

45°

**Convegno Nazionale
di Studi di Medicina Trasfusionale**

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**The value of large scale studies in
blood donors: from randomised
clinical trial to big data**

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Human Technopole, Milan | University of Cambridge, UK

Il sottoscritto, in qualità di Relatore
dichiara che

nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatore di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le sue funzioni al fine di trarne vantaggio.



What is the need of large scale studies?

- 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.

NHSBT: 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



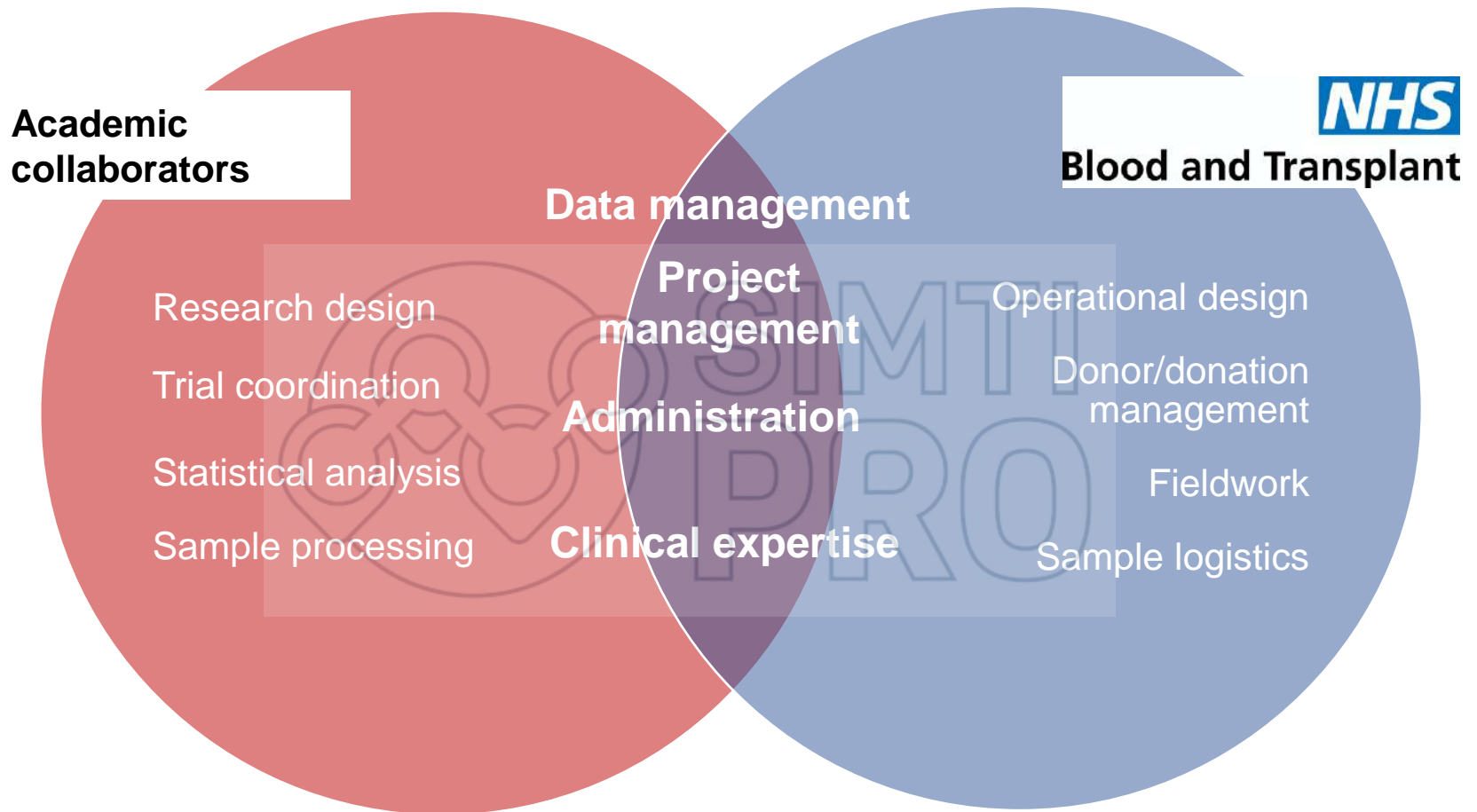
Altruism

Donors are unpaid volunteers



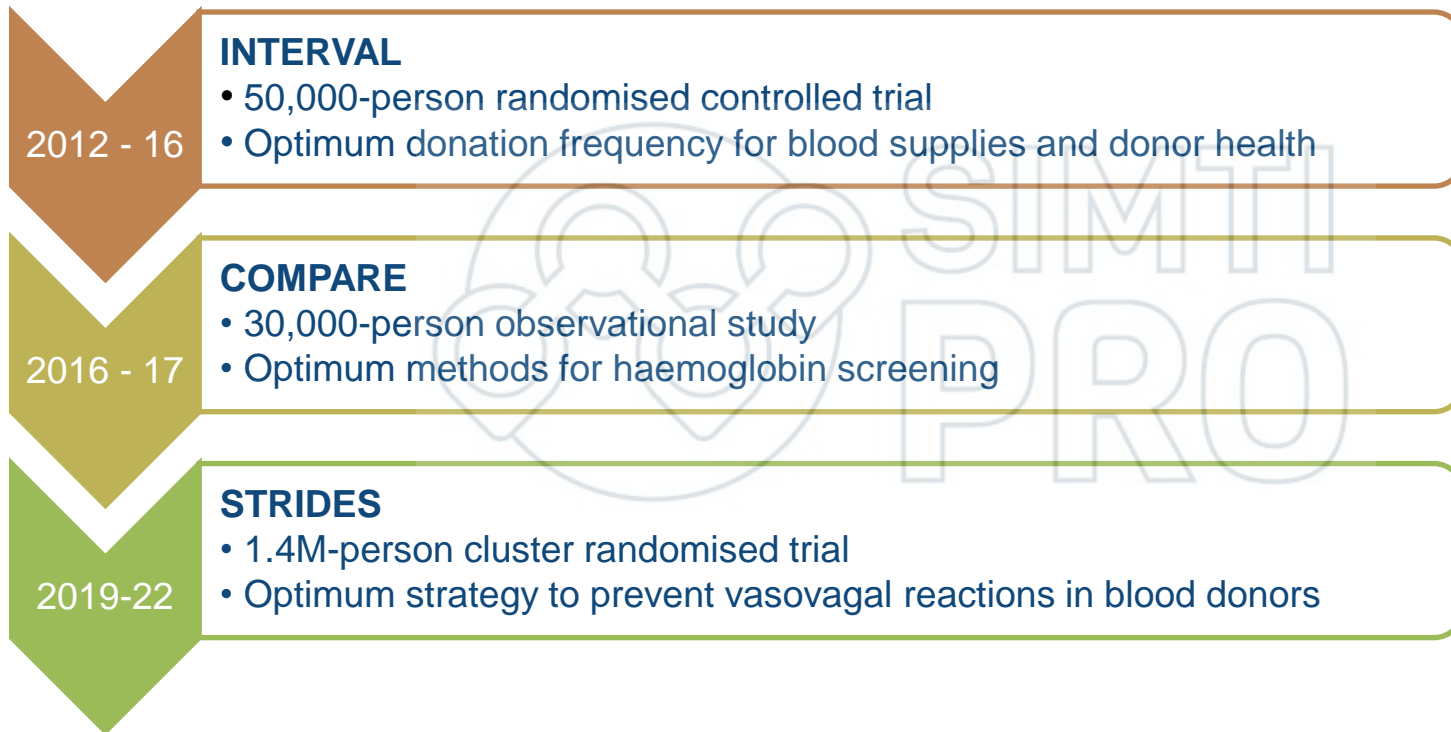
Blood and Transplant

Partnership between NHSBT and academia



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

Large scale studies in blood donors



Large scale studies in blood donors

2012 - 16

INTERVAL

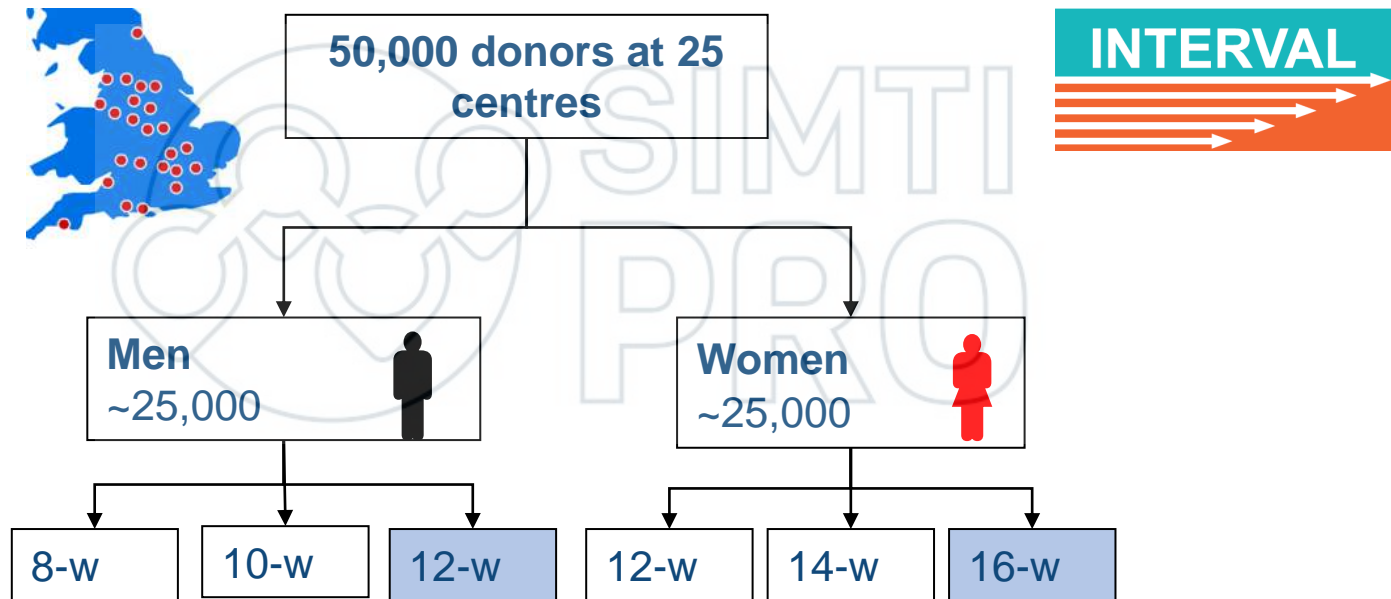
- 50,000-person randomised controlled trial
- Optimum donation frequency for blood supplies and donor health

INTERVAL



INTERVAL trial

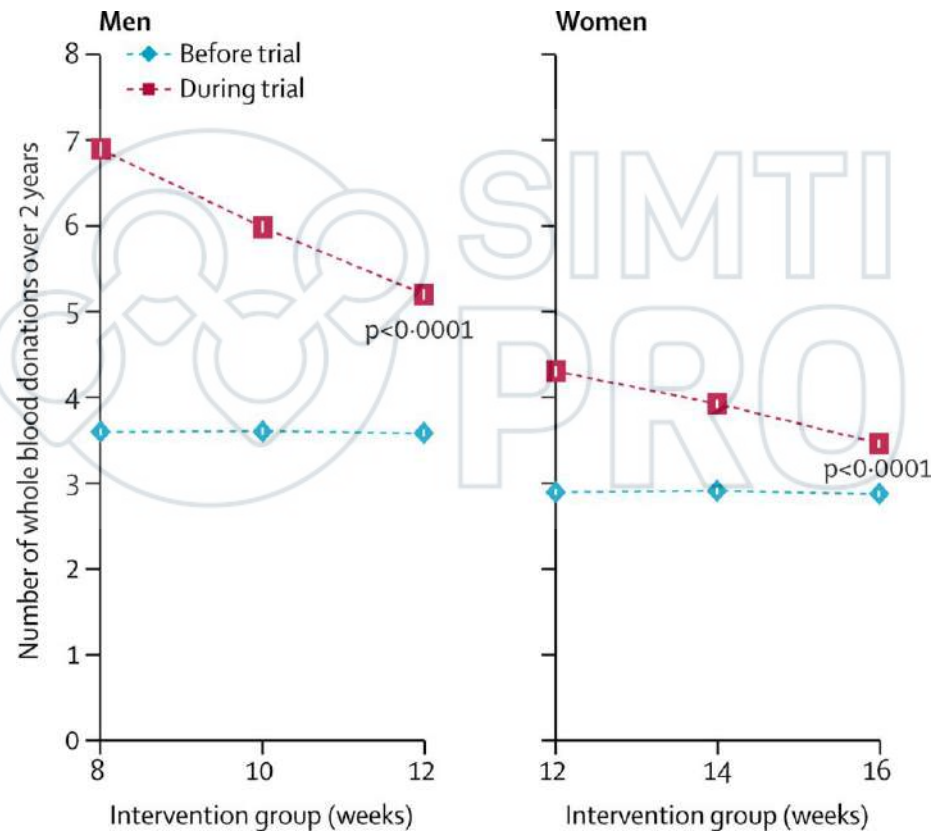
What is the optimum time period between blood donations for safety and efficiency?



