

Big Data in Donor Research

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What is the need?

Provide compelling evidence for blood services both nationally and internationally on major issues related to blood donation.

Provide a more personalised service.

Build major bioresources involving donors as enduring research platforms.

Large-scale studies in the English blood service

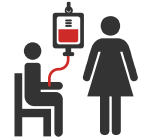
Scale

0.9M distinct individuals donate annually (1.7M donations)



Serial sampling

The typical donor attends about twice per year



Cost-effectiveness

>70 existing fixed and mobile centres
>23,000 donation sessions
>1500 existing phlebotomists

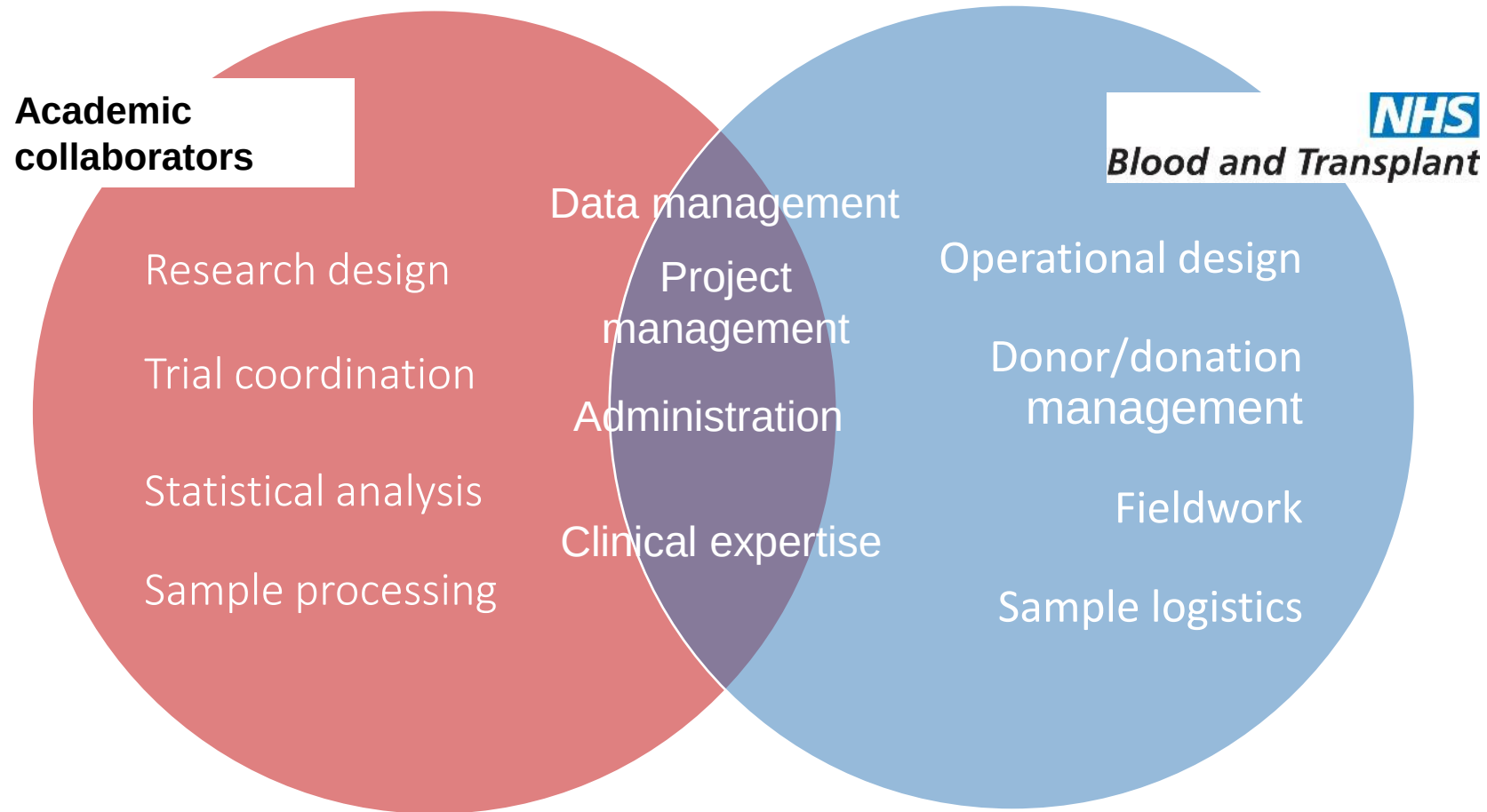


Altruism

Donors are unpaid volunteers



Partnership between NHSBT and academia



Building bioresources to help address questions relevant to blood donors and the wider population

Studies in blood donors

2012 - 16

- **INTERVAL**
- 50,000-person randomised controlled trial
- Optimum donation frequency for blood supplies and donor health

2016 - 17

- **COMPARE**
- 30,000-person observational study
- Optimum methods for Hb screening

2019-22

- **STRIDES**
- 1.4M-person cluster randomised trial
- Optimum strategy to prevent vasovagal reactions in blood donors

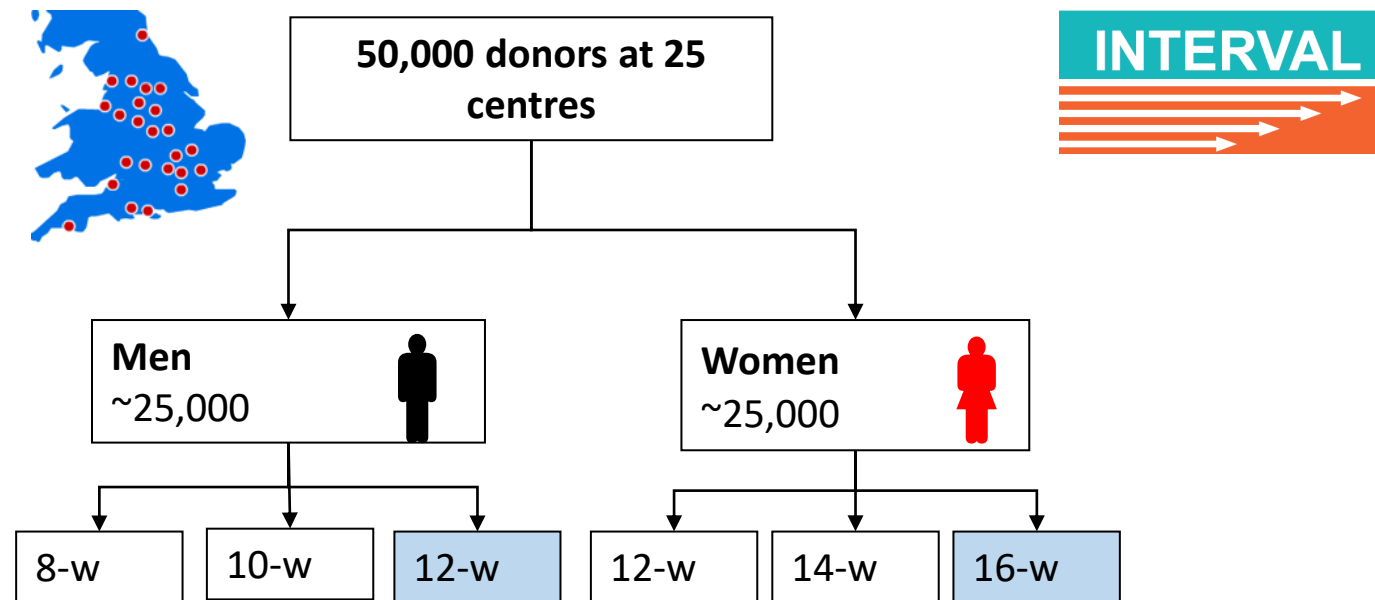
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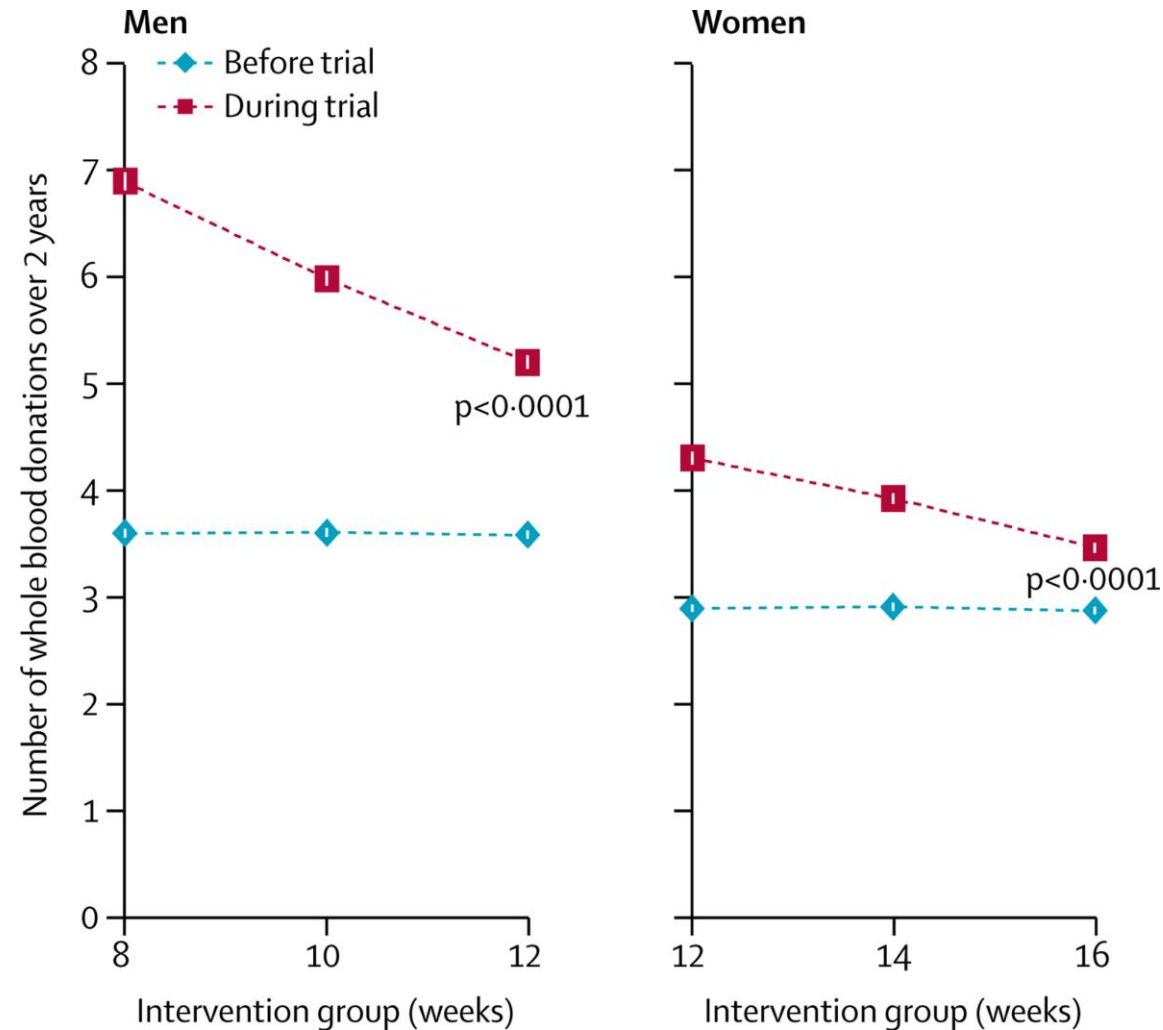
INTERVAL trial

