend it. Your health and wellbeing is really important. If donating blood isn't for you, think about whether you'd rather give plasma instead. During a plasma donation, your red cells (and therefore your iron) are given back to you.
Ask one of the team in the donor centre for more info, or head to **lifeblood.com.au/blood/learn-about-blood/plasma**

What else do I need to consider?

Don't take iron if you:

- are allergic to iron or any of the ingredients listed in the supplements, or
- have haemochromatosis or an iron-overload condition.

See your doctor before taking iron if you have:

- a history of any condition affecting the bowel or stomach,
- a history of bowel cancer or polyps, or
- a family history of haemochromatosis.

You must tell your pharmacist or doctor if you:

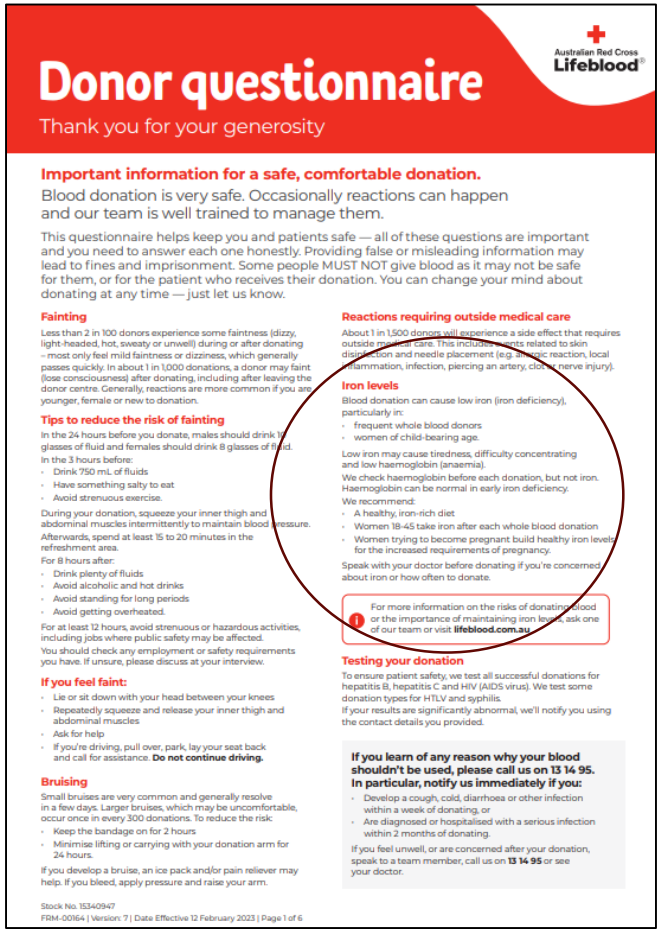
- are taking any medication, other supplements or multivitamins (including pre-pregnancy supplements), or
- have any health problems.

Not sure if iron supplements are right for you? Have a chat to your doctor first.

[1] Elemental iron is the amount of iron in the supplement that could be absorbed by your body.

13 14 95 lifeblood.com.au

INF-00005 | Version: 3 | Effective Date: November 2021 | Page 1 of 2



Australian Red Cross Lifeblood

Donor questionnaire

Thank you for your generosity

Important information for a safe, comfortable donation.

Blood donation is very safe. Occasionally reactions can happen and our team is well trained to manage them.

This questionnaire helps keep you and patients safe — all of these questions are important and you need to answer each one honestly. Providing false or misleading information may lead to fines and imprisonment. Some people MUST NOT give blood as it may not be safe for them, or for the patient who receives their donation. You can change your mind about donating at any time — just let us know.

Fainting

Less than 2 in 100 donors experience some faintness (dizzy, light-headed, hot, sweaty or unwell) during or after donating – most only feel mild faintness or dizziness, which generally passes quickly. In about 1 in 1,000 donations, a donor may faint (lose consciousness) after donating, including after leaving the donor centre. Generally, reactions are more common if you are younger, female or new to donation.

Tips to reduce the risk of fainting

In the 24 hours before you donate, males should drink 10 glasses of fluid and females should drink 8 glasses of fluid.
In the 3 hours before:

- Drink 750 mL of fluids
- Have something salty to eat
- Avoid strenuous exercise.

During your donation, squeeze your inner thigh and abdominal muscles intermittently to maintain blood pressure.
Afterwards, spend at least 15 to 20 minutes in the refreshment area.
For 8 hours after:

- Drink plenty of fluids
- Avoid alcoholic and hot drinks
- Avoid standing for long periods
- Avoid getting overheated.

For at least 12 hours, avoid strenuous or hazardous activities, including jobs where public safety may be affected.
You should check any employment or safety requirements you have. If unsure, please discuss at your interview.

If you feel faint:

- Lie or sit down with your head between your knees
- Repeatedly squeeze and release your inner thigh and abdominal muscles
- Ask for help
- If you're driving, pull over, park, lay your seat back and call for assistance. **Do not continue driving.**

Bruising

Small bruises are very common and generally resolve in a few days. Larger bruises, which may be uncomfortable, occur once in every 300 donations. To reduce the risk:

- Keep the bandage on for 2 hours
- Minimise lifting or carrying with your donation arm for 24 hours.

If you develop a bruise, an ice pack and/or pain reliever may help. If you bleed, apply pressure and raise your arm.

Reactions requiring outside medical care

About 1 in 1,500 donors will experience a side effect that requires outside medical care. This includes events related to skin disinfection and needle placement (e.g. allergic reaction, local inflammation, infection, piercing an artery, clot or nerve injury).

Iron levels

Blood donation can cause low iron (iron deficiency), particularly in:

- frequent whole blood donors
- women of child-bearing age.

Low iron may cause tiredness, difficulty concentrating and low haemoglobin (anaemia).
We check haemoglobin before each donation, but not iron. Haemoglobin can be normal in early iron deficiency.
We recommend:

- A healthy, iron-rich diet
- Women 18-45 take iron after each whole blood donation
- Women trying to become pregnant build healthy iron levels for the increased requirements of pregnancy.

Speak with your doctor before donating if you're concerned about iron or how often to donate.

For more information on the risks of donating blood or the importance of maintaining iron levels, ask one of our team or visit **lifeblood.com.au**

Testing your donation

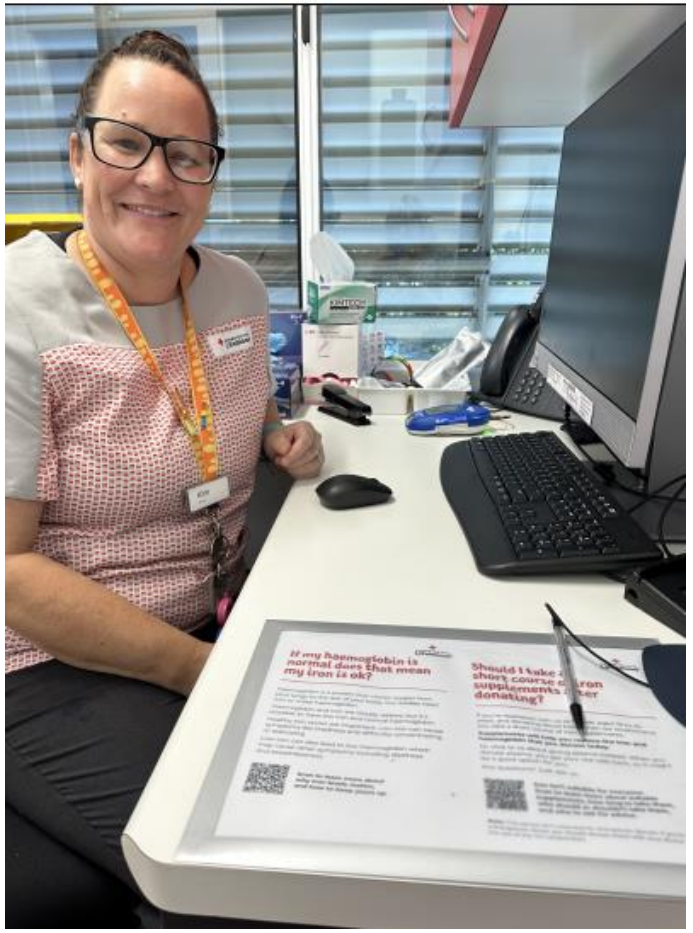
To ensure patient safety, we test all successful donations for hepatitis B, hepatitis C and HIV (AIDS virus). We test some donation types for HTLV and syphilis.
If your results are significantly abnormal, we'll notify you using the contact details you provided.

If you learn of any reason why your blood shouldn't be used, please call us on 13 14 95. In particular, notify us immediately if you:

- Develop a cough, cold, diarrhoea or other infection within a week of donating, or
- Are diagnosed or hospitalised with a serious infection within 2 months of donating.

If you feel unwell, or are concerned after your donation, speak to a team member, call us on **13 14 95** or see your doctor.

Stock No. 1534094?
FRM-00164 | Version: 7 | Date Effective 12 February 2023 | Page 1 of 6



Information about iron health is provided on our website, on the donor questionnaire, when the haemoglobin test is performed and via appointment confirmation emails.