Pragmatic, randomised controlled trial embedded within NHSBT framework

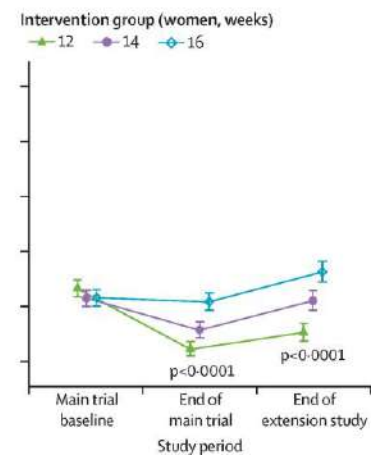
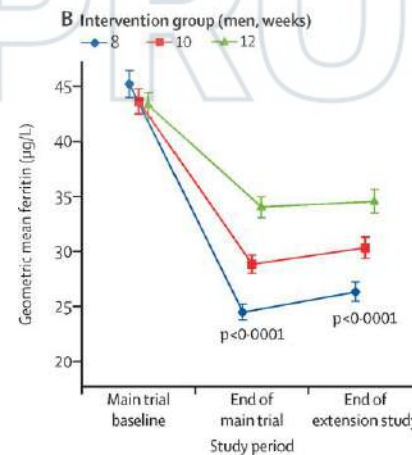
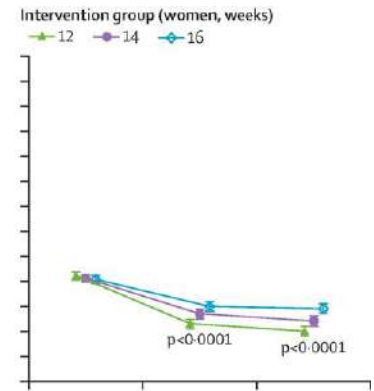
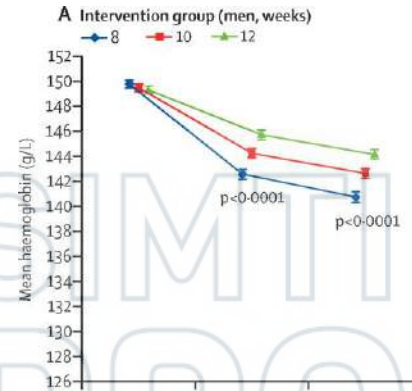
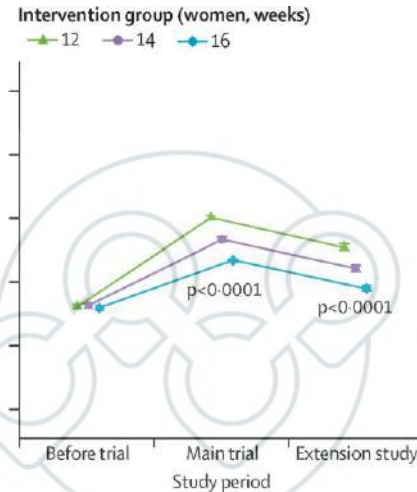
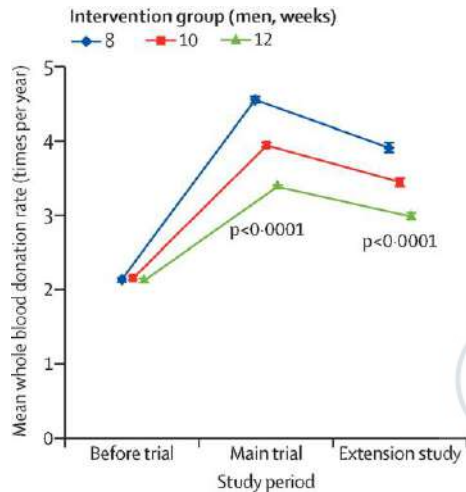
Moore C et al, *Trials* 2014