What is the optimum time period between blood donations for safety and efficiency?

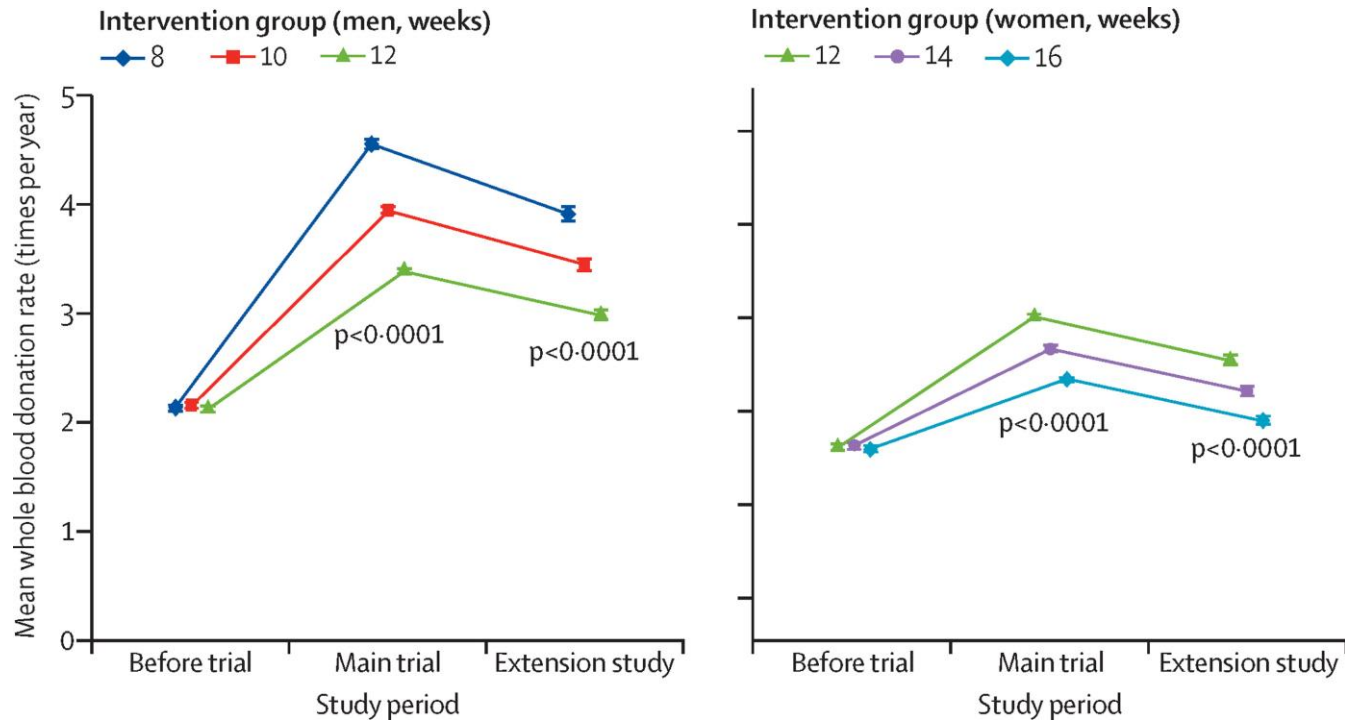


Pragmatic, randomised controlled trial embedded within NHSBT framework

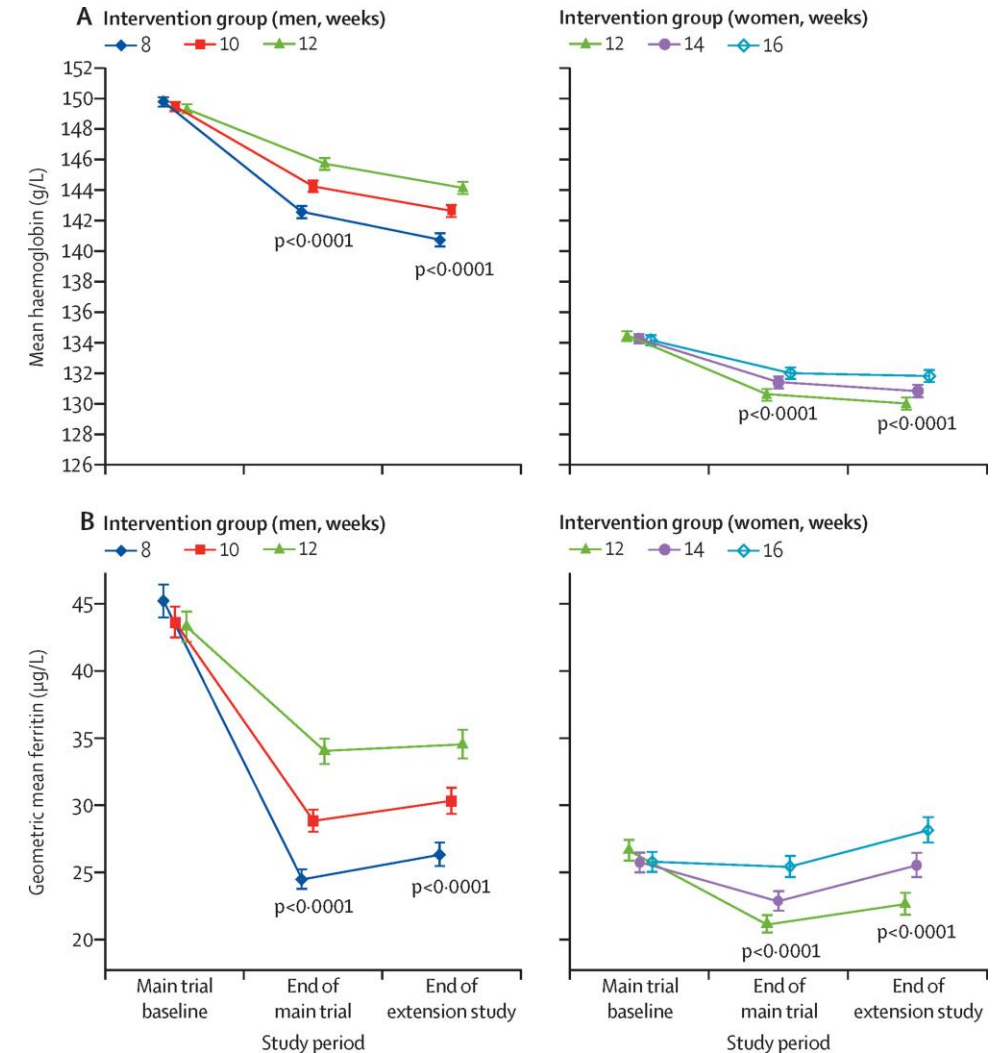
INTERVAL: primary outcome, efficiency of blood donation



