The Danish Blood Centers
- Innovating through Research

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DISCLOSURES

Unrestricted research grant from Abbott Diagnostics administered by Aarhus University Hospital

Unrestricted research grant from Novo Nordisk administered by Aarhus University Hospital

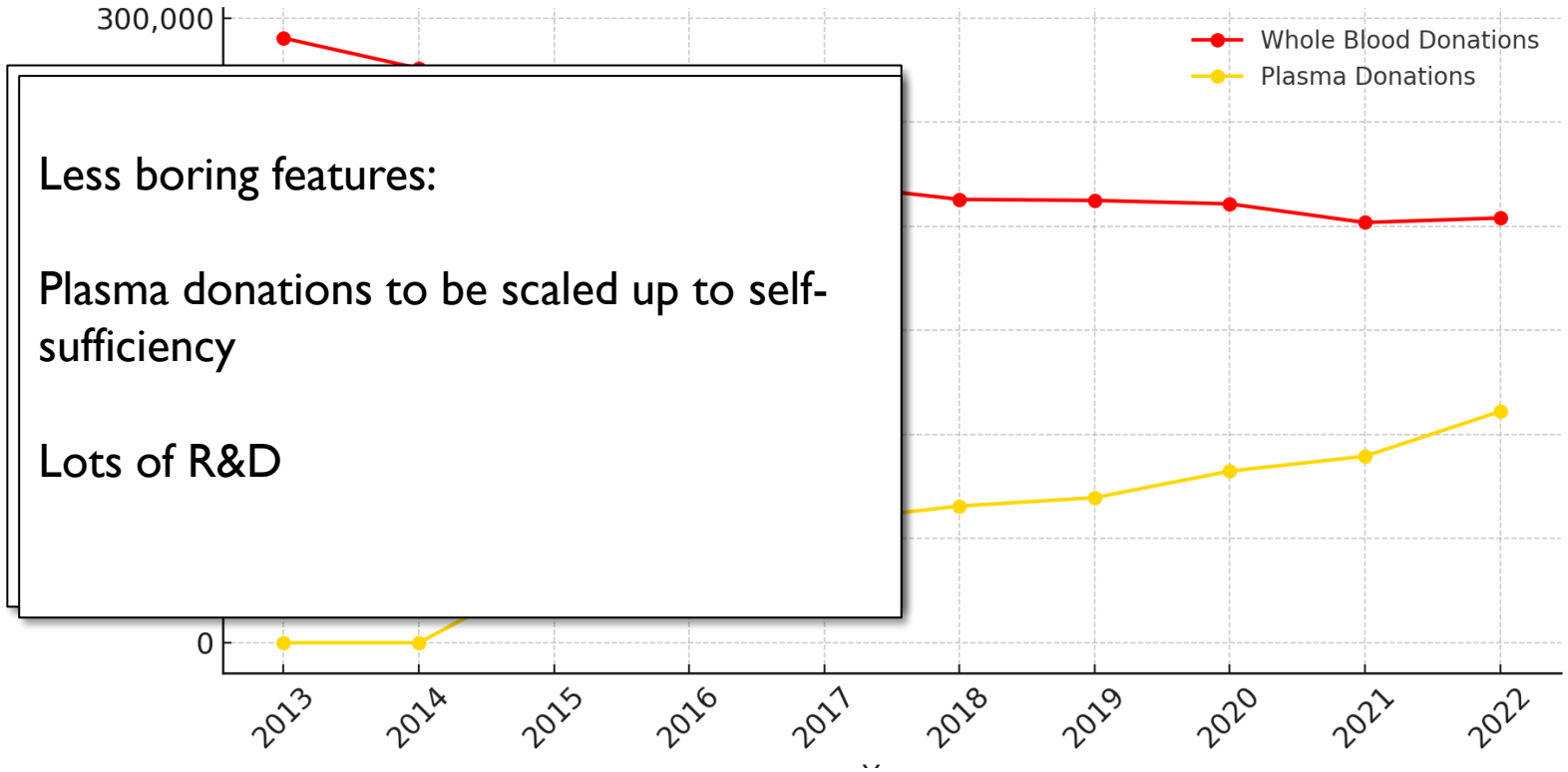
No personal fees



THE DANISH BLOOD CENTERS

Five regional blood centers

Hospital-based in the departments of clinical immunology



Less boring features:

Plasma donations to be scaled up to self-sufficiency

Lots of R&D

BLOOD CENTER FEATURES THAT FACILITATE RESEARCH AND DEVELOPMENT

Infrastructure supporting research in the blood bank:

- Blood, plasma, stem cell, faecal donors report for donations
- Linkage between donor and recipient built into our lab information system

A personal identification number (Central Person Register, CPR, introduced in 1968):