INTERVAL: primary outcome, efficiency of blood donation



Di Angelantonio E et al, *Lancet* 2017

Blood donation, haemoglobin and ferritin during the INTERVAL trial



More blood collected, but lower haemoglobin concentrations

Kaptoge S et al, *Lancet Haematol* 2019

Large scale studies in blood donors

2016 - 17

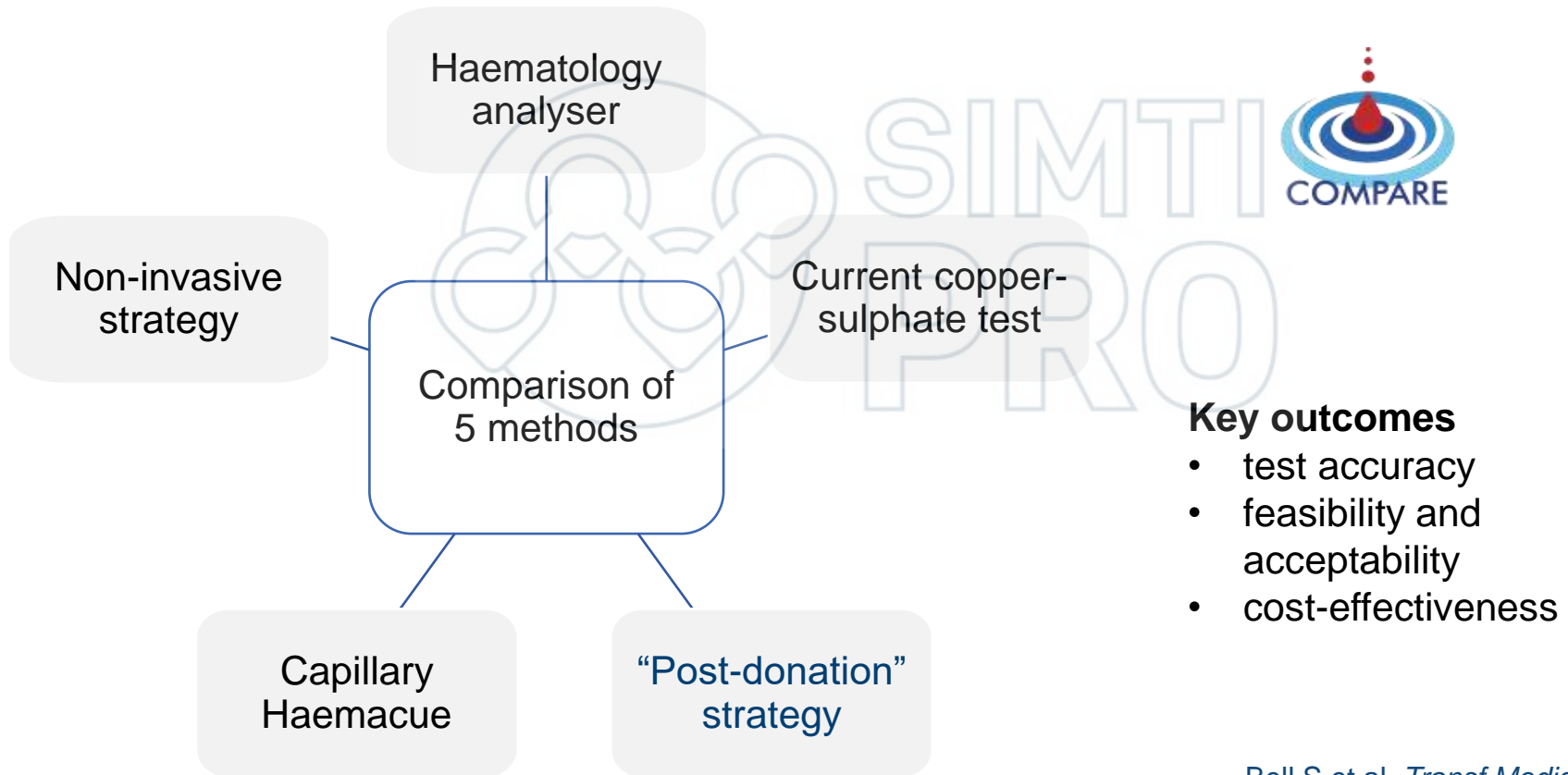
COMPARE

- 30,000-person observational study
- Optimum methods for haemoglobin screening



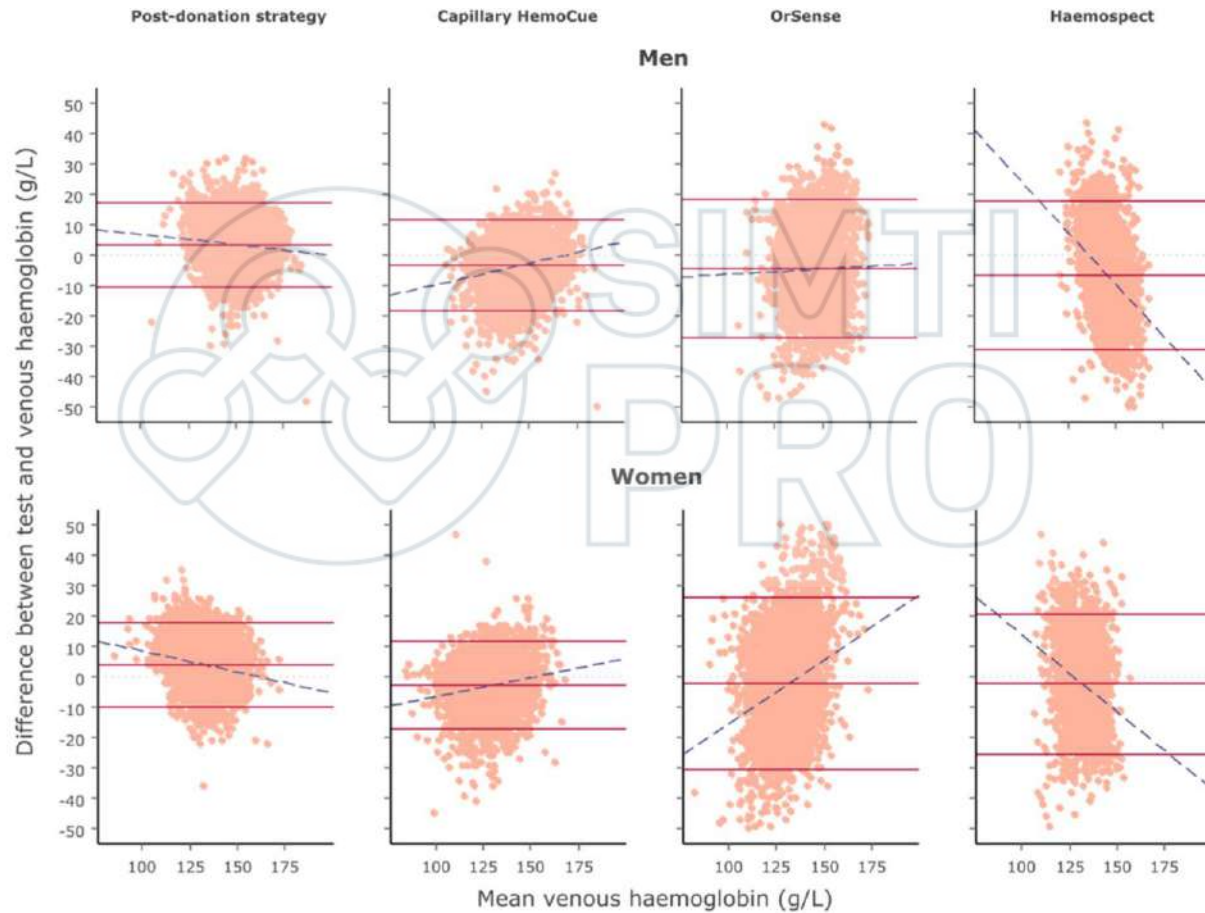
COMPARE study

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



Bell S et al, *Transf Medicine* 2021

Testing strategy vs reference test: Bland–Altman plot



Bell S et al, *Transf Medicine* 2021

Testing strategy vs reference test



Bell S et al, *Transf Medicine* 2021

Large scale studies in blood donors



2019-22

STRIDES

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



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%

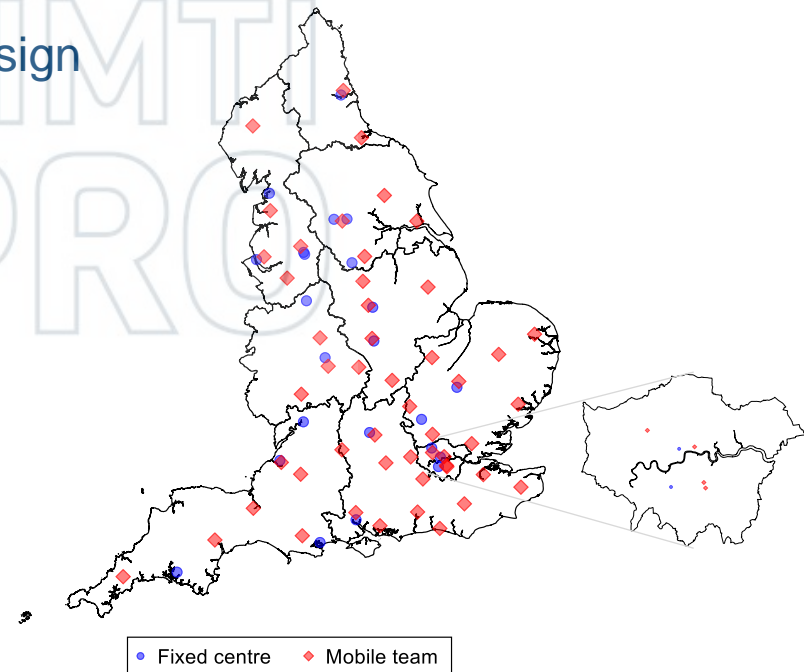
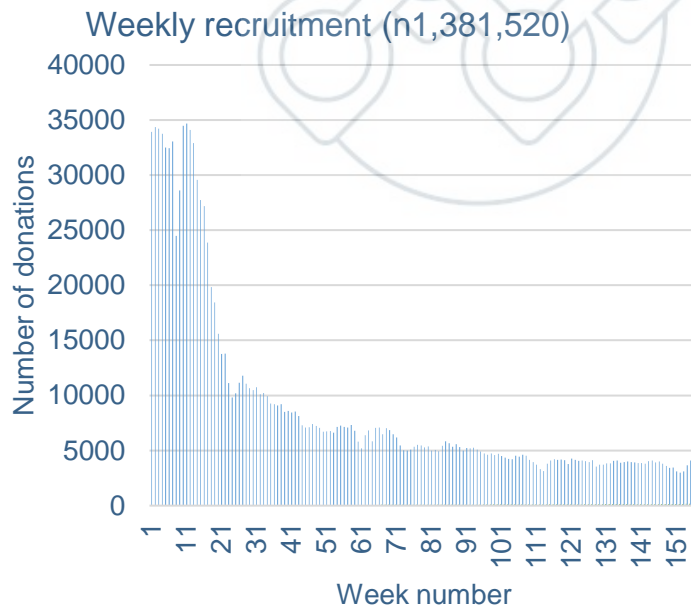
A cluster-randomised trial embedded in the English blood service

The STRIDES trial is a cluster-randomised trial of four interventions to prevent VVRs during routine blood donation:

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

STRategies to Improve Donor Experiences (STRIDES)

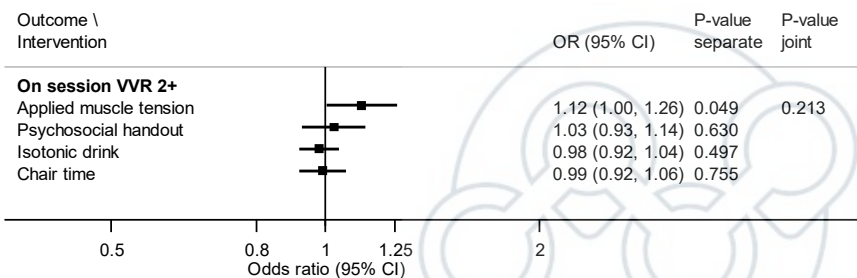
- 73 teams conducting routine blood collections (the entirety of NHSBT)
- November 2019 to November 2022
- Stepped-wedge, cross-over and factorial design