Blood donation, haemoglobin and ferritin during the INTERVAL trial



More blood collected, but lower haemoglobin concentrations

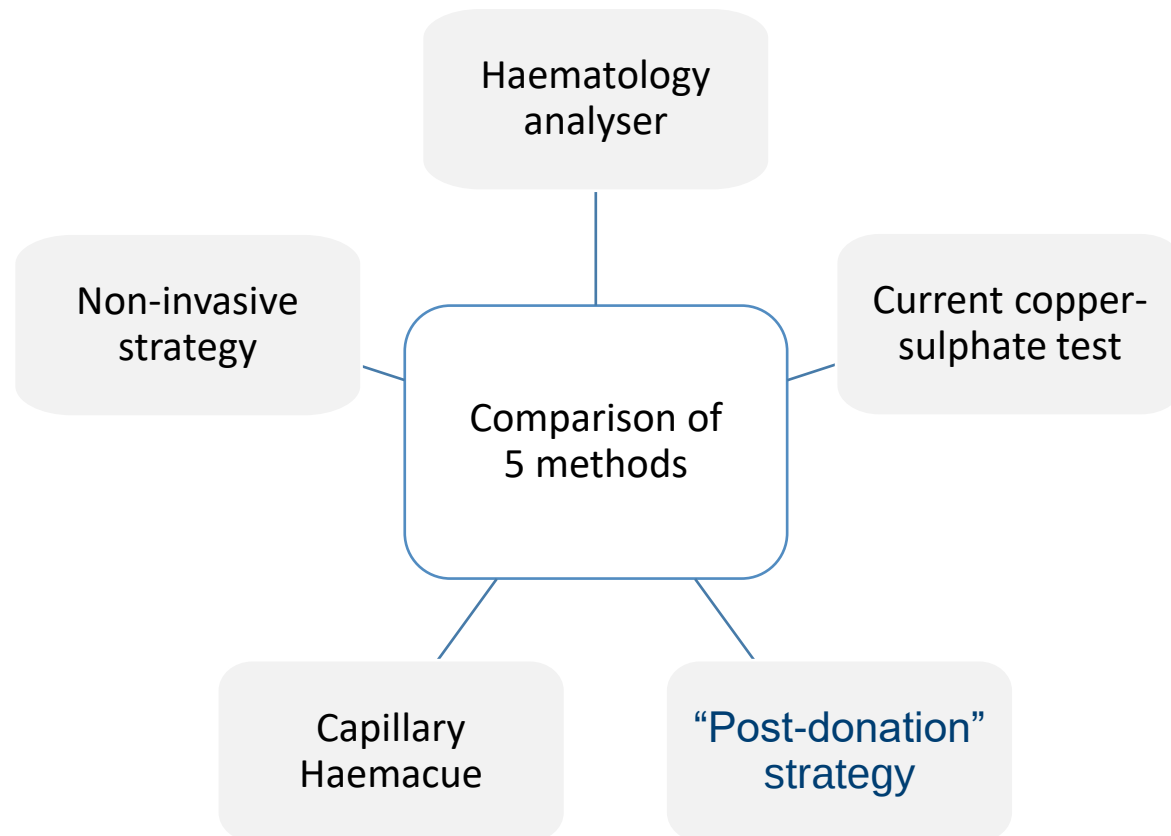


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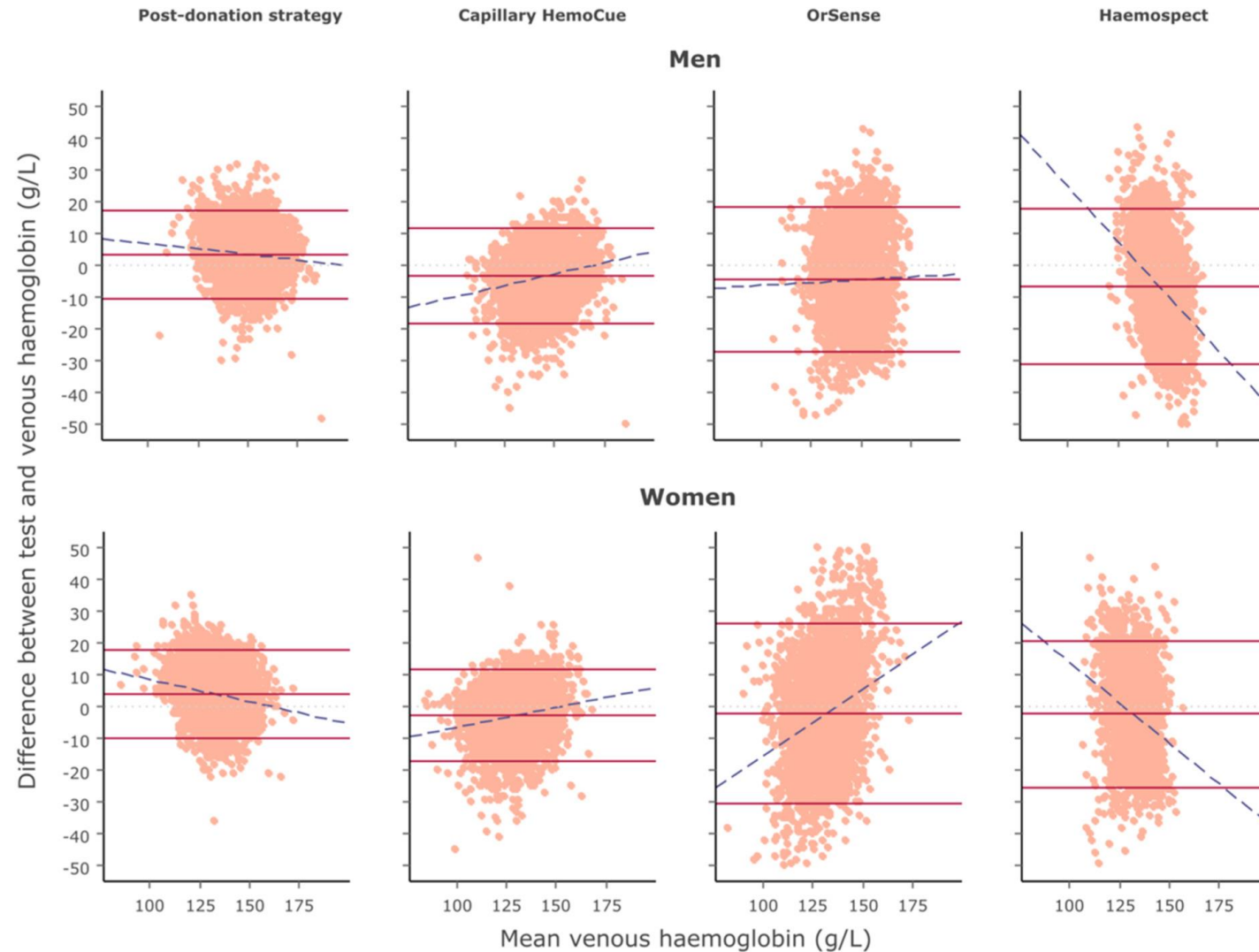
What is the optimum test to screen haemoglobin levels in blood donors?