Australian Red Cross Lifeblood

Donation-related iron loss

	Sample Volume	Residual kit volume		Total whole blood (equivalent) loss	Estimated iron loss
	Whole blood	Packed cells	Whole blood equivalent*		
Plasmapheresis	11mL	3.2mL	8mL	19mL	9.5mg
Plateletpheresis	17mL	30mL	75mL	92mL	46mg
Whole blood	30mL		470mL	500mL	250mg

**Based on Hct of 0.40*

Australian Red Cross Lifeblood

Iron loss:
Apheresis vs Whole Blood

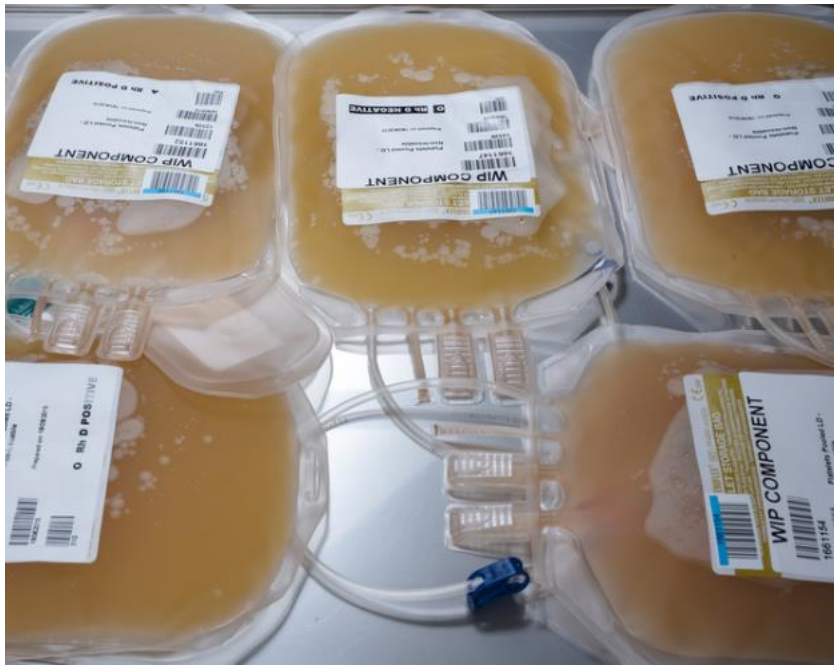
5 plateletpheresis donations ≈ one whole blood donation

Maximum donations per year

- 4 WB donations ≈1,000mg iron
- 26 plateletpheresis donations ≈1,200mg of iron

Permit cross over with following intervals

- Wait 4 weeks after WB before plateletpheresis
- Wait 2 weeks after plateletpheresis before WB
- Possible to give 18 platelets and 4 WB ≈ 1,828mg iron



Australian Red Cross Lifeblood

Are our plateletpheresis donors at risk of iron deficiency?

Investigate and mitigate the risk of iron deficiency in plateletpheresis, noting benefits for:

- Donor health and well being
- Return rates and eligibility
- Donors identified with non-anaemic iron deficiency during whole blood ferritin testing are eligible to give apheresis donations

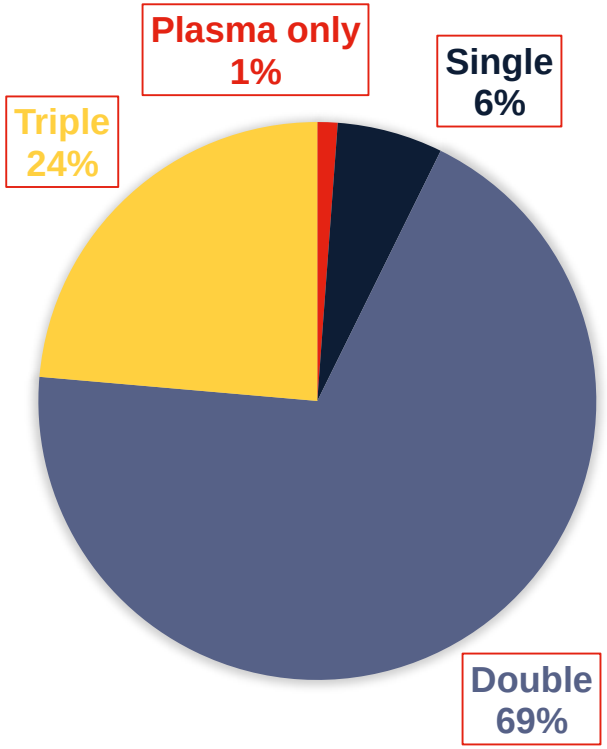
Australian Red Cross Lifeblood

Plateletpheresis

Collections

- 32% of platelets from apheresis
- 26,000 plateletpheresis donations per year
- 1.6% of total collections

Plateletpheresis – units collected



Australian Red Cross Lifeblood

Plateletpheresis – eligibility

Eligibility criteria

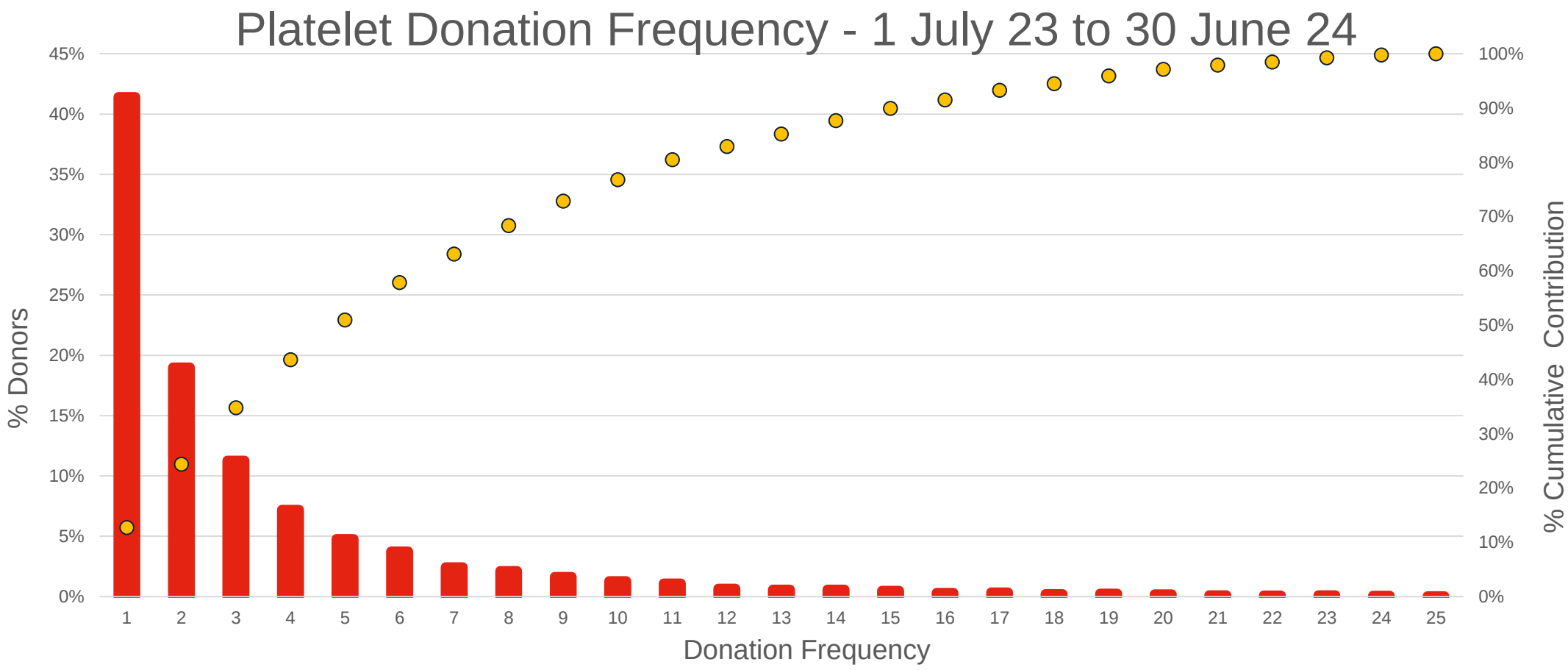
- Male
- Previous plasmapheresis collection
- Hb 125g/L -185g/L
- Minimum age 18 years
- Upper age limit – 75 for new donors and no upper age if returning
- 2 weekly intervals with maximum 26 collections per year

Routine testing

FBC sample collected with each donation and available post collection

Australian Red Cross Lifeblood

Contribution to the plateletpheresis numbers



5% of donors give >10 donations annually (23% of total collections)
49% of donors made at least one WB donation in last 12 months

Australian Red Cross Lifeblood

Plateletpheresis and ferritin testing

- FBC performed with each collection
- Currently no routine ferritin testing

- Ferritin testing is ordered if:
  - ✓ >20g/L drop in Hb from the last visit
  - ✓ FBC film/diff finding* such as:
    - ◯ Low MCV
    - ◯ High retic count
    - ◯ High platelet count
    - ◯ Low lymphocyte count

(*Ferritin ordered at the next visit)

Targeted ferritin testing in plateletpheresis

Donation history for donors with and without targeted ferritin testing in 2 years (Jul 2022 – Jun 2024)

	No ferritin test n=51,291	Ferritin test n=604	p value
Age (years)	46.43	47.43	0.087
Haemoglobin (g/L)	148.33	142.34	<0.0001
Prior WB collections	8.59	9.51	0.0273
Prior total platelet collections	24.80	32.41	<0.0001
Prior 1-year platelet collections	5.35	6.96	<0.0001
Prior 2- year platelet collections	8.86	11.45	<0.0001

Australian Red Cross Lifeblood

Targeted ferritin testing in plateletpheresis

Proportion of donors with iron deficiency based on the number of plateletpheresis collections in their last 12 months

Plateletpheresis collections in last 12 months (n)	**Ferritin tested n/(%)**	**Proportion (%) with iron deficiency** (Ferritin <30ug/L)
All	604	37.25
New donor	78 (0.85)	20.51
1-4	199 (1.00)	27.14
5-9	150 (1.29)	32.00
10-14	78 (1.29)	46.15
15-19	71 (2.17)	70.42
20-26	28 (2.33)	75.00

Plasma rinseback

Review feasibility and benefits of plasma rinseback to mitigate iron deficiency

- Plateletpheresis platform returns 30mL plasma (software upgrade will allow collection of additional 30mL for the rinseback, avoids component plasma loss)
- Has effect of returning 75% of the inline red cells which would otherwise not be returned
  - Mitigate iron deficiency in plateletpheresis donors, particularly important for;
    - Frequent plateletpheresis donors,
    - Those who also donate whole blood, and
    - In the context of our ferritin strategy that permits donors with non-anaemic iron deficiency to donate plasma and platelets.

