UNIVERSITY OF CAMBRIDGE

NHS Blood and Transplant

NHS National Institute for Health Research

Current and future directions in donor health

Use of large-scale blood donors bio-resources

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Large-scale blood donors bio-resources

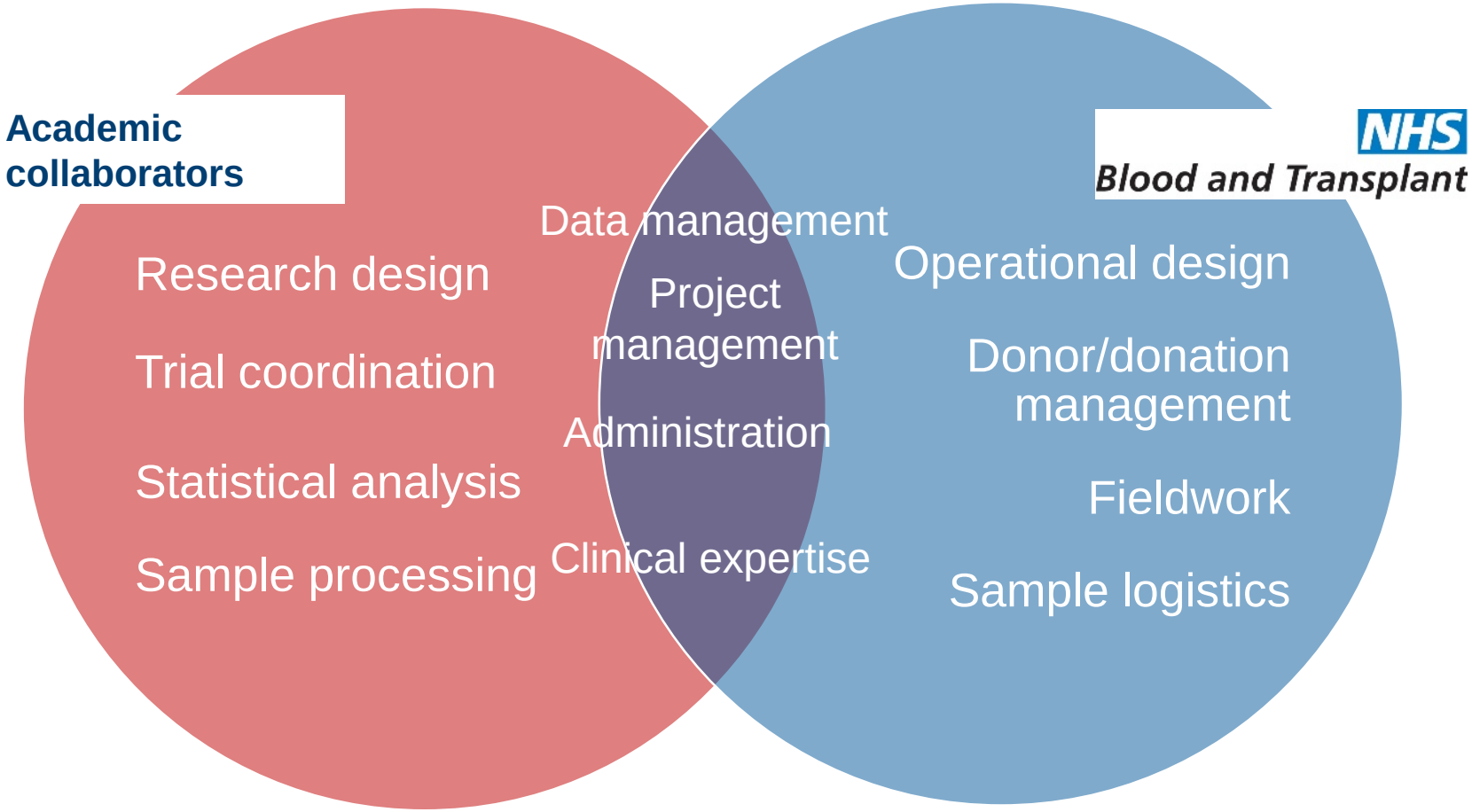
What is the need?

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

Provide a more personalised (stratified) service.

Build major bioresources involving donors as enduring research platforms.