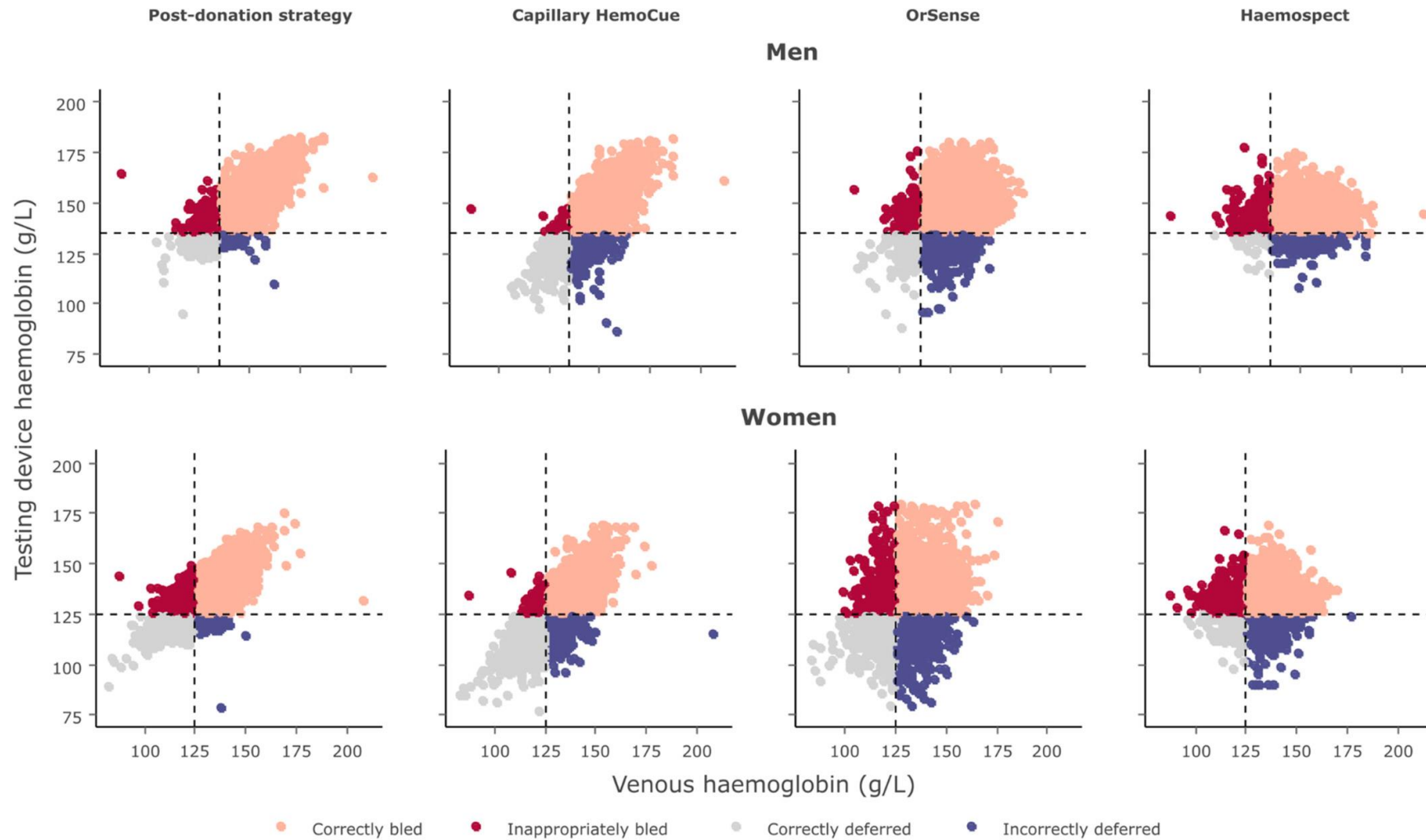
Key outcomes

- test accuracy
- feasibility and acceptability
- cost-effectiveness

Bland–Altman plot of each haemoglobin testing strategy by sex using venous haemoglobin values as the reference test.



Comparing testing device values vs venous blood samples



Studies in blood donors

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Clinical Significance of Vasovagal Reactions (VVRs)

- Worldwide: 14-70 moderate VVRs per 1000 donations, and 1.2-2.7 for severe reactions.
- NHBST: ~25,000 VVRs between 2017/ 2018, of which ~3000 severe reactions.
- These reactions cause the greatest degree of donor injury.
- Reduced likelihood of repeat donation by up to 50%

A cluster-randomised trial embedded in the English blood service

The STRIDES trial is a cluster-randomised trial of **four interventions to prevent vasovagal reactions (VVRs)** during routine blood donation.

1. **Isotonic hydration before donation (ISO)**, comparing 500ml isotonic drink vs current 500ml plain water;
2. **Time on donation chair after donation (CHA)**, comparing 3-minutes rest on donation chair before standing vs current 2-minutes;
3. **Modified applied muscle tension (AMT)**, comparing new AMT vs current practice of AMT;
4. **Psychosocial intervention (PSY)**, comparing provision of preparatory materials vs current practice of nothing.

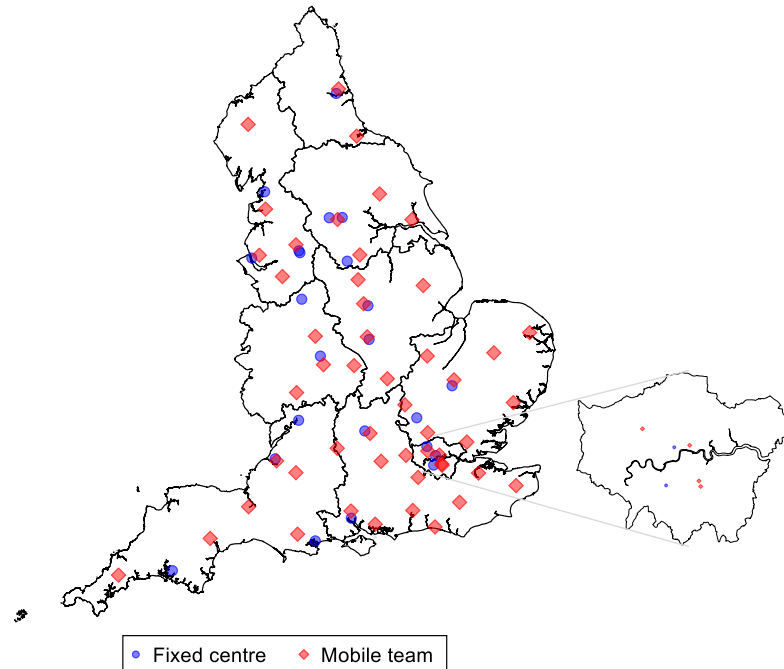
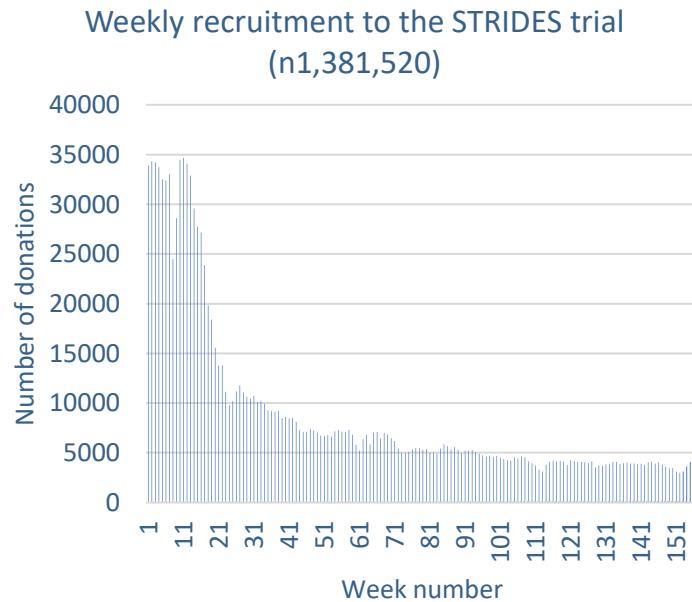


NHS
Blood and Transplant

NIHR | BioResource

STRategies to Improve Donor ExperienceS (STRIDES)

- 73 teams conducting routine blood collections in the entirety of NHSBT in England
- 04 November 2019 to 03 November 2022



Stepped-wedge (AMT, PSY)

Cluster	9 months	9 months	9 months	9 months
1	X	X	X	X
2	X	X	X	A
3	X	X	A	A
4	X	A	A	A

A: Intervention
X: Usual Practice

Cross-over (ISO, CHA)

Cluster	9 months	9 months	9 months	9 months
1	X	B	X	B
2	B	X	B	X

B: Intervention
X: Usual Practice

Factorial (AMT, PSY, ISO, CHA)

Cluster	9 months	9 months	9 months	9 months
1	X	B	X	B
2	B	X	B	X
3	X	B	X	A + B
4	B	X	B	A
5	X	B	A	A+B
6	B	X	A+B	A
7	X	A+B	A	A+B
8	B	A	A+B	A

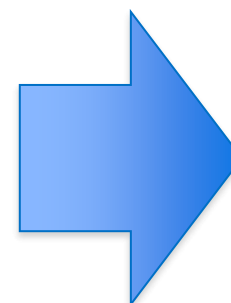
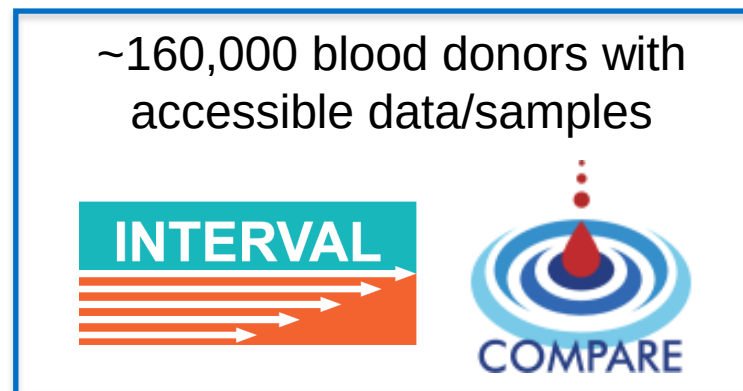
A or B: Intervention
X: Usual Practice