Australian Red Cross Lifeblood

Trial of Plasma Rinseback

- Rinseback trial completed in a single centre
- 108 plateletpheresis collections – 236 doses
- Using our current software - 30mL was taken from the 650mL collection volume
- No adverse events occurred during rinseback
- 2-3 minutes additional time for single/double
- Mean bleed duration of 80.44 minutes

Other benefits of plasma rinseback – reduce lymphopenia

- Plateletpheresis associated lymphopenia is not a new issue
- Renewed interest based on studies that show:
  - Donors with a high donation frequency and/or a high number of total collections have a higher risk of low CD4 counts
  - Lymphopenia more common if a leukoreduction system (LRS) chamber is used
  - Lymphocytes remains both in the LRS chamber and in-line tubing
  - Evidence to suggest plasma rinseback is effective in reducing lymphopenia in platforms with an LRS
- There is no definitive evidence of clinical impacts

Plateletpheresis associated lymphopenia

Australian Red Cross Lifeblood®

Frequency of significant lymphopenia based on number of plateletpheresis collections in prior 12 months

Platelet collections in 2022	Number of donors	Donors with lymphocyte count <0.7 x 10^9/L.		Donors with lymphocyte count <0.5 x10^9/L.	
		N	%	N	%
0-9	7,236	64	0.88	3	0.04
10-19	372	32	8.60	2	0.54
≥20	24	5	20.83	0	0.00
Total	7,632	101	1.32	5	0.07

RCPA Reference Range for lymphocytes for an adult is 1.5-4 x10^9/L

Plateletpheresis associated lymphopenia

Frequency of significant lymphopenia based on the number of career (total) collections

Number of career collections (to end 2023)	Number of donors	Donors with lymphocyte count <0.7 x 10^9/L		Donors with lymphocyte count <0.5 x10^9/L	
		N	%	N	%
0-49	7,100	52	0.73	2	0.03
50-99	406	27	6.65	0	0.00
100-149	95	12	12.63	2	2.11
150-199	26	8	30.77	1	3.85
≥200	5	2	40.00	0	0.00
Total	7,632	101	1.32	5	0.07

Australian Red Cross Lifeblood

Lifeblood approach – lymphopenia

FBC each donation

Defer and refer donors with lymphocyte count <0.5 X 10^9/L

Repeat at next donation if count 0.5-0.7 X 10^9/L +/- ferritin

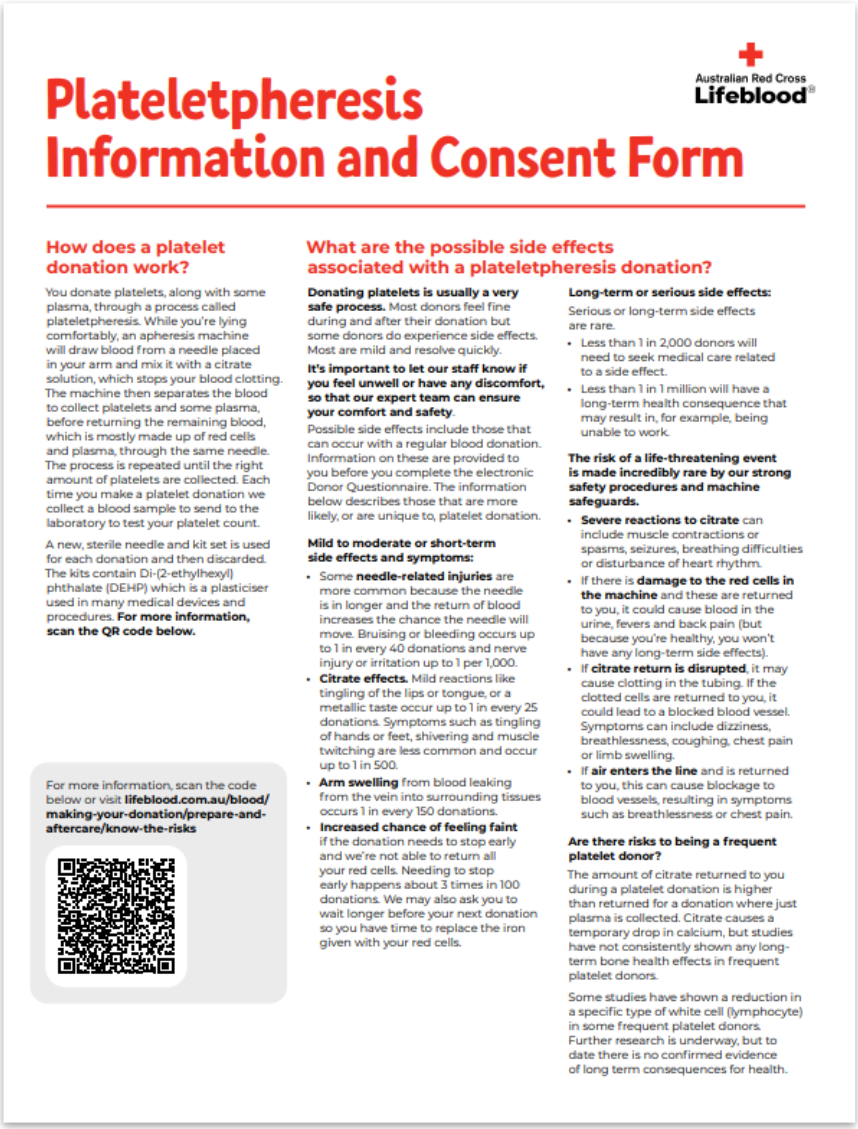
Consent form

Specific plateletpheresis information and consent form

Updated in 2023

Are there risks to being a frequent platelet donor?

Some studies have shown a reduction in a specific type of white cell (lymphocyte) in some frequent platelet donors. Further research is underway, but to date there is no confirmed evidence of long term consequences for health.



Plateletpheresis Information and Consent Form

Australian Red Cross Lifeblood

How does a platelet donation work?

You donate platelets, along with some plasma, through a process called plateletpheresis. While you're lying comfortably, an apheresis machine will draw blood from a needle placed in your arm and mix it with a citrate solution, which stops your blood clotting. The machine then separates the blood to collect platelets and some plasma, before returning the remaining blood, which is mostly made up of red cells and plasma, through the same needle. The process is repeated until the right amount of platelets are collected. Each time you make a platelet donation we collect a blood sample to send to the laboratory to test your platelet count.

A new, sterile needle and kit set is used for each donation and then discarded. The kits contain Di-(2-ethylhexyl) phthalate (DEHP) which is a plasticiser used in many medical devices and procedures. **For more information, scan the QR code below.**

For more information, scan the code below or visit **lifeblood.com.au/blood/making-your-donation/prepare-and-aftercare/know-the-risks**

What are the possible side effects associated with a plateletpheresis donation?

Donating platelets is usually a very safe process. Most donors feel fine during and after their donation but some donors do experience side effects. Most are mild and resolve quickly.

It's important to let our staff know if you feel unwell or have any discomfort, so that our expert team can ensure your comfort and safety.

Possible side effects include those that can occur with a regular blood donation. Information on these are provided to you before you complete the electronic Donor Questionnaire. The information below describes those that are more likely, or are unique to, platelet donation.

Mild to moderate or short-term side effects and symptoms:

- Some **needle-related injuries** are more common because the needle is in longer and the return of blood increases the chance the needle will move. Bruising or bleeding occurs up to 1 in every 40 donations and nerve injury or irritation up to 1 per 1,000.
- **Citrate effects.** Mild reactions like tingling of the lips or tongue, or a metallic taste occur up to 1 in every 25 donations. Symptoms such as tingling of hands or feet, shivering and muscle twitching are less common and occur up to 1 in 500.
- **Arm swelling** from blood leaking from the vein into surrounding tissues occurs 1 in every 150 donations.
- **Increased chance of feeling faint** if the donation needs to stop early and we're not able to return all your red cells. Needing to stop early happens about 3 times in 100 donations. We may also ask you to wait longer before your next donation so you have time to replace the iron given with your red cells.

Long-term or serious side effects:

Serious or long-term side effects are rare.

- Less than 1 in 2,000 donors will need to seek medical care related to a side effect.
- Less than 1 in 1 million will have a long-term health consequence that may result in, for example, being unable to work.

The risk of a life-threatening event is made incredibly rare by our strong safety procedures and machine safeguards.

- **Severe reactions to citrate** can include muscle contractions or spasms, seizures, breathing difficulties or disturbance of heart rhythm.
- If there is **damage to the red cells in the machine** and these are returned to you, it could cause blood in the urine, fevers and back pain (but because you're healthy, you won't have any long-term side effects).
- If **citrate return is disrupted**, it may cause clotting in the tubing. If the clotted cells are returned to you, it could lead to a blocked blood vessel. Symptoms can include dizziness, breathlessness, coughing, chest pain or limb swelling.
- If **air enters the line** and is returned to you, this can cause blockage to blood vessels, resulting in symptoms such as breathlessness or chest pain.

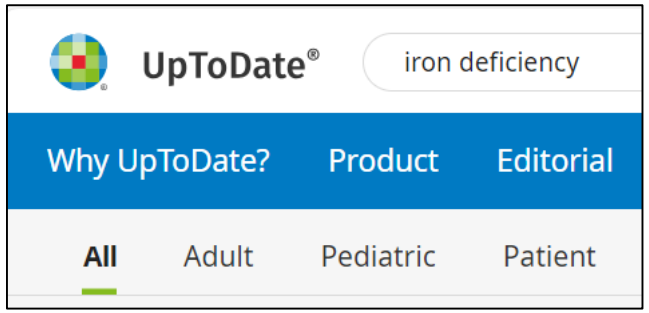
Are there risks to being a frequent platelet donor?

The amount of citrate returned to you during a platelet donation is higher than returned for a donation where just plasma is collected. Citrate causes a temporary drop in calcium, but studies have not consistently shown any long-term bone health effects in frequent platelet donors.

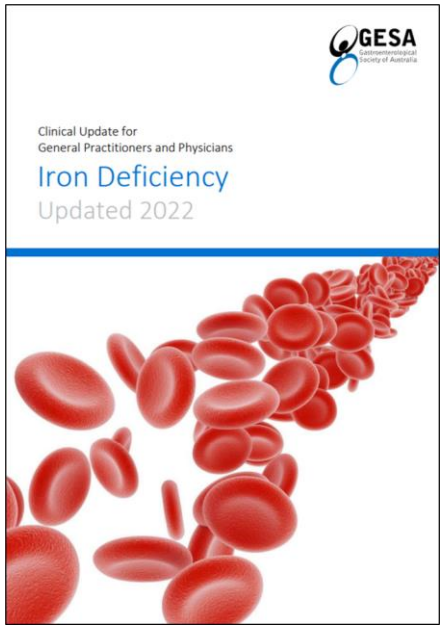
Some studies have shown a reduction in a specific type of white cell (lymphocyte) in some frequent platelet donors. Further research is underway, but to date there is no confirmed evidence of long term consequences for health.

Is there adequate clinical awareness of iron loss with plateletpheresis?