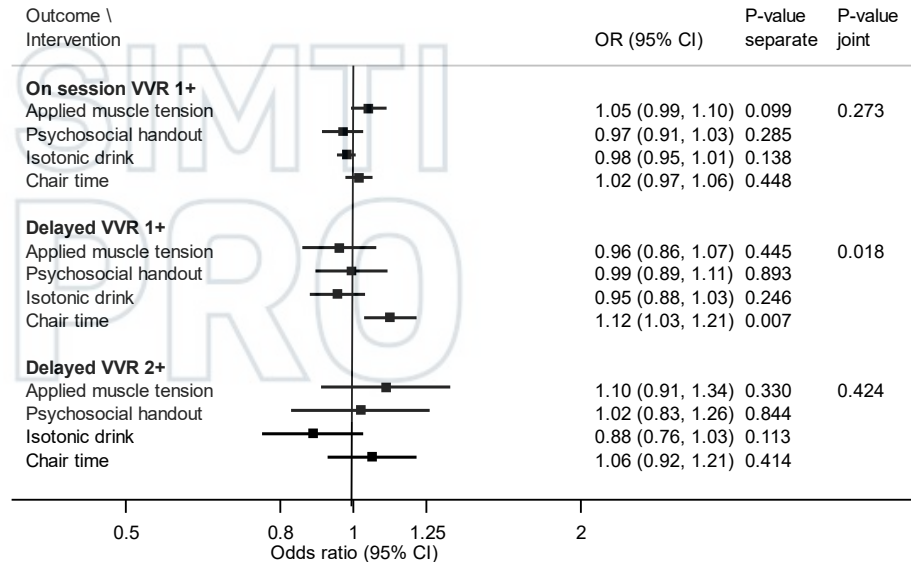
McMahon, *Trials* 2023

STRIDES: primary and secondary outcomes

Primary outcome



Secondary outcomes



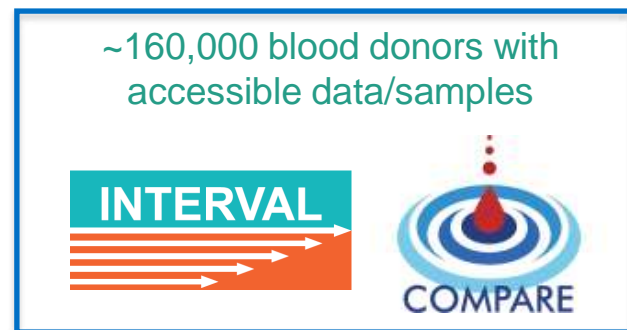
McMahon, under review

Participants characteristics, consent and e-health records

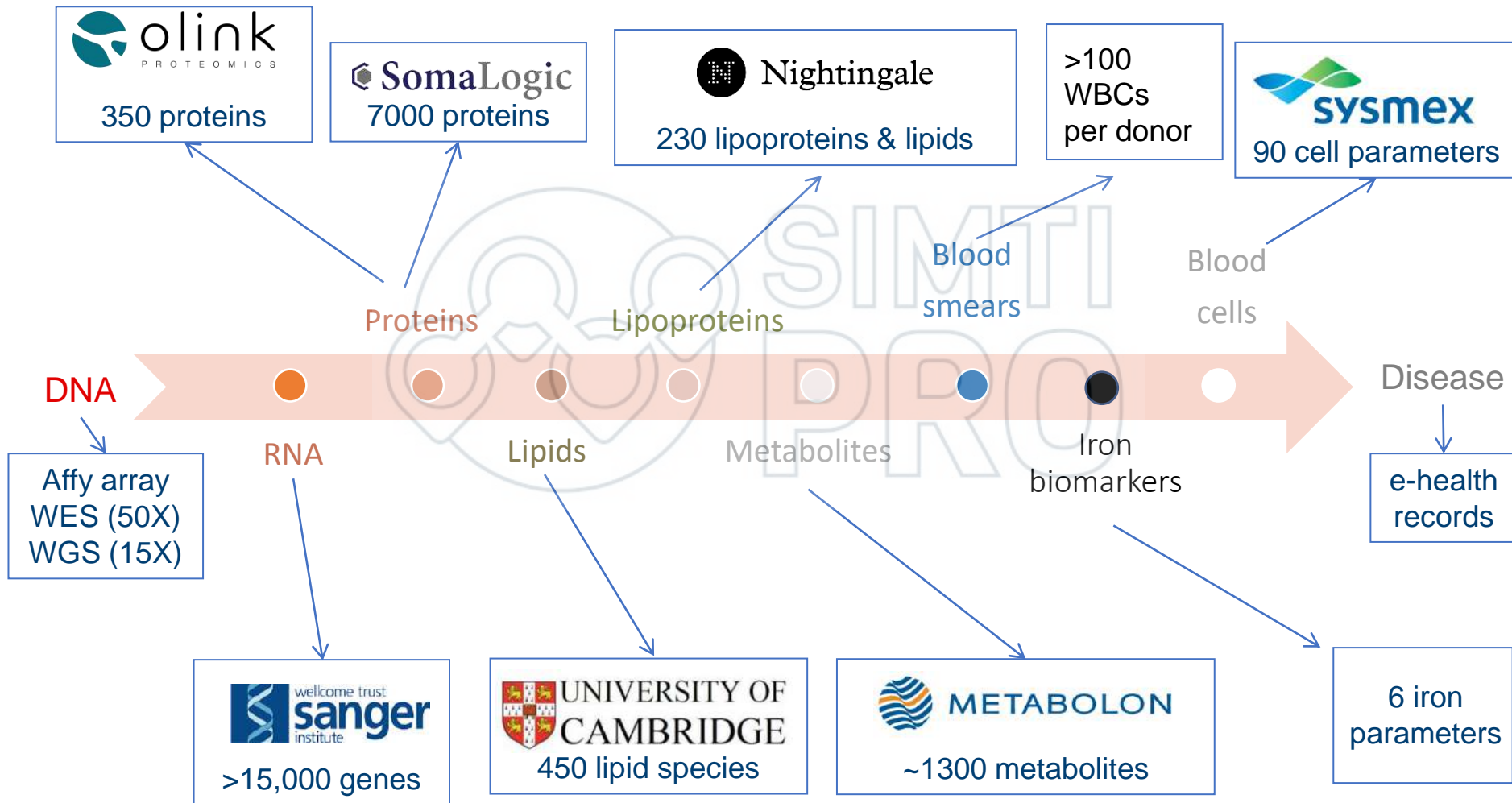
Characteristics and consent