Participants characteristics, consent and e-health records

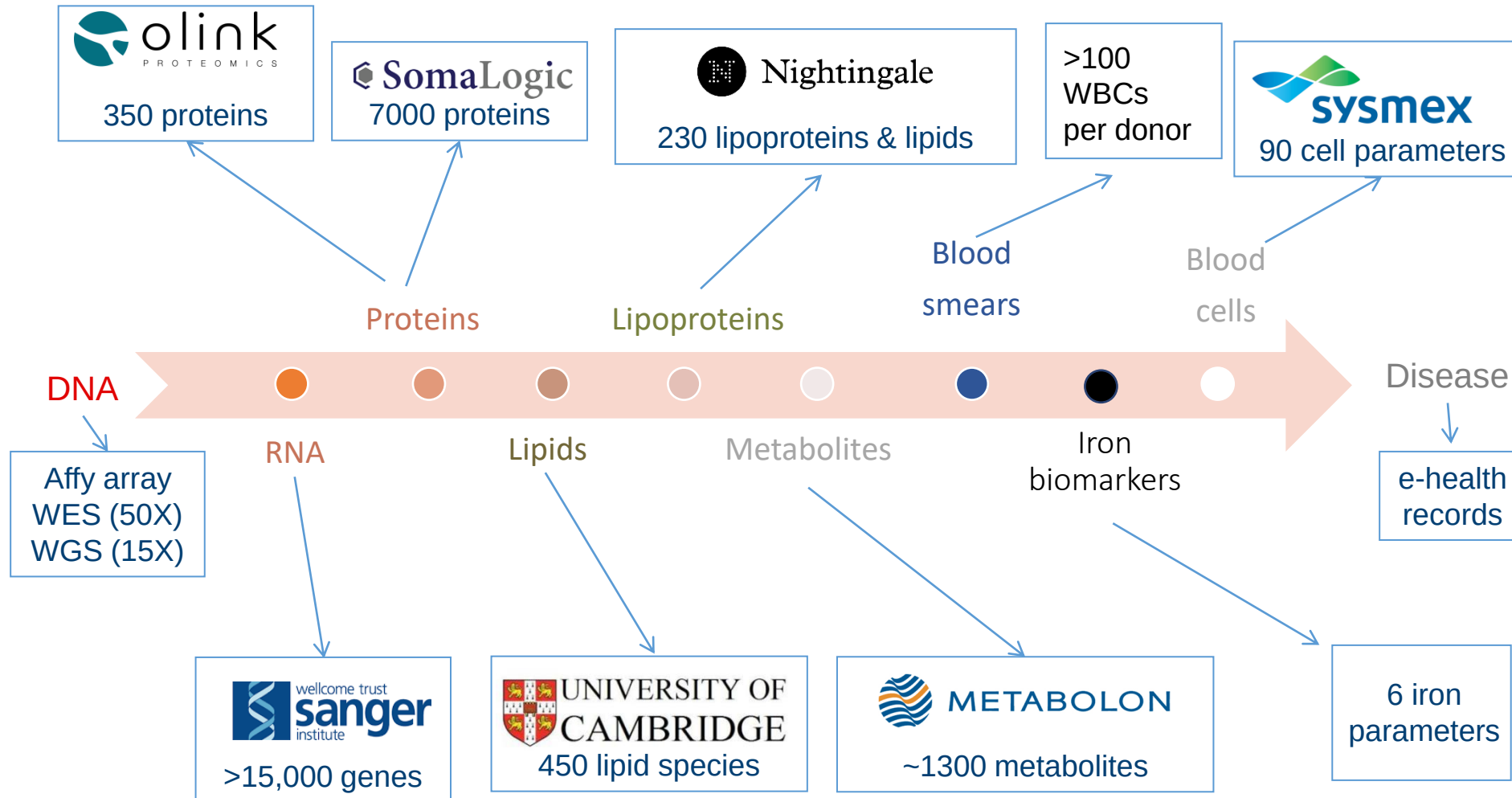
Characteristics and consent

- ❑ Whole blood donors ≥ 18 years old, ~50% women
- ❑ Internet access and email address
- ❑ Wide geographical distribution
- ❑ Long-term, anonymised storage of blood samples
- ❑ Recall for targeted mechanistic (and other) studies

Linkage to health records

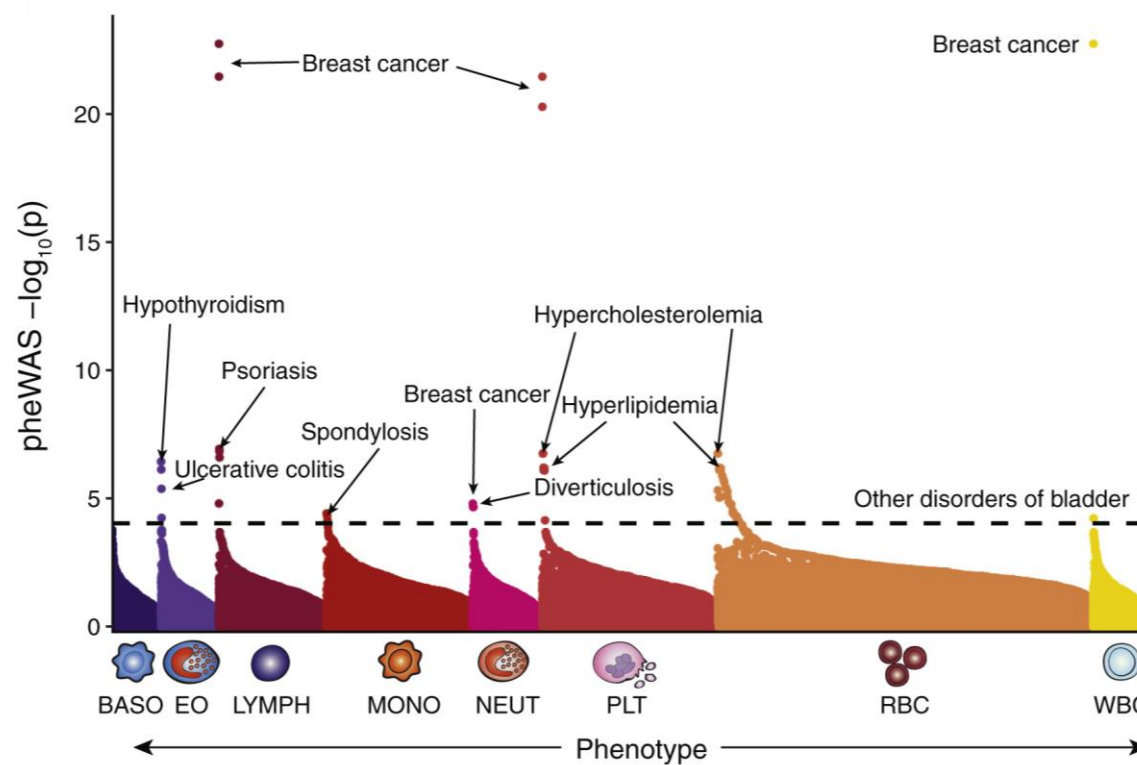
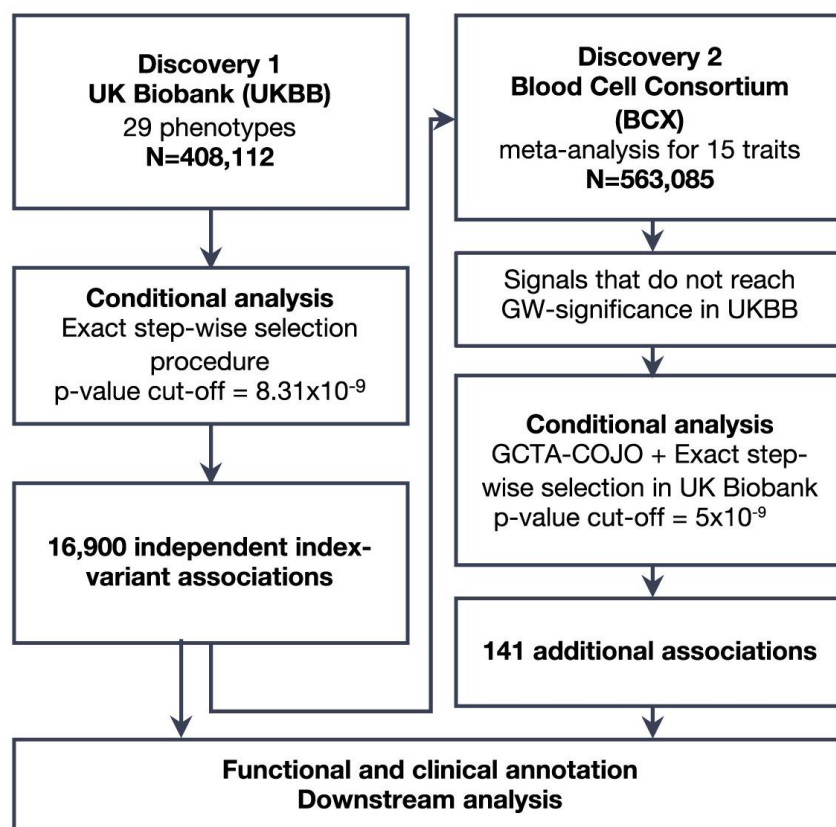