- Well recognised that blood loss is iron loss, and that regular blood donation may cause iron deficiency
- Less well recognised that regular plateletpheresis donation may cause iron deficiency



"In contrast to standard whole blood donation, apheresis donation is performed as a way to collect platelets or plasma without removing red blood cells (RBCs)"



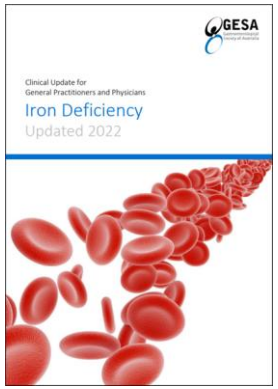
"Other situations causing blood loss may be regular blood donation…"

Australian Red Cross Lifeblood

Are plateletpheresis donors at risk of over-investigation for iron deficiency?

Diagnosis of the cause

Diagnosis of the cause of iron deficiency requires taking a careful history and usually involves referral to a specialist gastroenterologist for consideration of upper and lower endoscopies and, if these are normal, capsule endoscopy. Coeliac serology should be performed for most individuals.



#N2Y (never too young) to have bowel cancer

Future directions

- Roll-out of plasma rinseback nationally in mid-2025 when new software updates in place
- Consider routine ferritin testing in frequent plateletpheresis donors
- Donation intervals based on iron loss – tailored based on WB, plasma and red cell loss

In conclusion

- Frequent plateletpheresis donors are at risk of iron deficiency
- Frequent plateletpheresis donors and those with >150 total donations have higher rates of lymphopenia, clinical significance is uncertain

- Plasma rinseback reduces red cell loss and lymphocyte loss, is well tolerated and only adds 2-3 minutes of additional collection time. No loss of plasma component volume.

- Well recognised that blood loss is iron loss and whole blood donation may cause iron deficiency
- Iron deficiency in frequent platelepheresis donors (samples and residual red cells in the collection kit) may be disregarded as a cause because the red cell loss is not as obvious

Thank you

Australian governments fund Australian Red Cross Lifeblood to provide blood, blood products and services to the Australian community.

Sanquin

Change in hemoglobin to identify a functionally relevant ferritin cut-off for iron deficiency

A study in blood donor populations

Amber Meulenbeld
15-01-2025

In collaboration with Esa Turkulainen, Hongchao Qi, Wanjin Li, Elias Allara, Emanuele DiAngelantonio, Ronel Swanevelder, Tinus Brits, Yared Paalvast, Hanke Matlung, Dorine Swinkels, Katja van den Hurk, Alton Russell, Mikko Arvas, and Mart Janssen

For Life.

No conflicts of interest to declare.

Prevent anemia & iron deficiency in blood donors The Netherlands

	Hb		Ferritin	Deferral
Males	≥ 8.4 mmol/L	All	<15 ng/mL	12 Months
Females	≥ 7.8 mmol/L		15 - ≤30 ng/mL	6 Months

Iron deficiency

WHO iron deficiency definition:

Ferritin < 15 ng/mL

- Based on liver biopsies and bone marrow staining
- Certainty of evidence from systematic reviews is low to very low

→ Risk of bias, indirectness and imprecision

- Other cut-offs in guidelines vary from 12-100 ng/mL

Iron deficiency

Absolute iron deficiency
Severe reduction/absence of iron stores.

Functional iron deficiency
Inability to utilize available iron, and thus, for example unable to recover Hb

Iriarte-Gahete et al., Blood Reviews, 2024
Tawfik et al., JAMA Netw Open, 2024

Aim

Find a functional iron deficiency cut-off for ferritin based on change in Hb

Methods

Blood bank data:

- Sanquin
- SANBS
- Vitalant

Cohorts:

- FinDonor
- INTERVAL

Methods: ferritin measurement

Country	Manufacturer/platform
Finland	Abbott Architect Ci8200 Roche Cobas c501
The Netherlands	Abbott Architect Ci8200
South Africa	Beckman Coulter UniCell Dxl 800
United Kingdom	Roche Cobas e801
United States	Beckman Coulter AU680

Methods: ferritin measurement

Reference materials exist to calibrate routine assays performed in laboratories.

WHO international standards (IS):

- First (liver)
- Second (spleen)
- Third (recombinant)
- Fourth (recombinant)

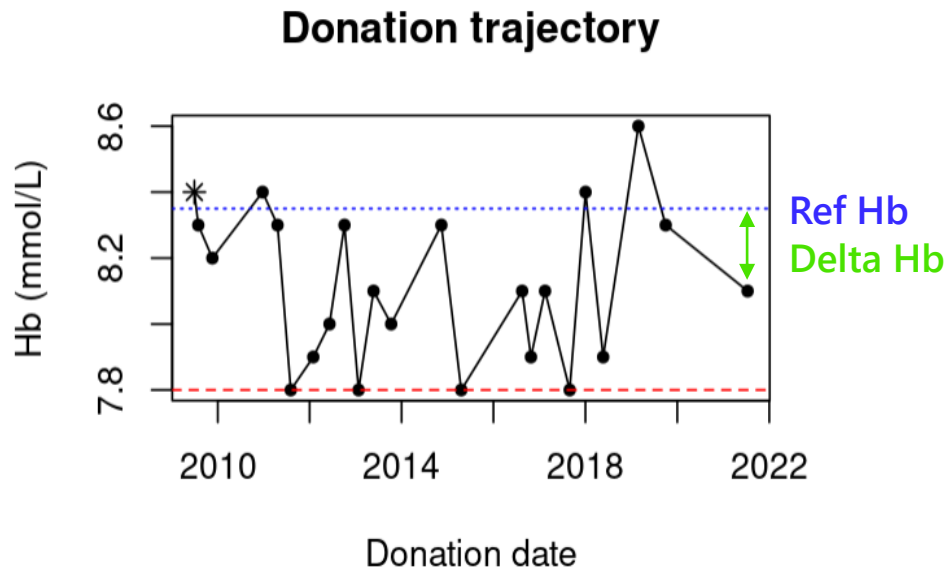
Methods: data selection

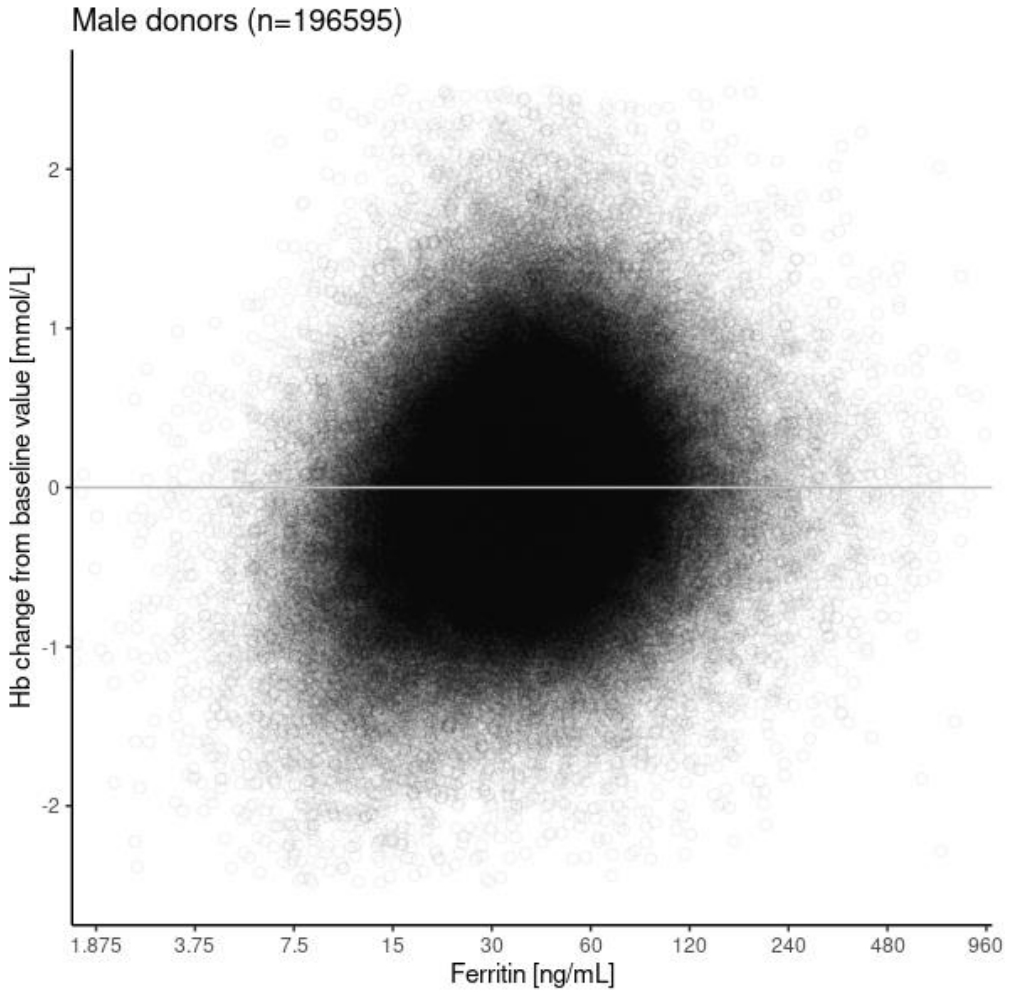
Reference Hb	Follow-up Hb or ferritin
Used to calculate changes in Hb at follow-up. Should be unaffected by prior blood donation. R1: No donation in a prior 2-year period OR R2: Average of Hb measured at the first two blood bank visits. R3: Use most proximal reference Hb for each visit.	Hb and Ferritin levels measured at a donation. Valid for any blood product or donation outcome. F1: Preceded by a donation with reference Hb level AND F2: Both ferritin and Hb were measured AND F3: At least one successful RBC-containing donation in previous 2-years.