- ❑ 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

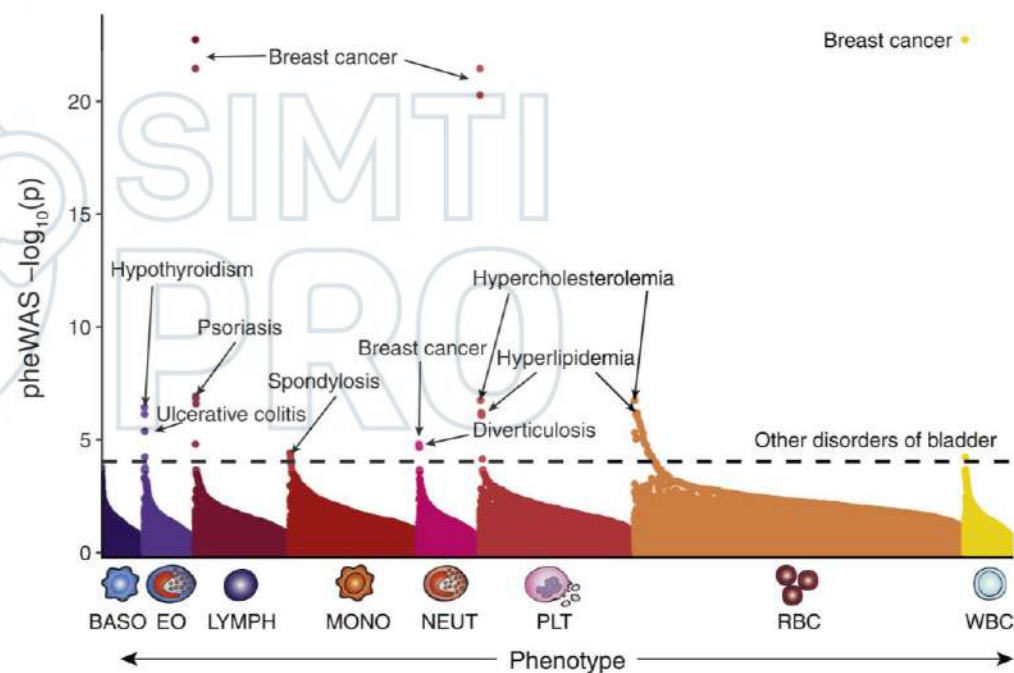
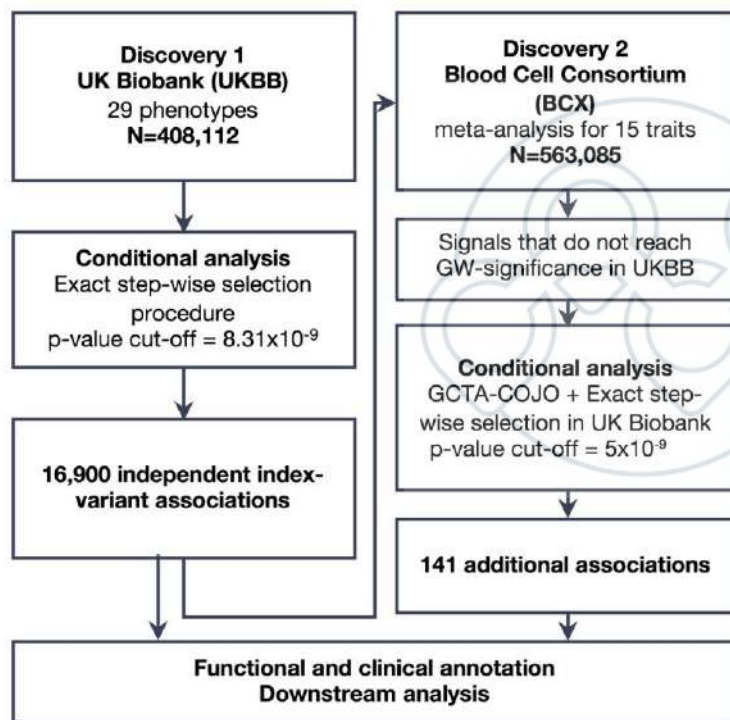


Deep molecular phenotyping



Blood Traits and Genomics

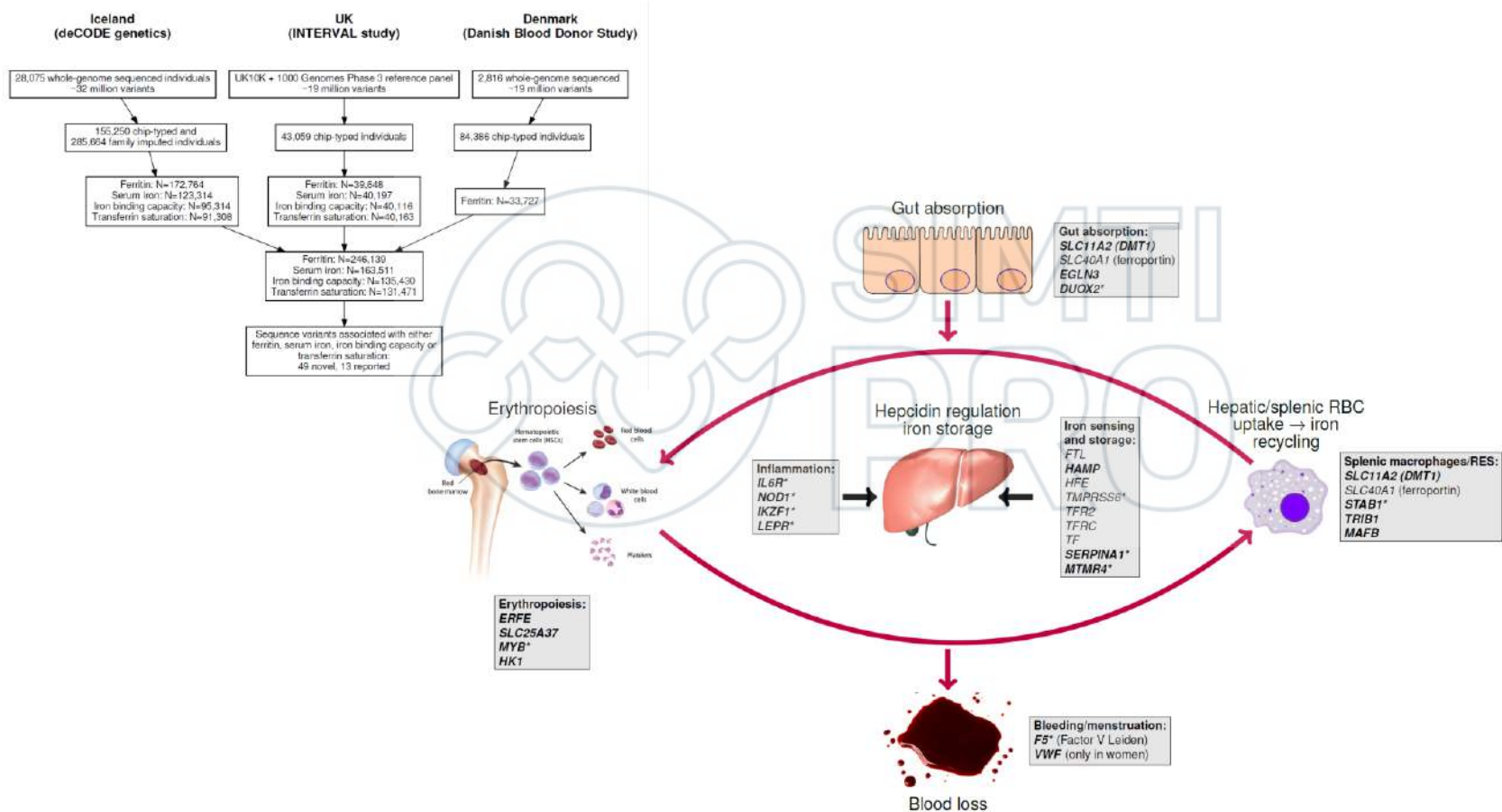
Largest genome-wide association study of blood cell traits to date
 >560K participants, >5000 new independent genetic variants, 29 blood cell phenotypes