Deep molecular phenotyping



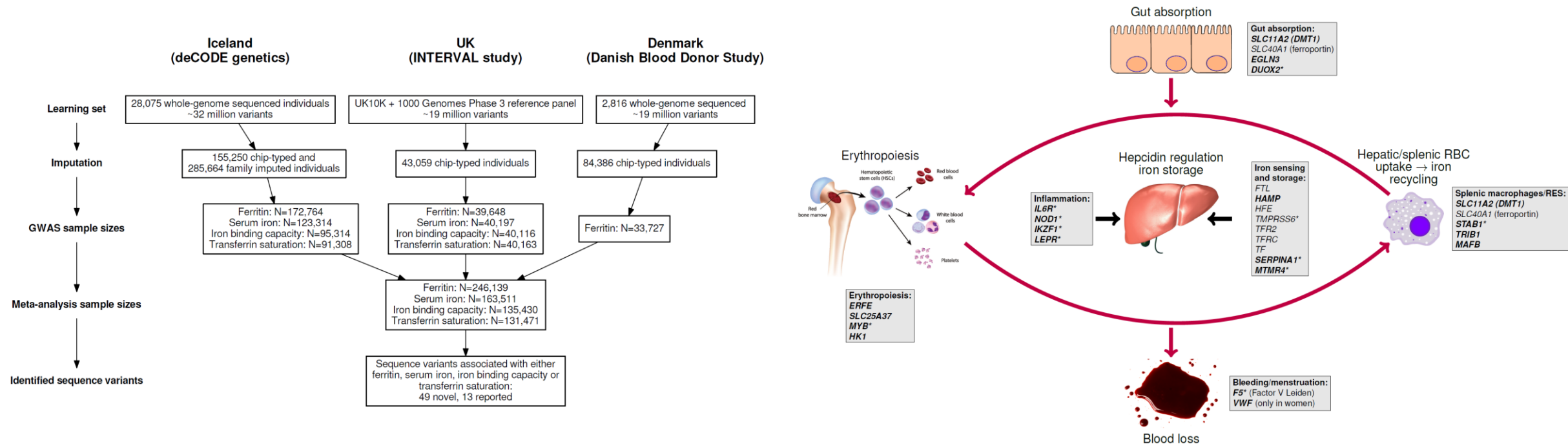
Blood Traits and Genomics

Largest genome-wide association study of blood cell traits to date
>560K participants, >5000 new independent genetic variants, 29 blood cell phenotypes



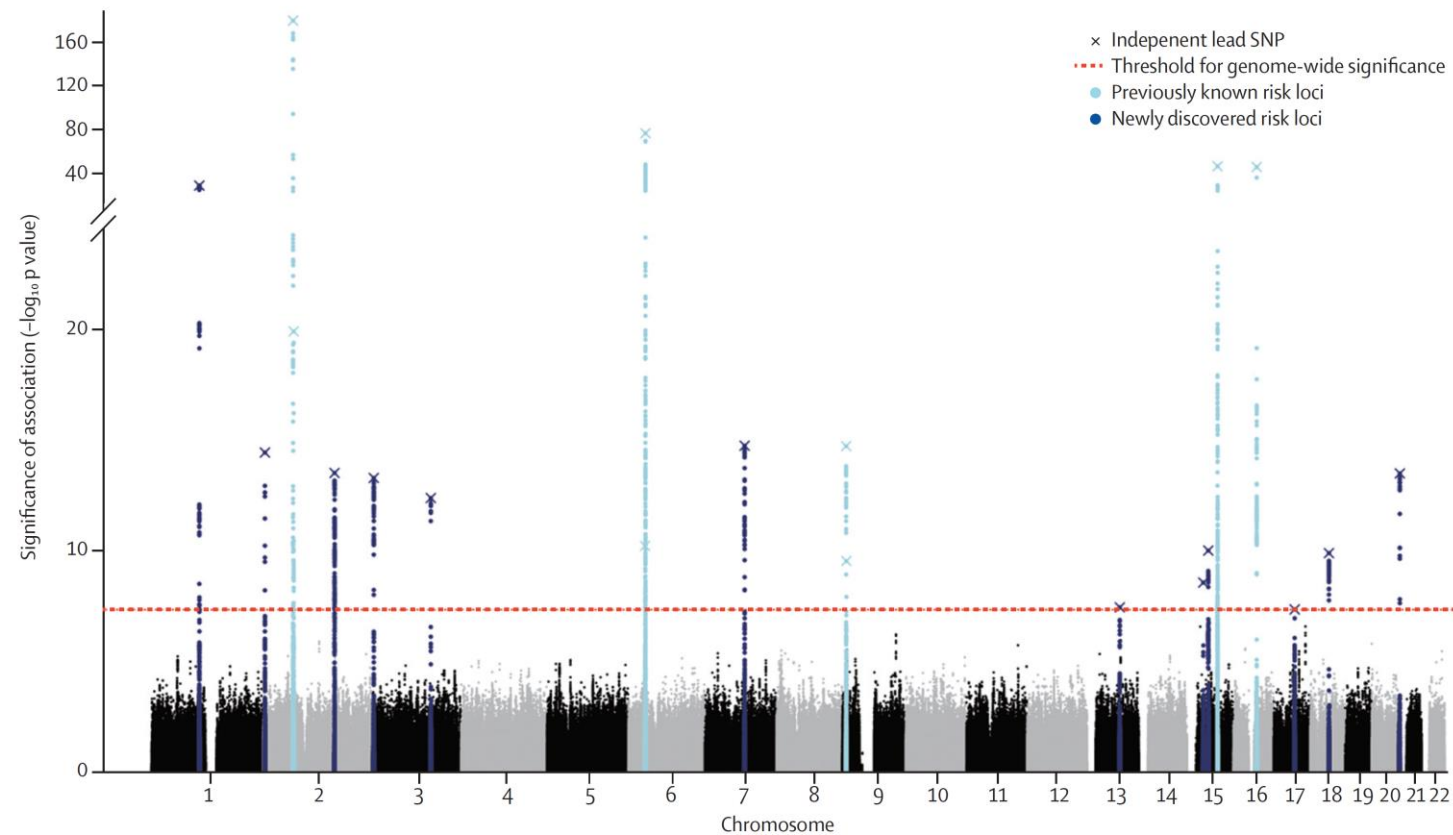
Genetic determinants of iron homeostasis

46 new loci associating with biomarkers of iron homeostasis



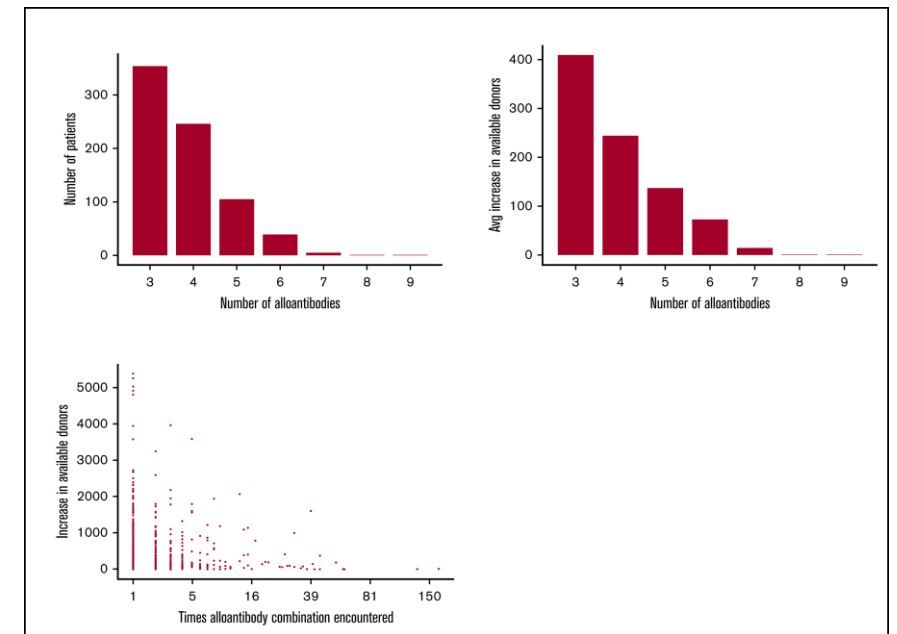
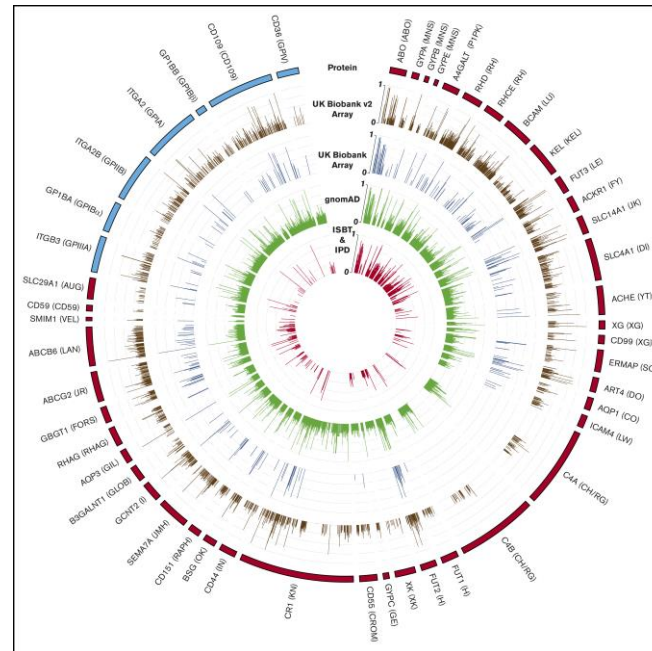
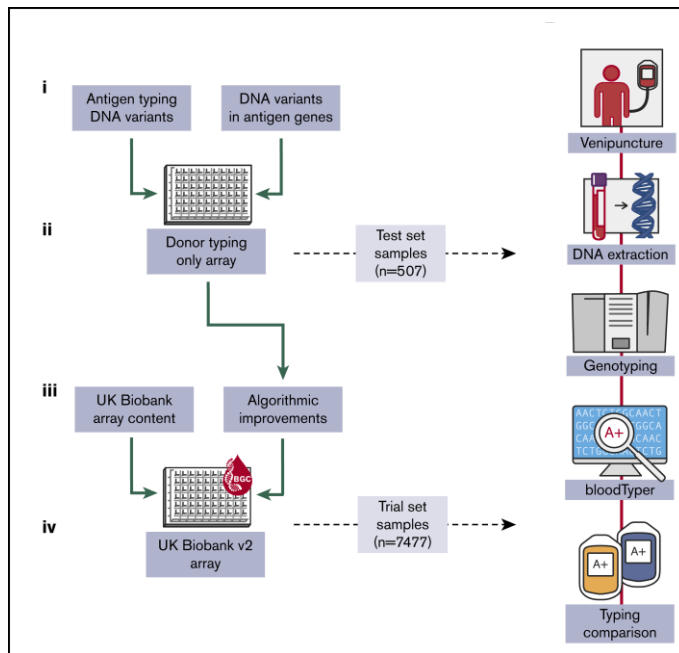
Genomic determinants of restless legs syndrome?