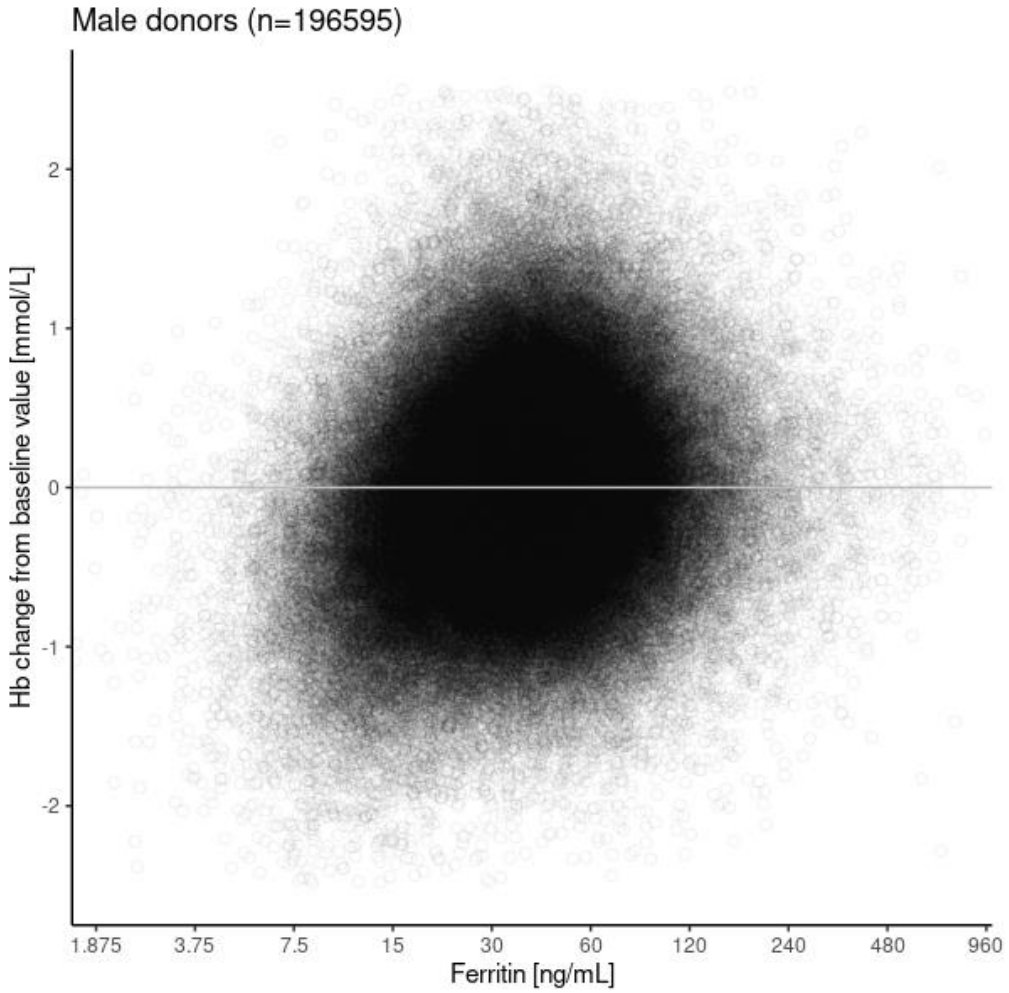
Methods

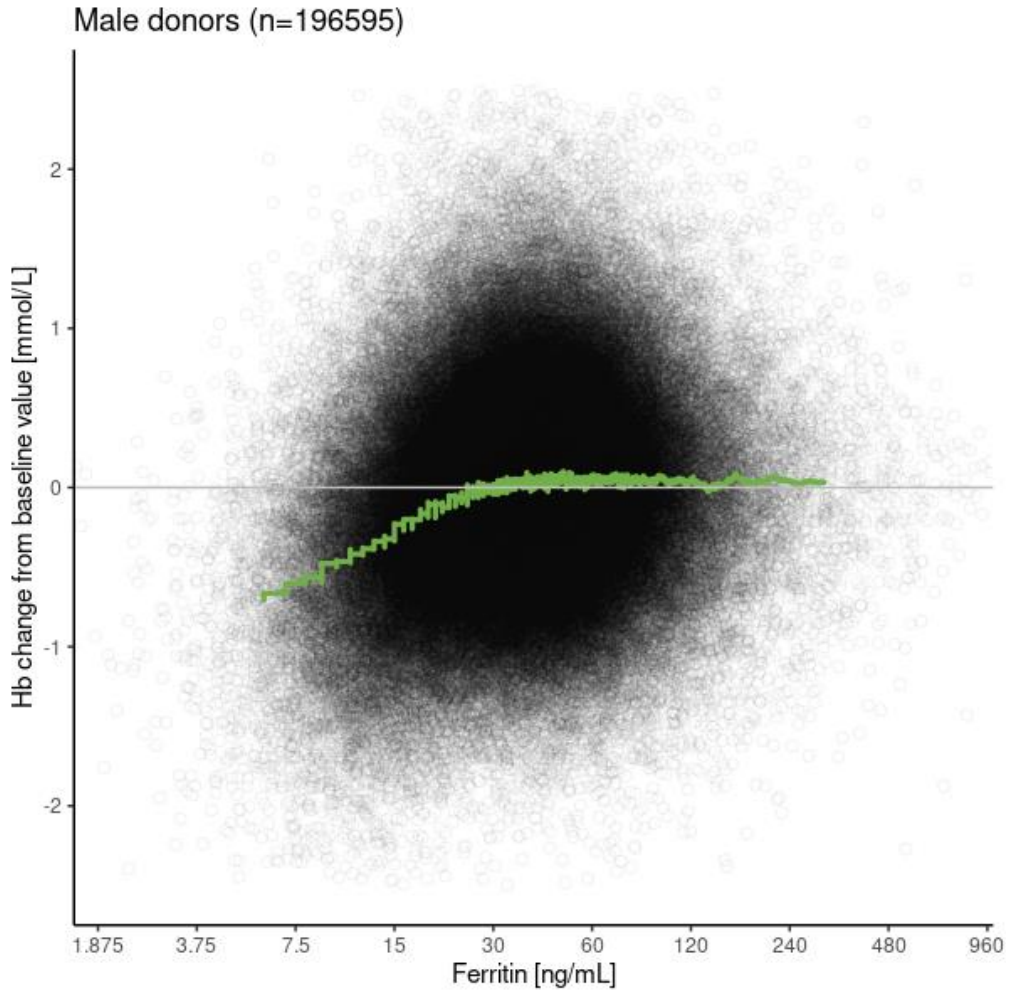
Ferritin: log transformed
Hb change:

$$\Delta\text{Hb} = Follow\ up\ Hb\ - Reference\ Hb$$



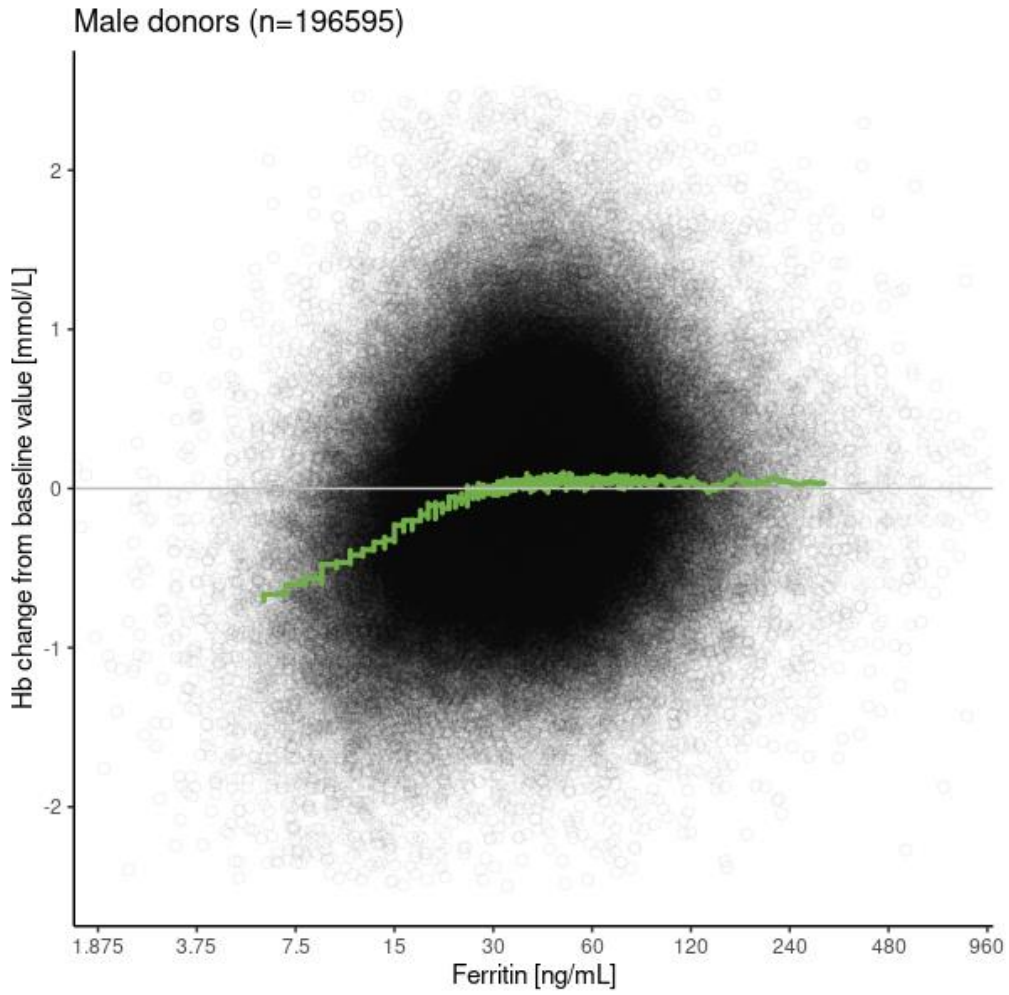

Male donors (n=196595)
Hb change from baseline value [mmol/L]
2
1
0
-1
-2
1.875
3.75
7.5
15
30
60
120
240
480
960
Ferritin [ng/mL]


Male donors (n=196595)
Hb change from baseline value [mmol/L]
2
1
0
-1
-2
1.875
3.75
7.5
15
30
60
120
240
480
960
Ferritin [ng/mL]


Male donors (n=196595)
Hb change from baseline value [mmol/L]
2
1
0
-1
-2
1.875
3.75
7.5
15
30
60
120
240
480
960
Ferritin [ng/mL]