Partnership between NHSBT and academia



Summary of studies in blood donors

2009

- **Cambridge Cardioresource**
- 2500-person feasibility study
- Feasibility of embedding research into routine NHSBT framework

2012 - 6

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

2016 - 7

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

Future

- **STRIDE** (fainting prevention)

Summary of studies in blood donors

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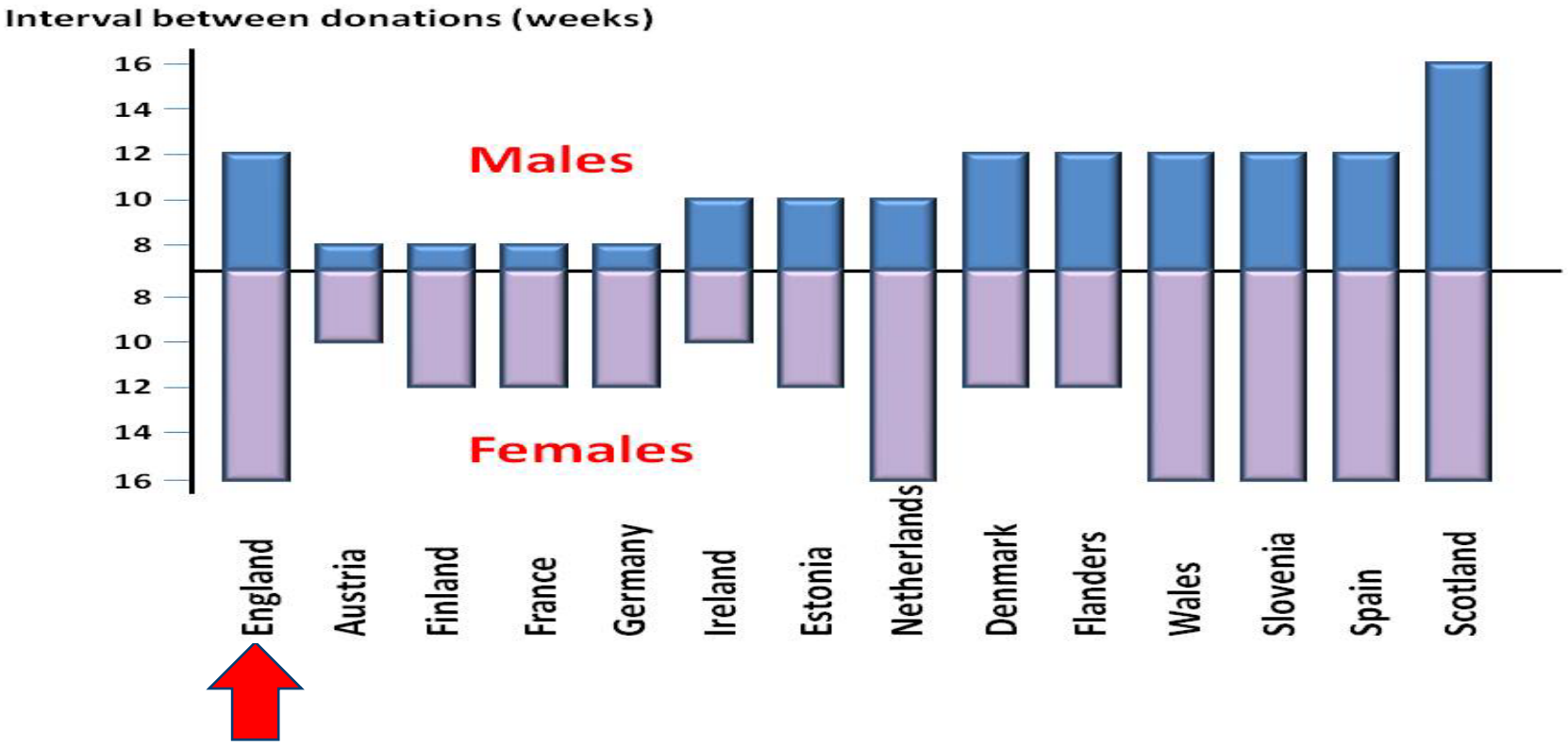
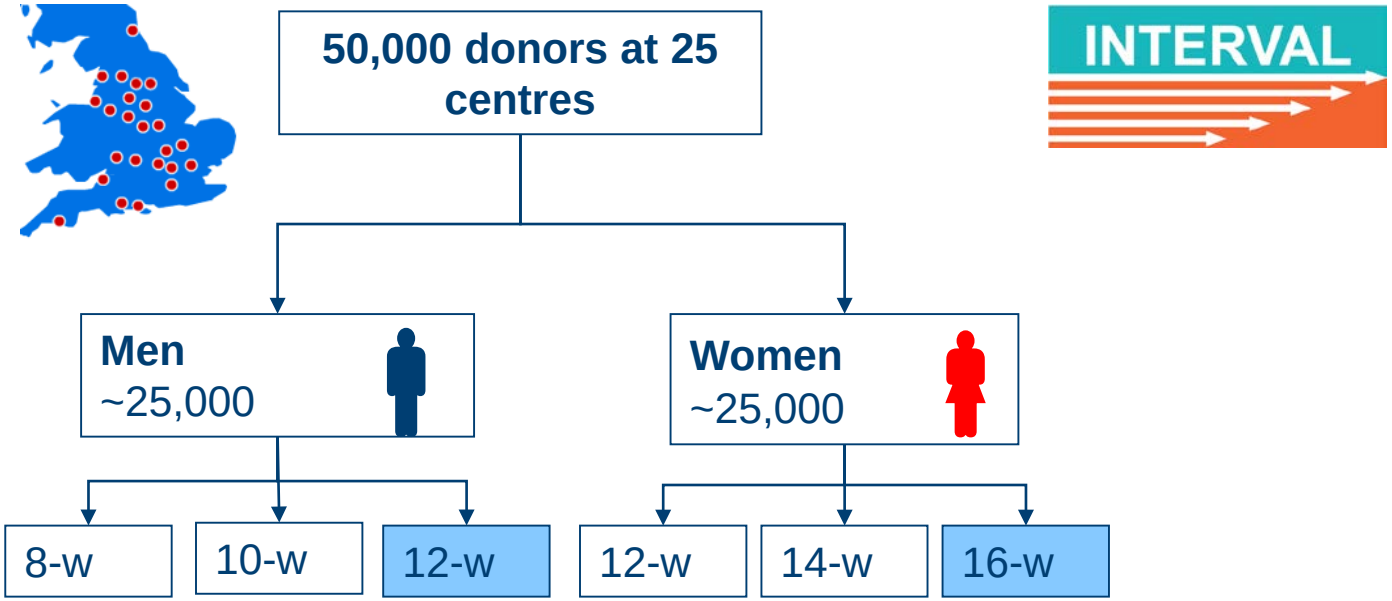
INTERVAL trial: rationale