Vuckovic D *Cell* 2020

Genetic determinants of iron homeostasis

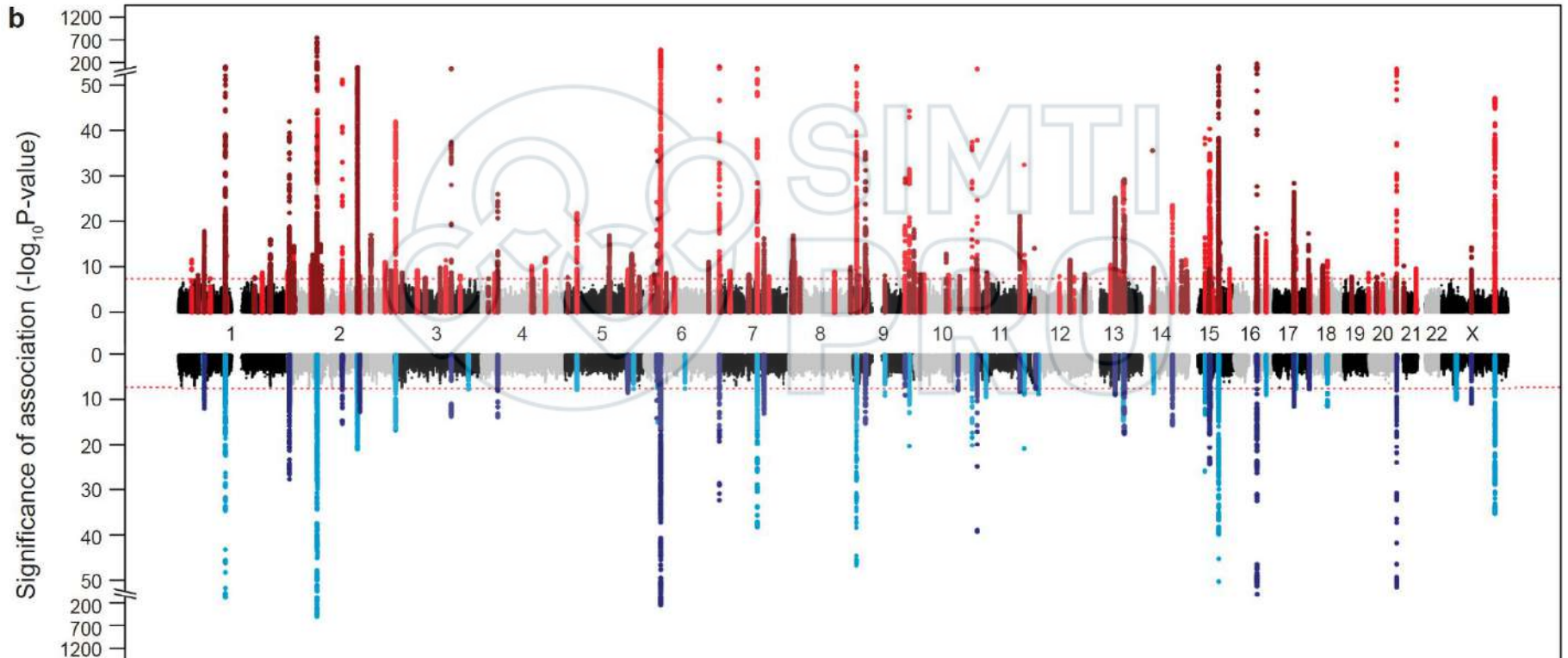
46 new loci associating with biomarkers of iron homeostasis



Bell S Comms Bio 2021

Genomic determinants of restless legs syndrome

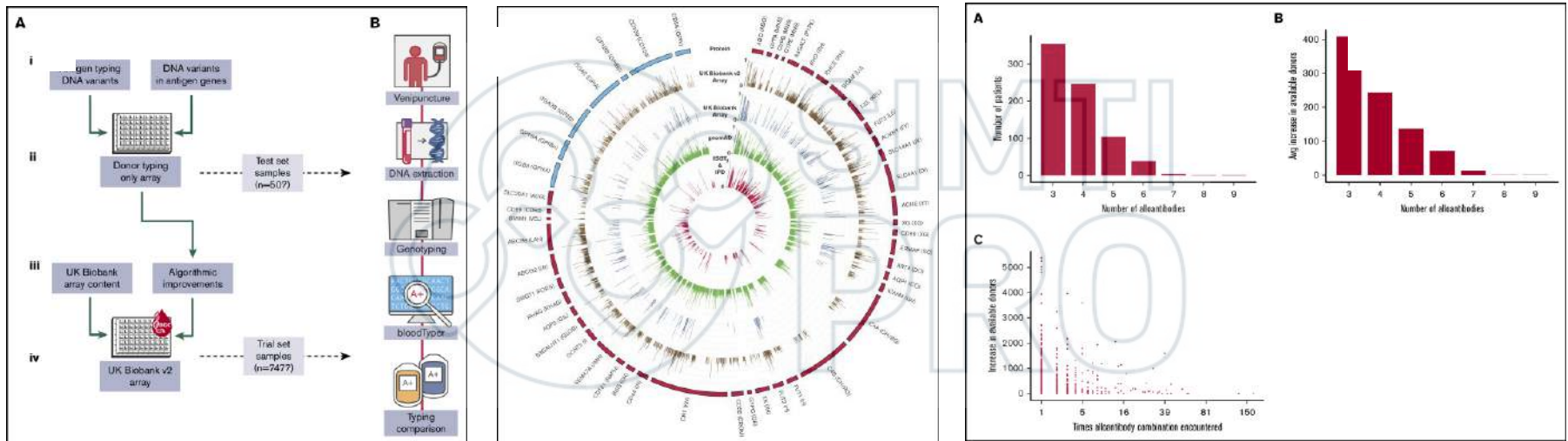
164 new risk loci in 116,647 cases and 1,546,466 controls



Schormair, *Lancet Neurol* 2017
Schormair, *Nat Gen* in press

Blood groups genotyping

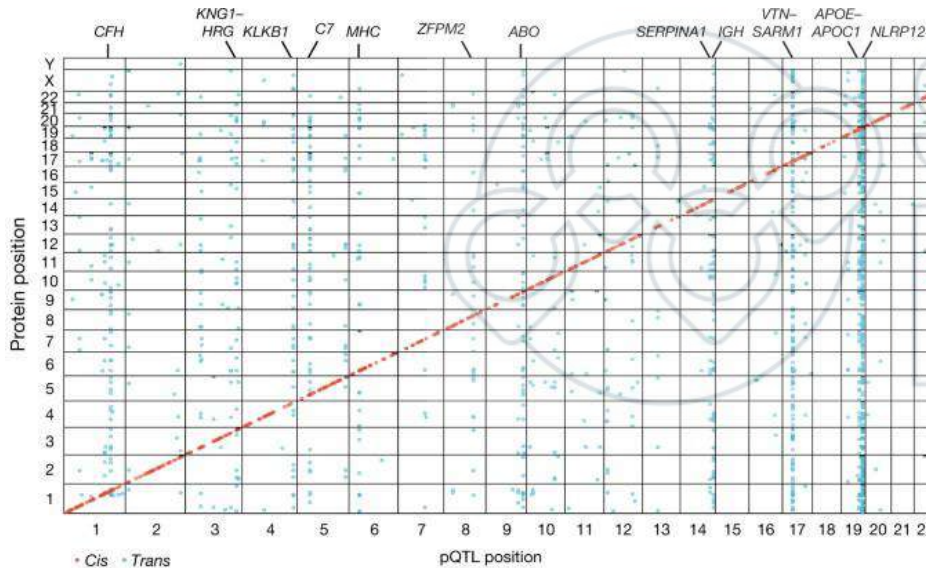
Development and validation of a universal blood donor genotyping platform