Methods

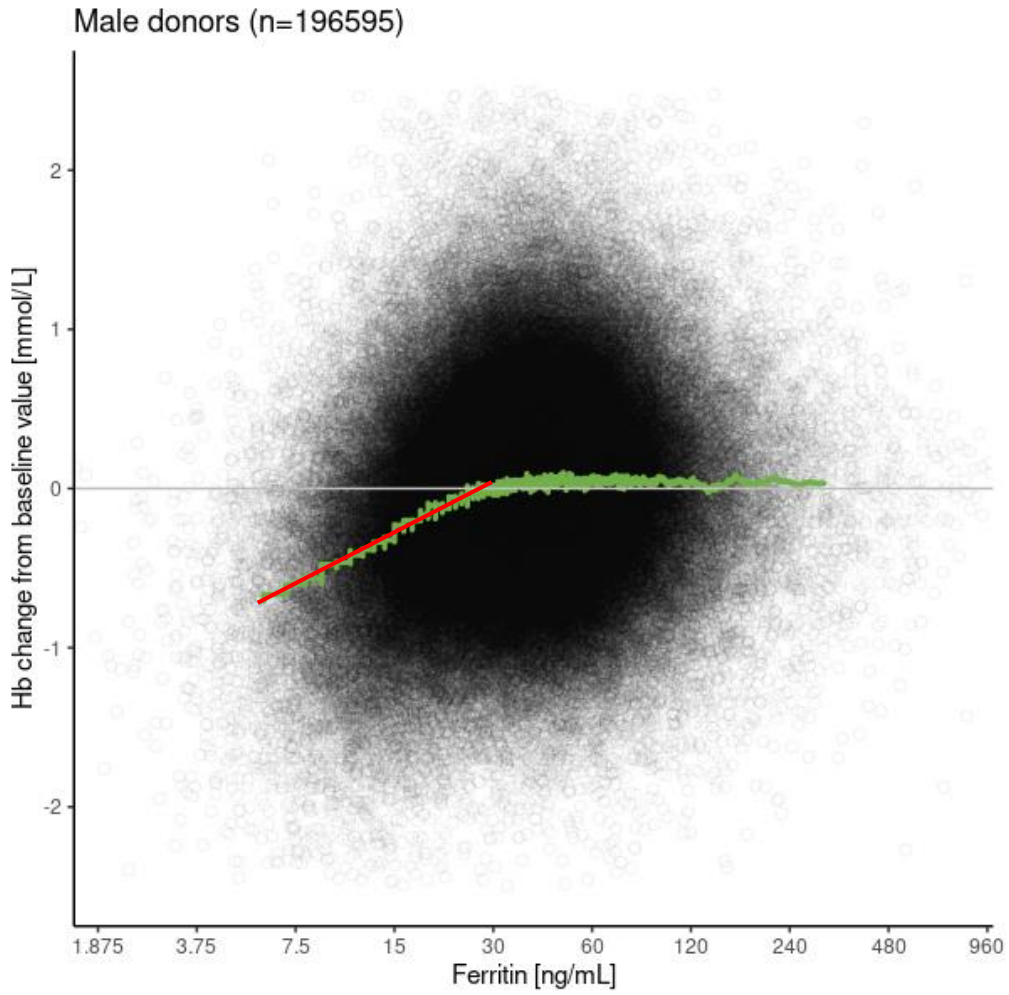
We fit a line:



Methods

We fit a line:

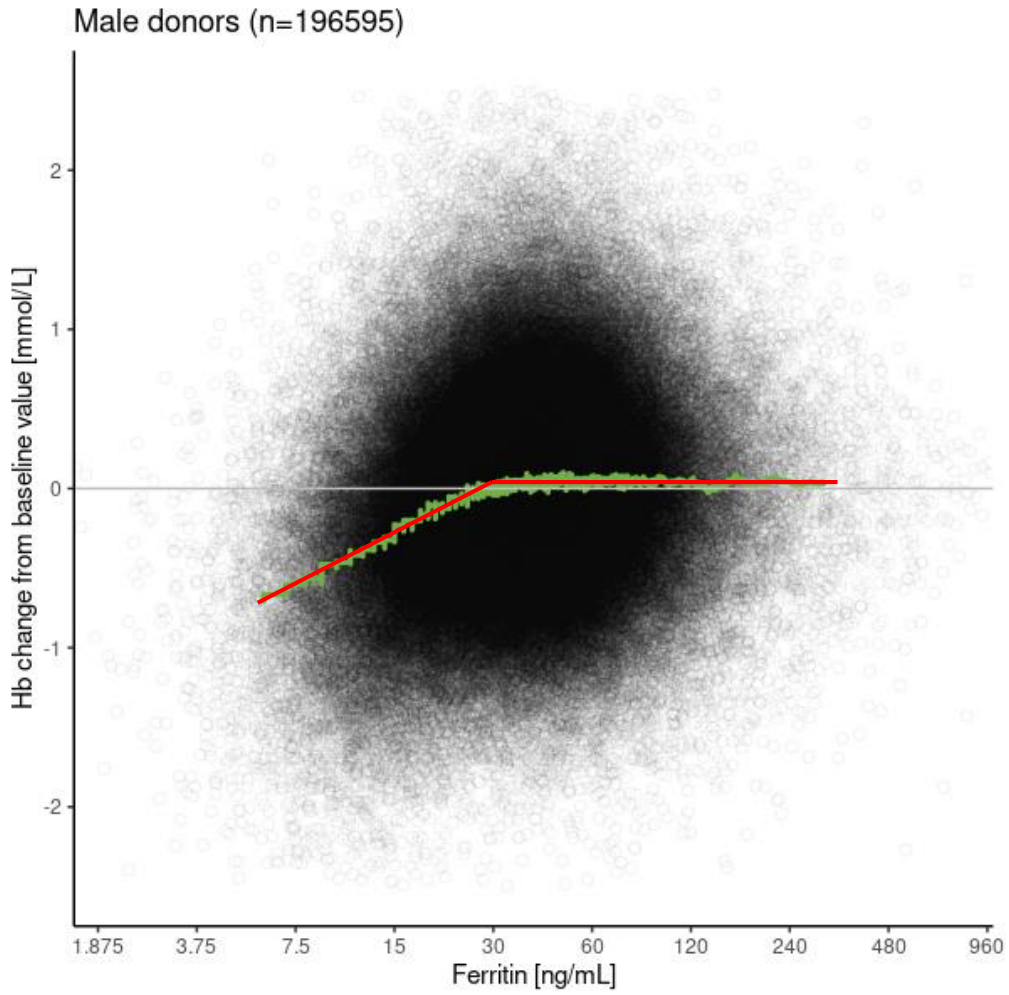
- First segment



Methods

We fit a line:

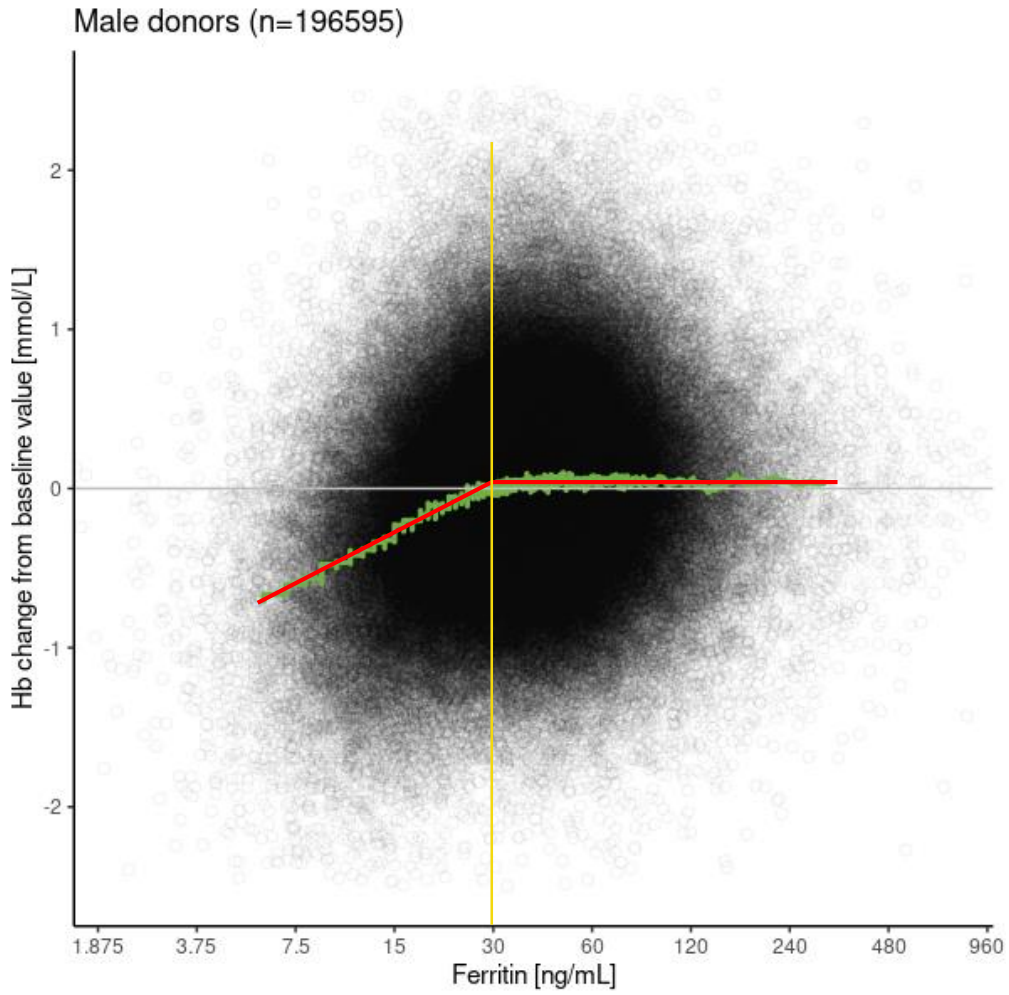
- First segment
- Second segment



Methods

We fit a line:

- First segment
- Second segment
- Changepoint (cut-off)