13 new risk loci in 15,505 cases and 95,741 controls



Blood groups genotyping

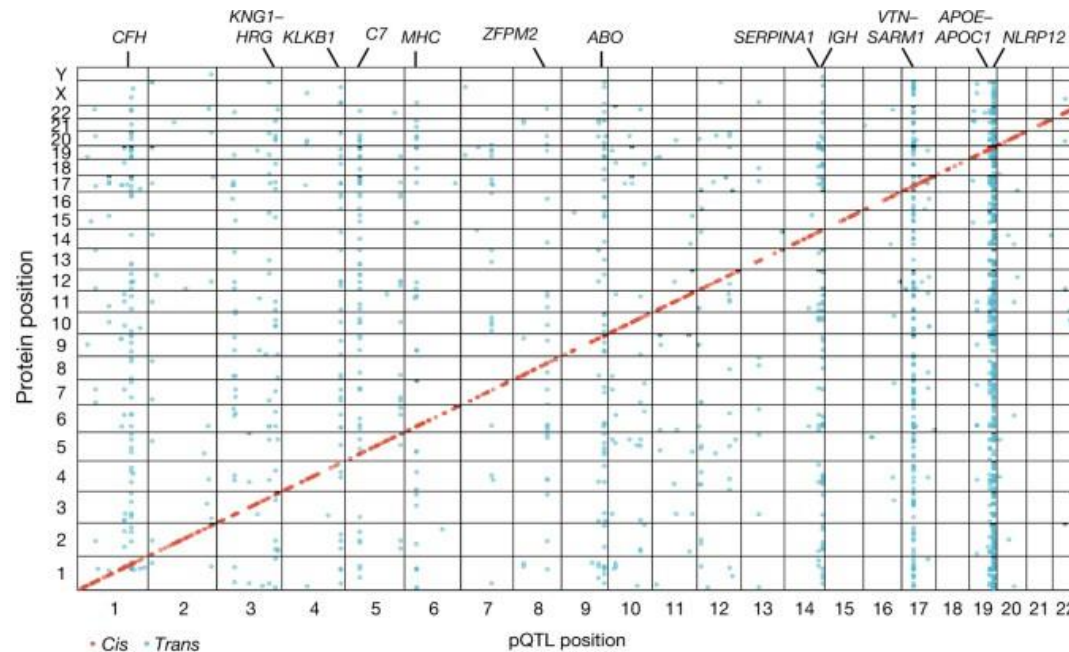
Development and validation of a universal blood donor genotyping platform



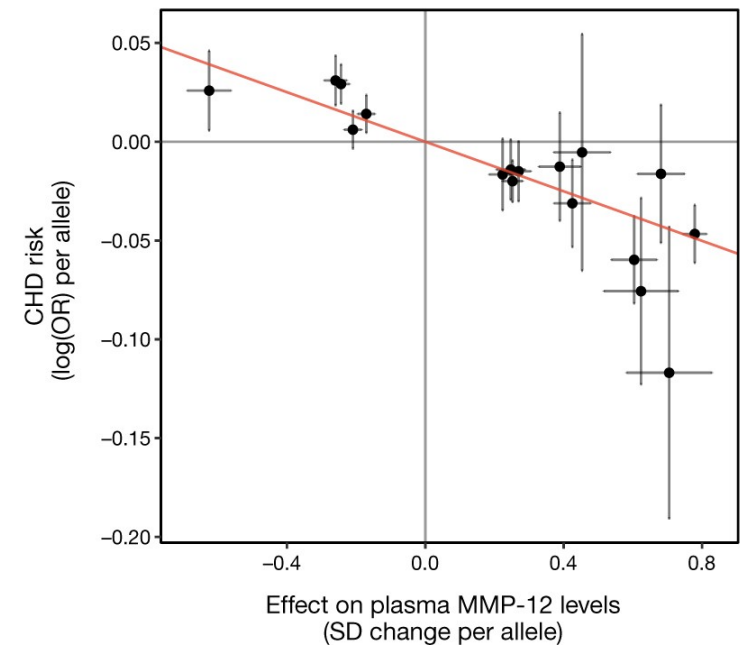
Significantly increases the number of available units for patients with multiple RBC antibodies

Combining multi-omics with genomics and clinical data at scale

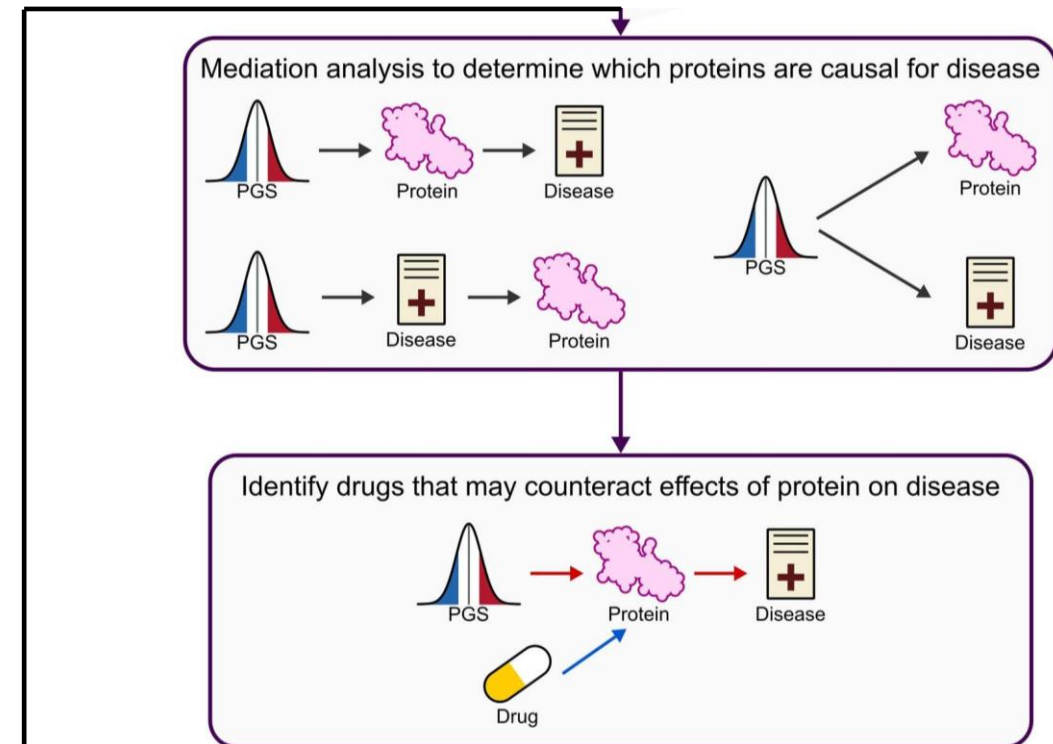
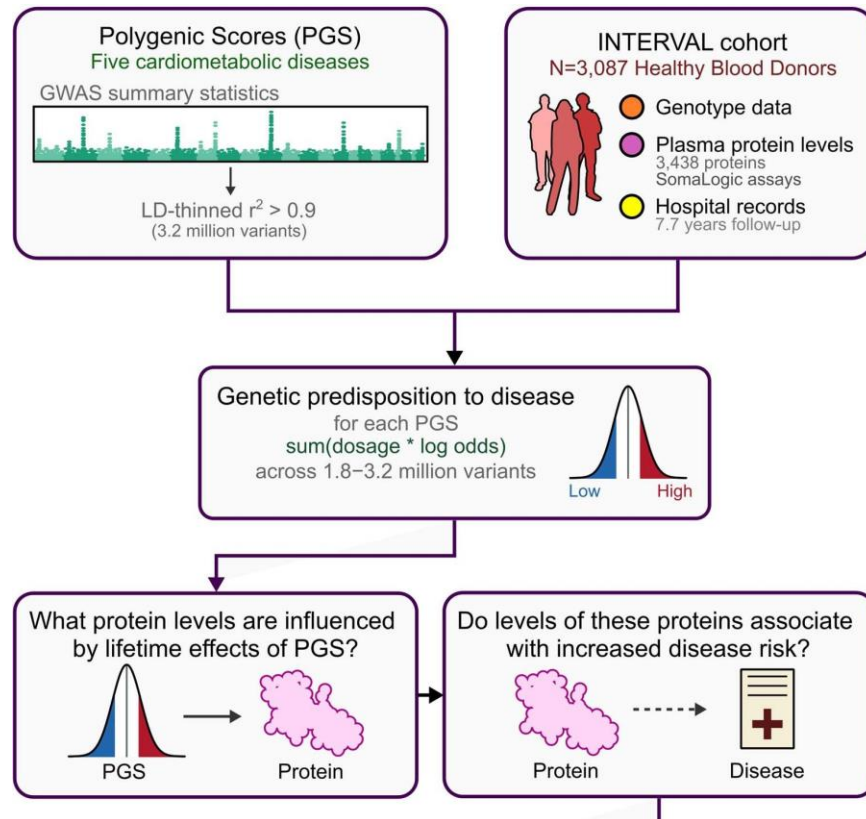
A genomic atlas of the human plasma proteome