No RCTs / definitive data to inform policies on donation frequency

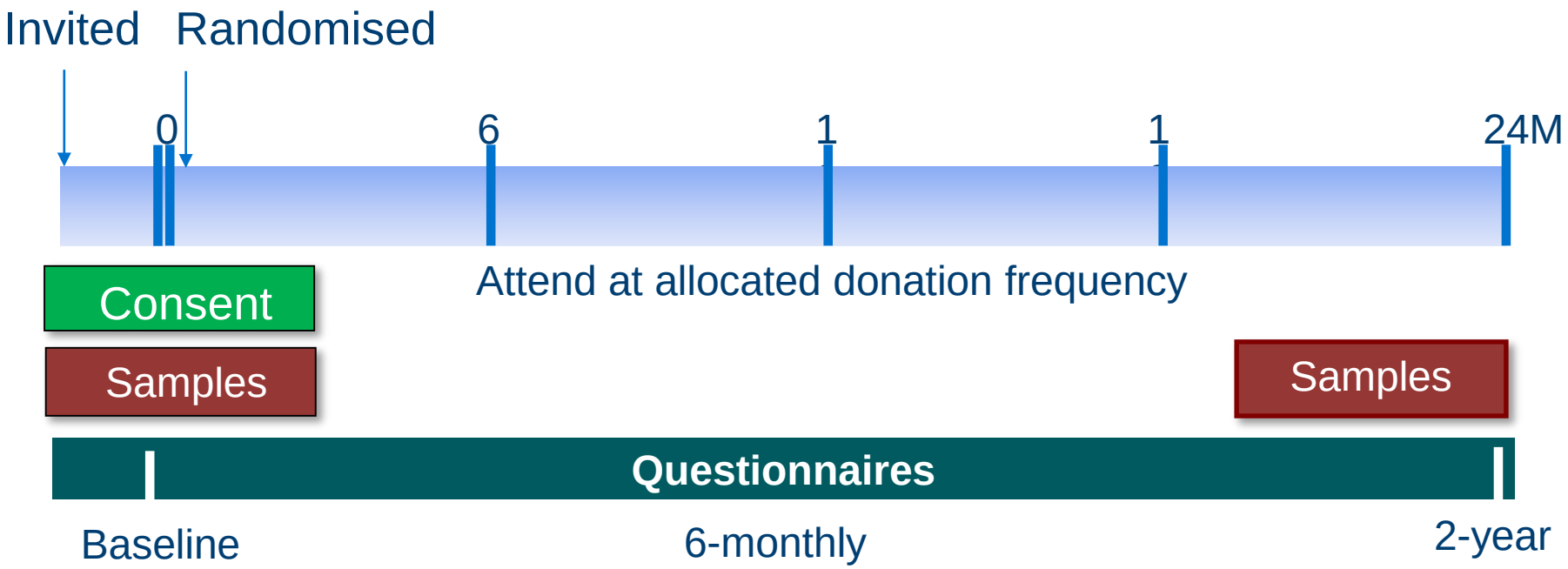
INTERVAL trial

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

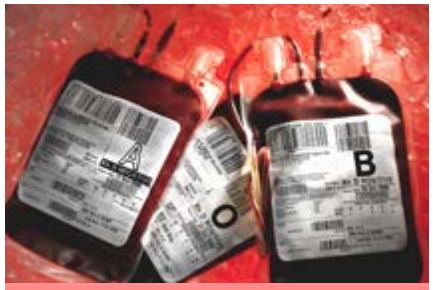


Moore C et al. Trials. 2014;15:363

INTERVAL trial design

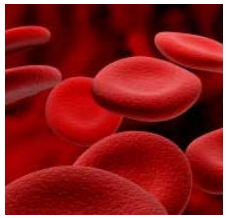


INTERVAL trial: outcomes



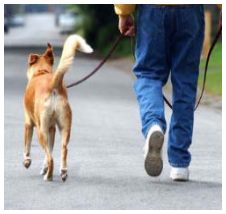
Blood donations (primary)

Well-being (key secondary)



Iron status

Cognitive function



Physical activity

Cardiometabolic traits

Cost effectiveness

Published online September 20, 2017

INTERVAL trial: outcomes

Published online September 20, 2017

COMPARE study: what is the need?

European directive 2004/33/EC Article 4:

"Blood establishments shall ensure that donors of whole blood and blood components comply with the eligibility criteria set out in Annex III."

ANNEX III

ELIGIBILITY CRITERIA FOR DONORS OF WHOLE BLOOD AND BLOOD COMPONENTS

(as referred to in Article 4)

1. ACCEPTANCE CRITERIA FOR DONORS OF WHOLE BLOOD AND BLOOD COMPONENTS

1.2. **Haemoglobin levels in donor's blood**

Haemoglobin	for females ≥ 125 g/l	for males ≥ 135 g/l	*Applicable to allogeneic donors of whole blood and cellular components*

Haemoglobin screening: rationale

Recipient protection:

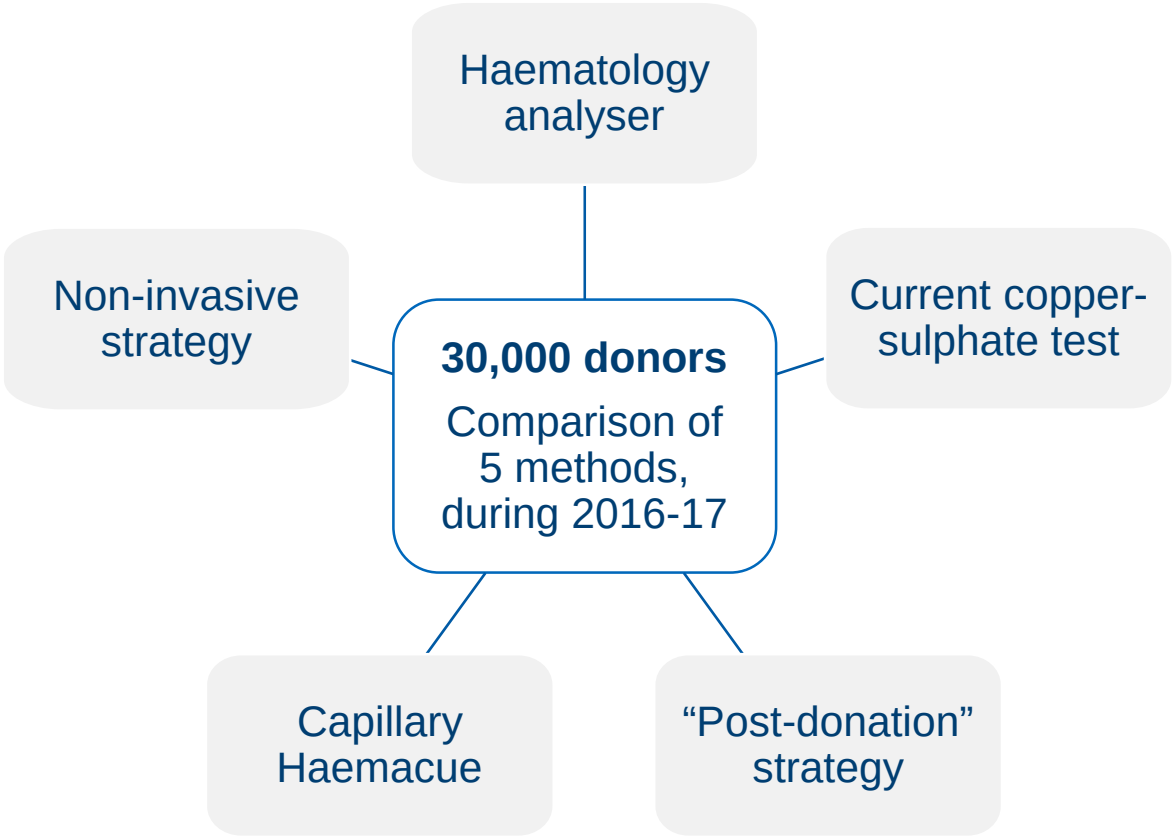
- Ensure a minimum haemoglobin dose/whole blood transfusion
- Detect RBC or congenital haemoglobin abnormalities

Donor protection:

- Assess donor suitability: non specific measure of donor health
- Prevent anaemia in donors as a consequence of blood donation