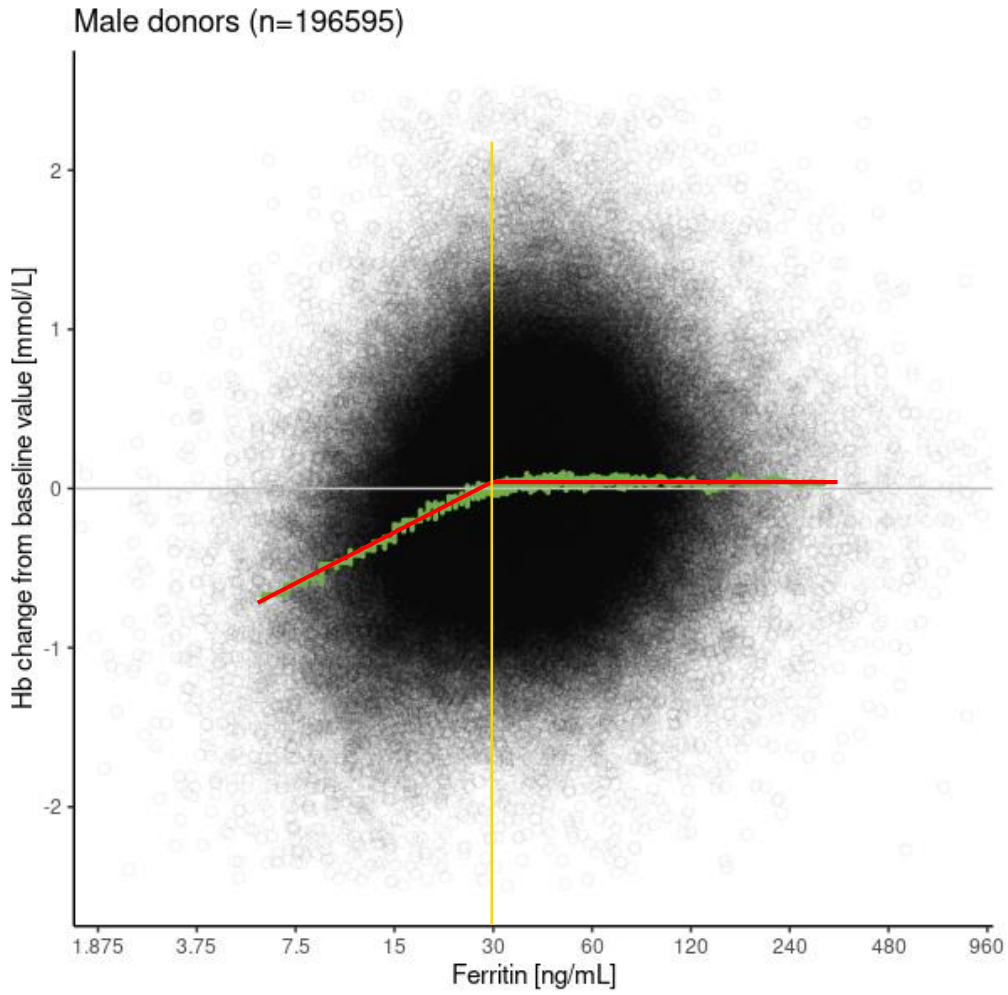


Methods

We fit a line:

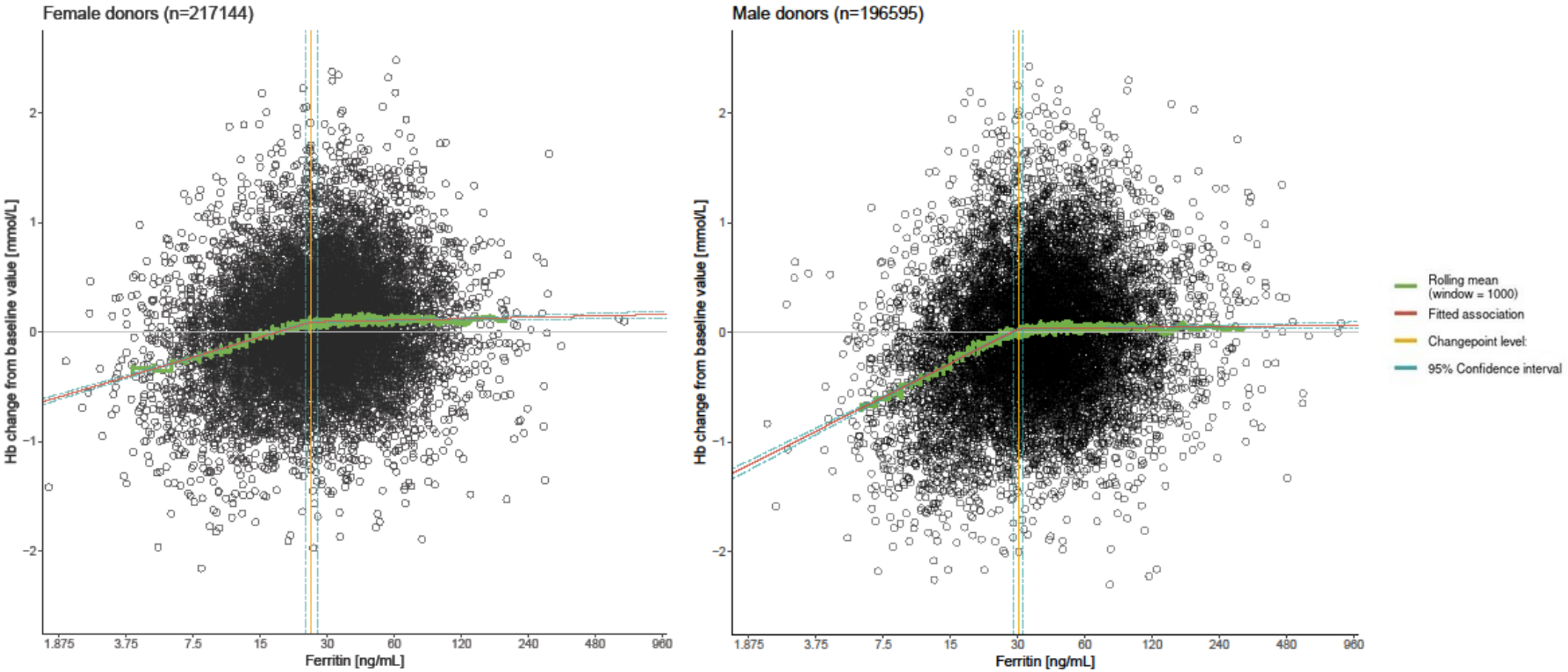
- First segment
- Second segment
- Changepoint (cut-off)

Seperately analysed males, females, premenopausal females and postmenopausal females