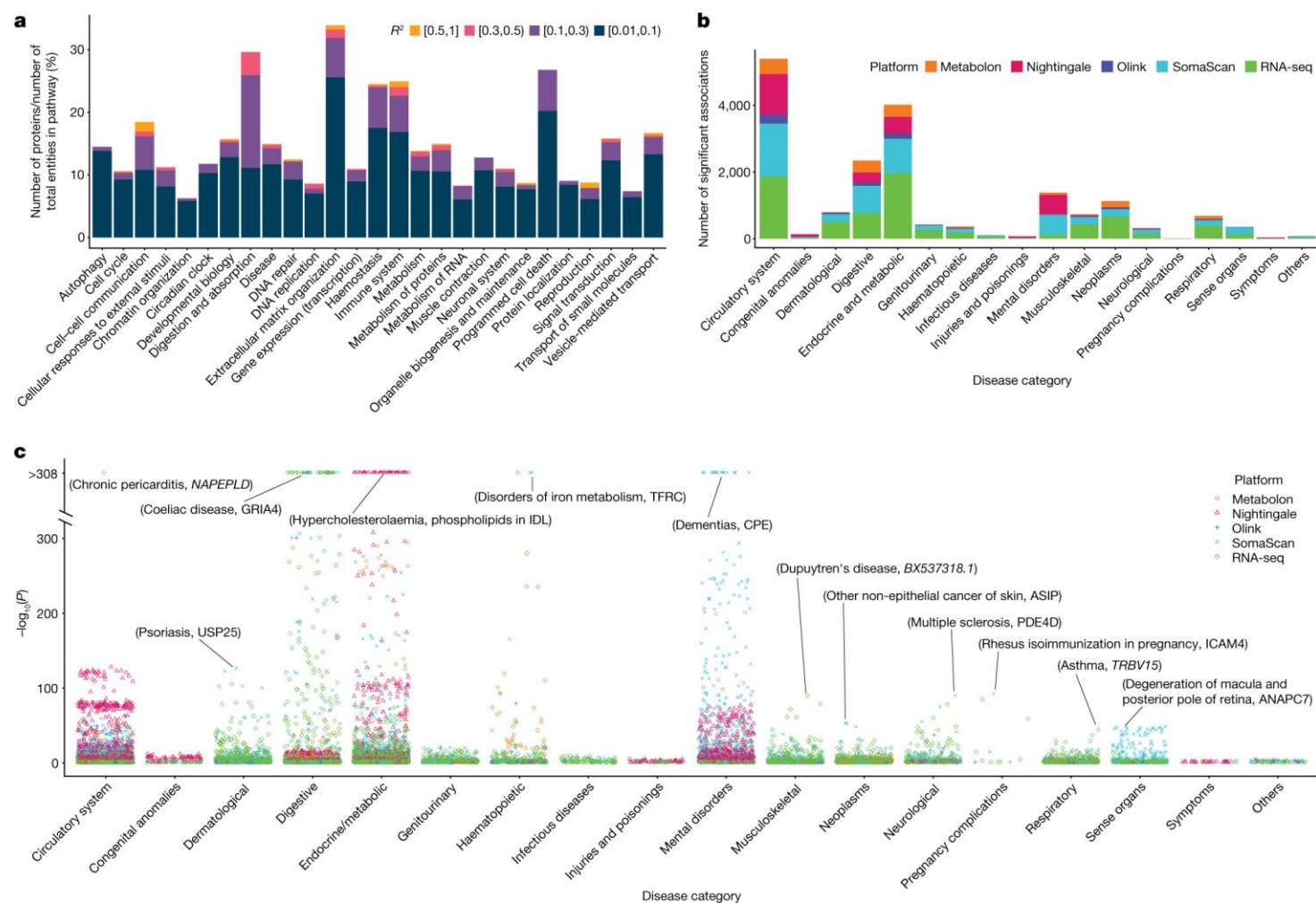
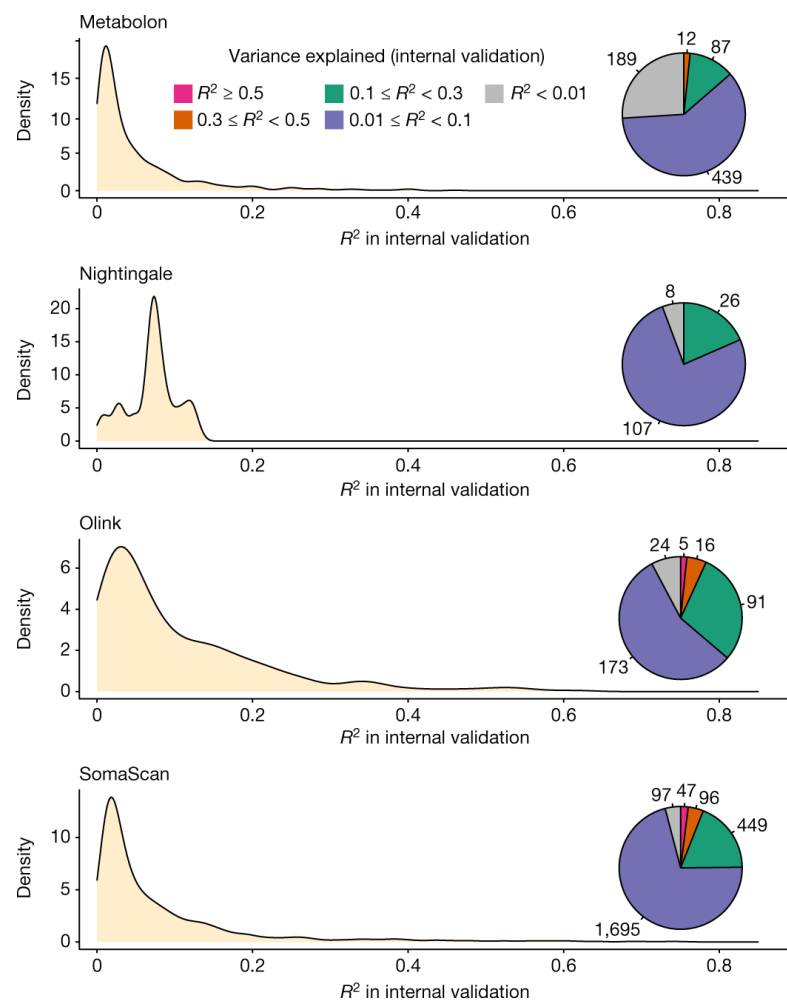
A likely protective role for matrix metalloproteinase-12 in coronary disease



Integrative analysis of plasma proteome and cardiometabolic diseases



Atlas of genetic scores to predict multi-omic traits



Summary

INTERVAL, COMPARE and STRIDES have provided compelling evidence for blood services on major issues related to blood donation and donor health, and have informed NHSBT policy and practice.

Studies of genetic, other “omics” and biomarkers in donors will contribute to improving blood donation, blood transfusion products and practices.

Large-scale studies and bioresources involving donors as enduring research platforms can provide resources that enable further research relevant both to blood donor health and the general population.

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