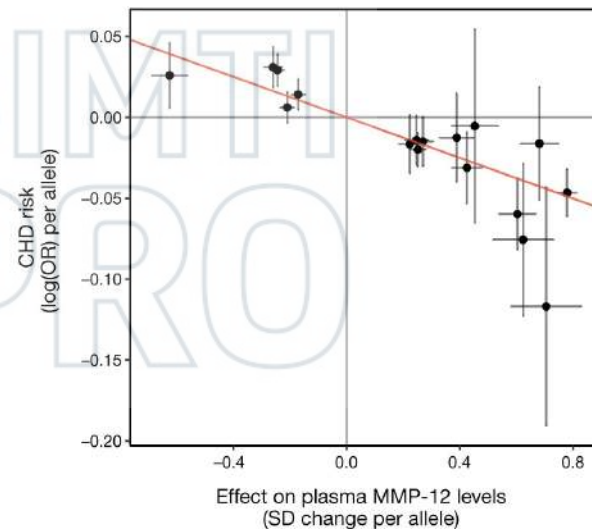
Significantly increases the number of available units for patients with multiple RBC antibodies

Combining multi-omics with genomics and clinical data at scale

A genomic atlas of the human plasma proteome

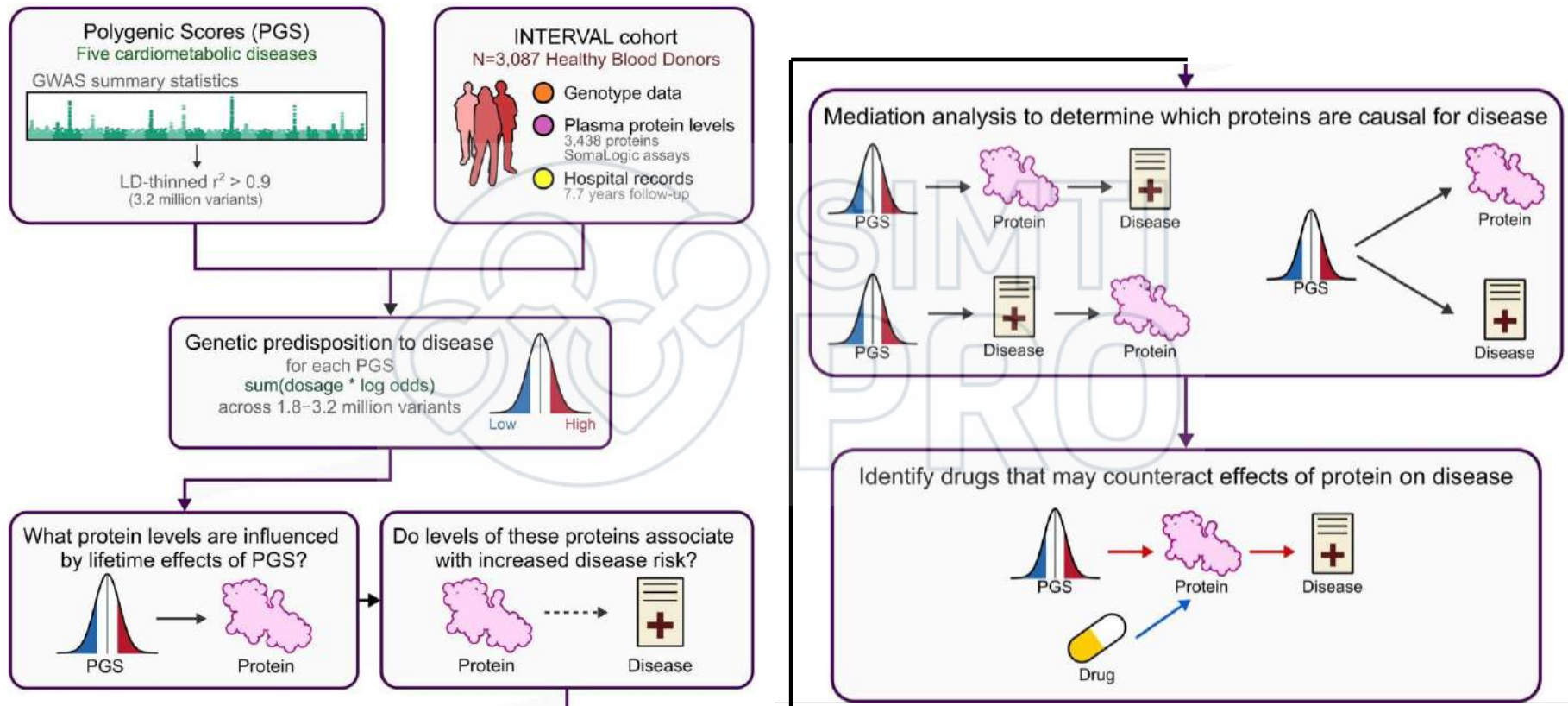


A likely protective role for matrix metalloproteinase-12 in coronary disease



Sun B, *Nature* 2018

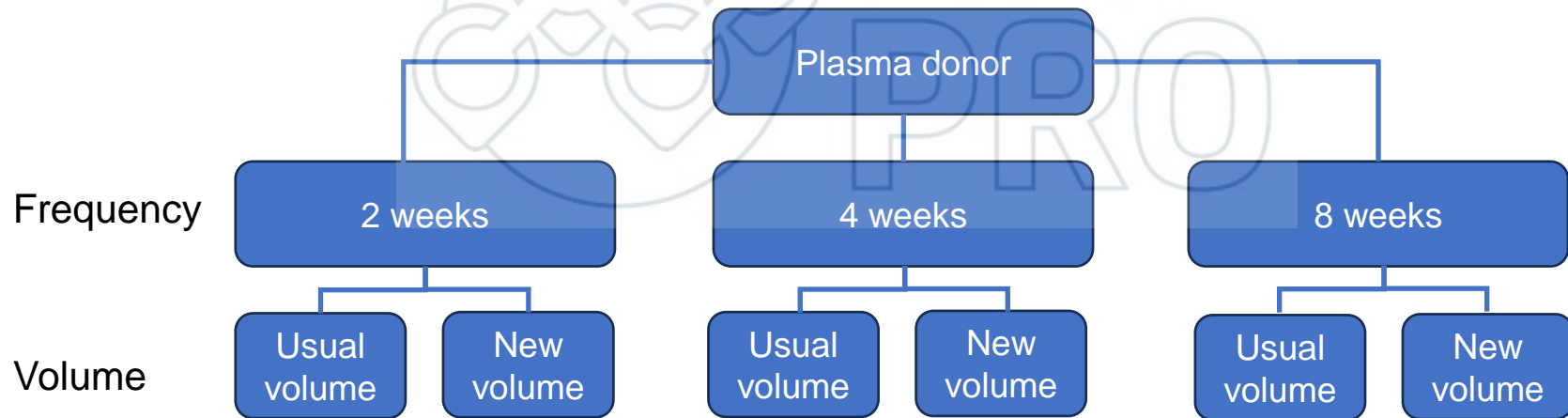
Integrative analysis of plasma proteome and cardiometabolic diseases



Ritchie S, Nature Metabolism 2021

...back to trial improving safety of donation

What is the optimum frequency and volume for the safety and efficiency of plasma donation?



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.

www.donorhealth-btru.nihr.ac.uk/

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Unit in Donor Health and Behaviour
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