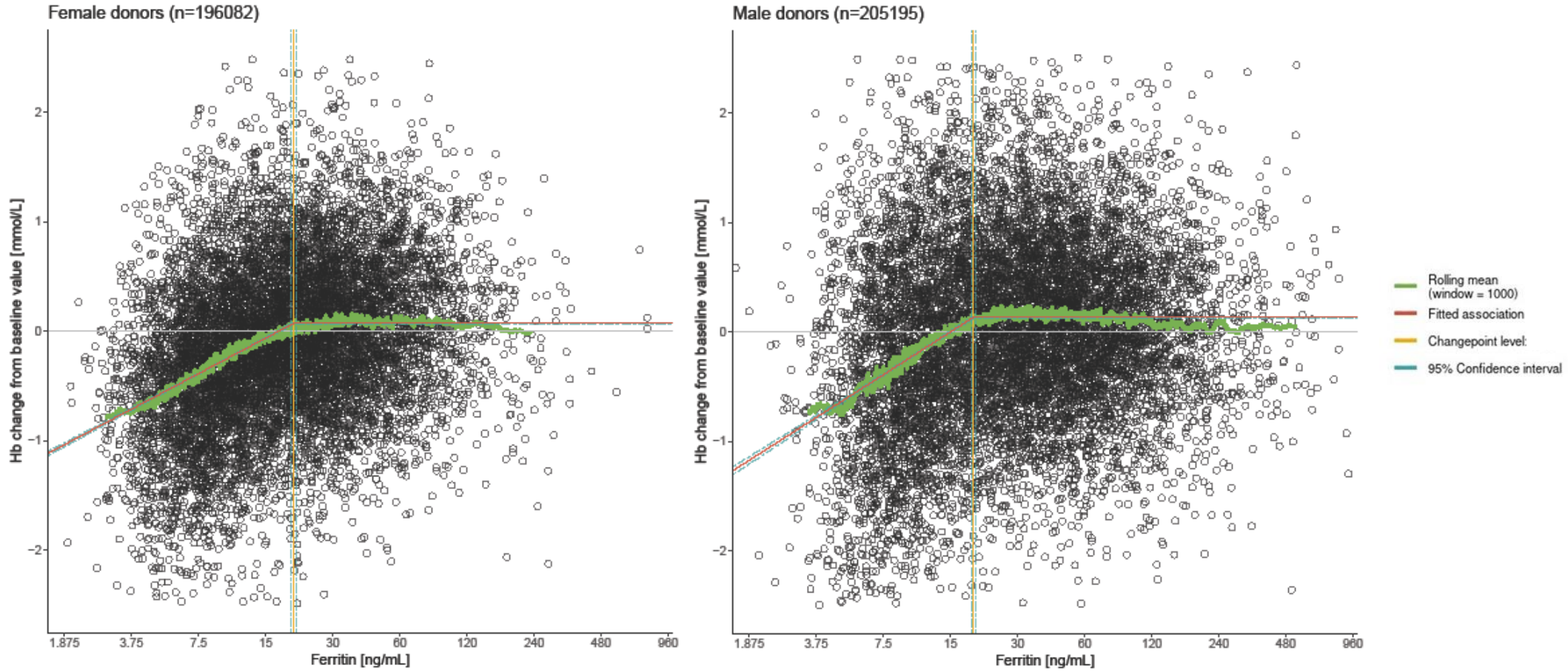


Results

The Netherlands

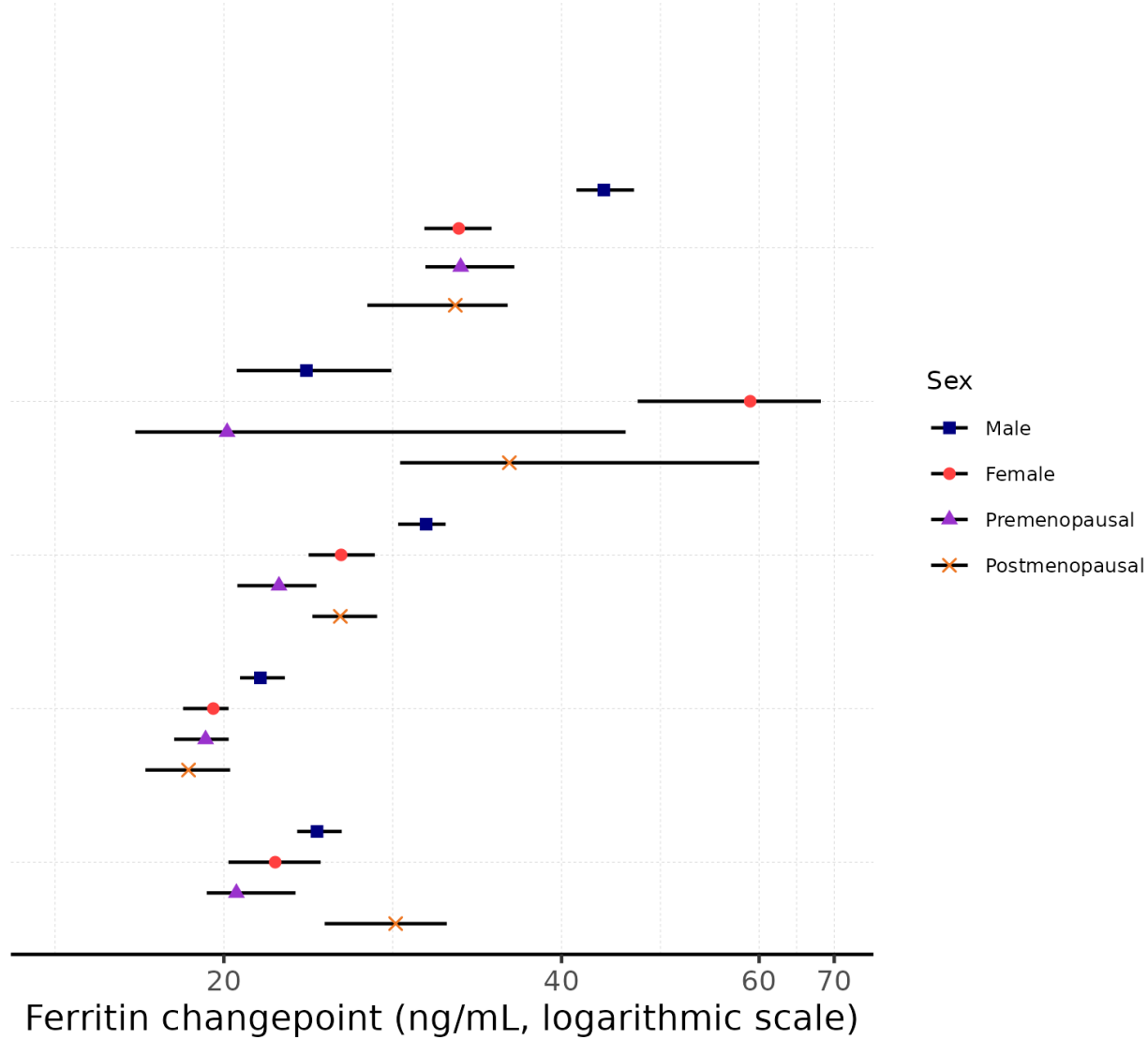


South Africa



Cut-off for functional iron deficiency

Country	Changepoint (95% CI)	N (donations)
ENG	43.6 (41.2 - 46.4)	20,975
	32.4 (30.2 - 34.6)	19,697
	32.5 (30.2 - 36.3)	10,613
	32.2 (26.8 - 35.8)	9,084
FIN	23.7 (20.5 - 28.2)	3,462
	58.9 (46.8 - 68.1)	3,457
	20.1 (16.7 - 45.6)	1,867
	35.9 (28.7 - 60.0)	1,590
NL	30.3 (28.6 - 31.5)	196,595
	25.4 (23.8 - 27.3)	217,144
	22.4 (20.6 - 24.2)	138,623
	25.4 (24.0 - 27.4)	78,521
SA	21.6 (20.7 - 22.7)	205,195
	19.6 (18.4 - 20.2)	196,082
	19.3 (18.1 - 20.2)	149,368
	18.6 (17.0 - 20.3)	46,714
USA	24.2 (23.2 - 25.5)	65,052
	22.2 (20.2 - 24.4)	100,616
	20.5 (19.3 - 23.2)	76,670
	28.5 (24.6 - 31.6)	23,946



Discussion

Cut-offs found may not be relevant for iron deficiency-related symptoms

Discussion

Cut-offs found may not be relevant for iron deficiency-related symptoms

Within country differences (sex differences):

- Generally lower for females
- Potential role for iron supplementation
- Exact mechanism needs further investigation

Discussion

Cut-offs found may not be relevant for iron deficiency-related symptoms

Within country differences (sex differences):

- Generally lower for females
- Potential role for iron supplementation
- Exact mechanism needs further investigation

Between country differences:

- Population differences
- Policy differences
- Differences in ferritin measurement?

Discussion

Country	Manufacturer/platform	Standard
Finland	Abbott Architect Ci8200 Roche Cobas c501	1st
The Netherlands	Abbott Architect Ci8200	1st
South Africa	Beckman Coulter UniCell Dxl 800	3rd
United Kingdom	Roche Cobas e801	1st
United States	Beckman Coulter AU680	3rd

! Big differences observed between platforms that report using the same standard and between labs that use the same platform

Conclusion

We can define a ferritin cut-off below which Hb starts to decrease (functional ID) in multiple settings

Conclusion

We can define a ferritin cut-off below which Hb starts to decrease (functional ID) in multiple settings

Cut-off differs across countries, probably because of:

- Population differences
- Policy differences
- Differences in ferritin measurement

Conclusion

We can define a ferritin cut-off below which Hb starts to decrease (functional ID) in multiple settings

Cut-off differs across countries, probably because of:

- Population differences
- Policy differences
- Differences in ferritin measurement

Implications:

- Donor management strategies may focus on minimizing change in Hb instead of general cut-offs
- Focus on reporting, calibration and use of (recent) standards

Conclusion

We can define a ferritin cut-off below which Hb starts to decrease (functional ID) in multiple settings

Cut-off differs across countries, probably because of:

- Population differences
- Policy differences
- Differences in ferritin measurement

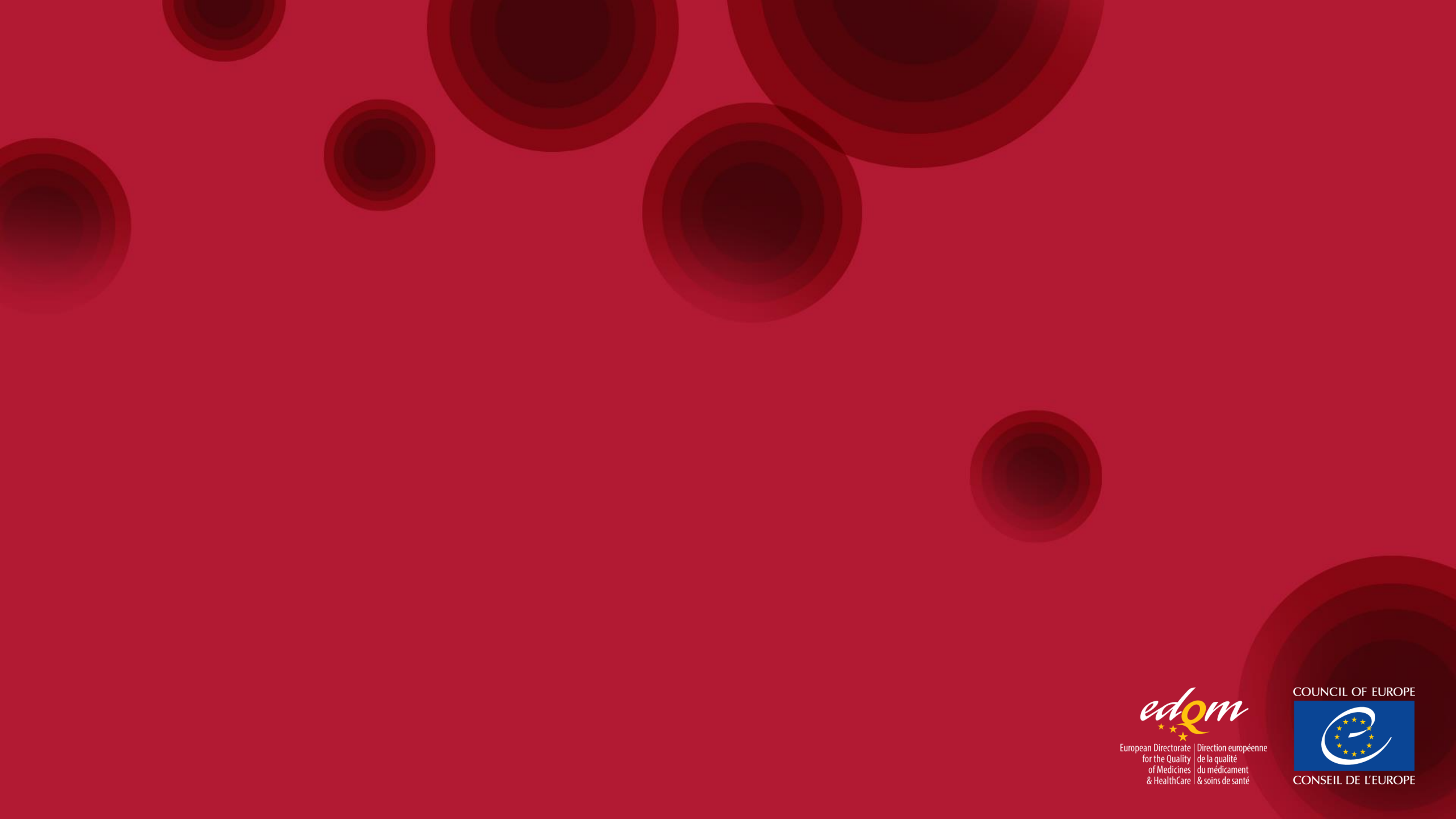
Implications:

- Donor management strategies may focus on minimizing change in Hb instead of general cut-offs
- Focus on reporting, calibration and use of (recent) standards

Recommendation for now: ID cut-offs defined per country/blood establishment

Sanquin

For Life.


edqm
European Directorate for the Quality of Medicines & HealthCare
Direction européenne de la qualité du médicament & soins de santé
COUNCIL OF EUROPE
CONSEIL DE L'EUROPE