COMPARE study

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



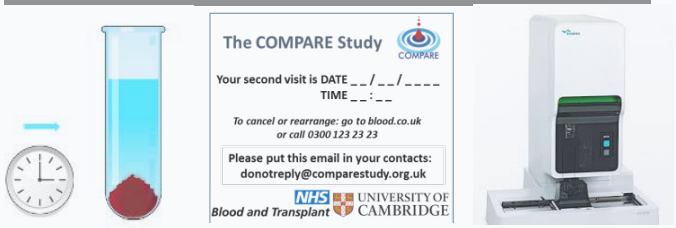
COMPARE

Key outcomes

- test accuracy
- feasibility and acceptability
- cost-effectiveness

COMPARE study design

18,000 donors



STAGE 1 – first visit

~1300 participants per week using 10 different teams

STAGE 1 – second visit

Expect a 30 % drop out rate

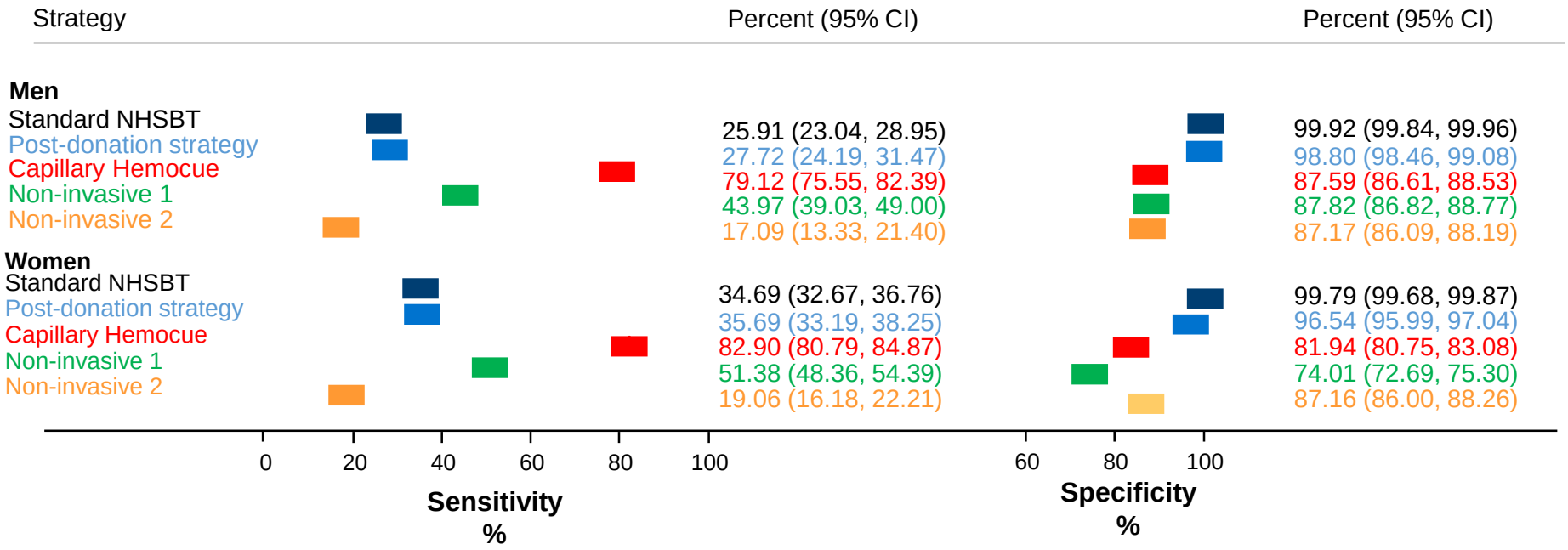
12,500 donors

STAGE 2

New donors recruited, look at skin colour and tone on non-invasive devices

13,000 donors

COMPARE study: preliminary results



Participants: characteristics/consent

Characteristics

- ❑ Whole blood donors ≥18 years old
- ❑ Internet access and email address
- ❑ Approximately 50% men
- ❑ Wide geographical distribution

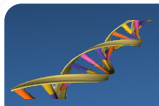
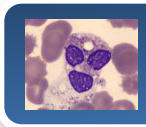
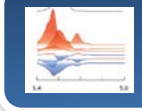
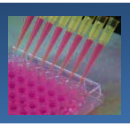
Consent: permission for

- ❑ Retrieval of relevant sections of blood donation records
- ❑ Long-term, anonymised storage of blood samples (incl. DNA)
- ❑ Retrieval of health records
- ❑ Contact, no more than three times a year, by study team about further studies

Baseline data and sample collection

Data/sample	Timepoint	INTERVAL	COMPARE
Donation data		✓	✓
Questionnaire data	Baseline	General characteristics, well-being and lifestyle	General characteristics, well-being, AEs and symptoms, lifestyle, skin type
	Interim	Well-being, adverse events (AEs) and symptoms	✗
	Endpoint	As above + donor beliefs, RPAQ and cognitive function	Feedback on experiences of different Hb screening methods
Blood sample tubes	Baseline & endpoint	EDTA, Serum TEMPUS	EDTA, Serum TEMPUS
Blood sample aliquots		Serum, plasma, buffy coat	Serum, Plasma, buffy coat
DNA extracted		✓	Ongoing

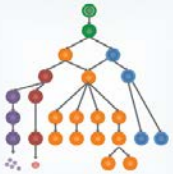
Deep molecular phenotyping

	Variables
 Genome-wide genotyping (→ sequencing)	75M →3bn
 Extended haematology assay	~200
 Blood smears (RBC overview and 100 WBCs per donor)	
 Soluble biomarkers (inc. iron-related)	~20
 Metabolomics / Proteomics	~5000

Example of research questions

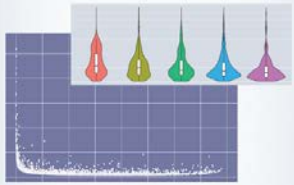
What are the genomic regulators of erythropoiesis (and other blood cell traits)?

GWAS discoveries



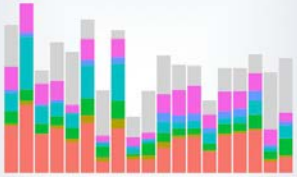
173,480 participants
36 blood cell indices
2,706 variants discovered

Allelic spectrum and heritability



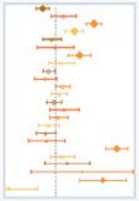
130 rare variants
210 low-frequency

Epigenome integration



Integration with chromatin states and molecular traits

Causal contribution to complex disease

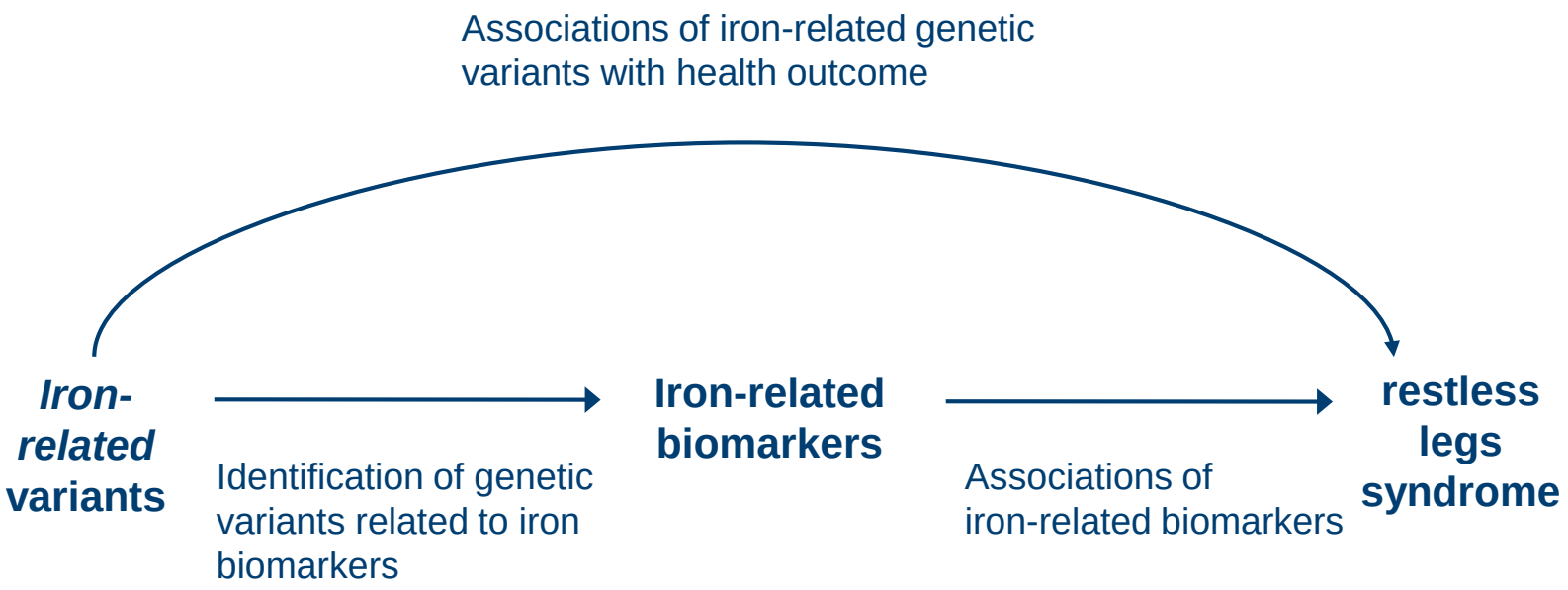


Cardiovascular, autoimmune, neuropsychiatric disease

Astle et al, Cell 2016

Example of research questions

Human genetic test for causality: iron and restless legs syndrome



Conclusions

- INTERVAL and COMPARE will provide compelling evidence for blood services on major issues related to blood donation, and inform NHSBT policy and practice.

- Studies of genetic and biomarkers in donors will contribute to improving blood donation, blood transfusion products and practices.

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

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Acknowledgments