- Universal identifier, traceable across data sources

Legal framework:

- Facilitates in-depth analysis and merging of data from a wealth of sources

National health registers:

- High quality data

Building on the infrastructure:
THE DANISH BLOOD DONOR STUDY

>170,000 blood donors have been included

>117,000 donors typed for 650,000 SNPs

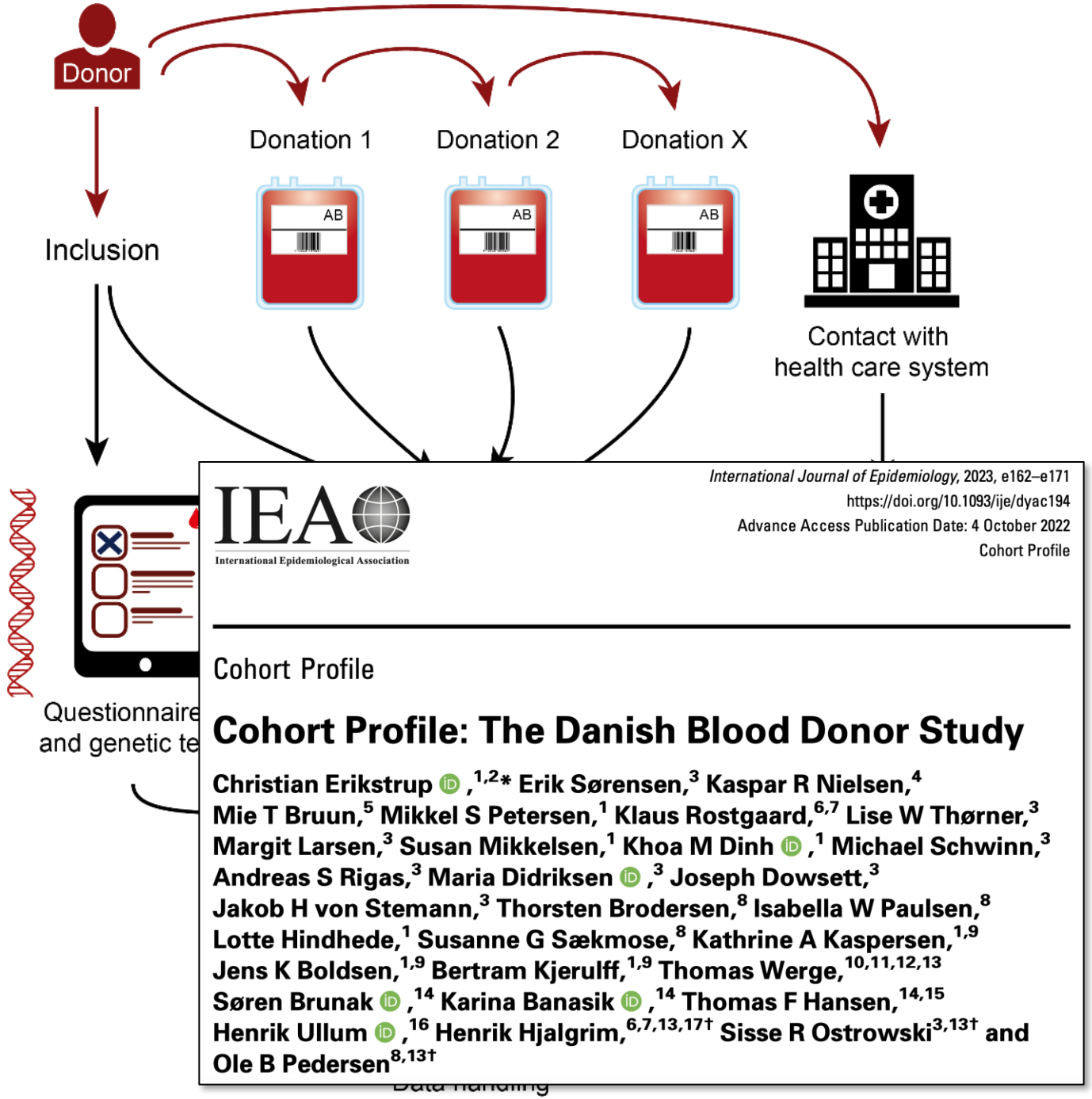
One thing that signifies blood donor studies:
Multiple visits

Sequential Samples: Analyzing changes in biomarkers over time to understand health trends.

>3 million plasma archive samples from every donation available for research

Re-questioning: Assessing lifestyle and health trait trajectories to identify correlations and impacts.

>450,000 questionnaires collected



International Journal of Epidemiology, 2023, e162–e171
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Advance Access Publication Date: 4 October 2022
Cohort Profile

IEA
International Epidemiological Association

Cohort Profile

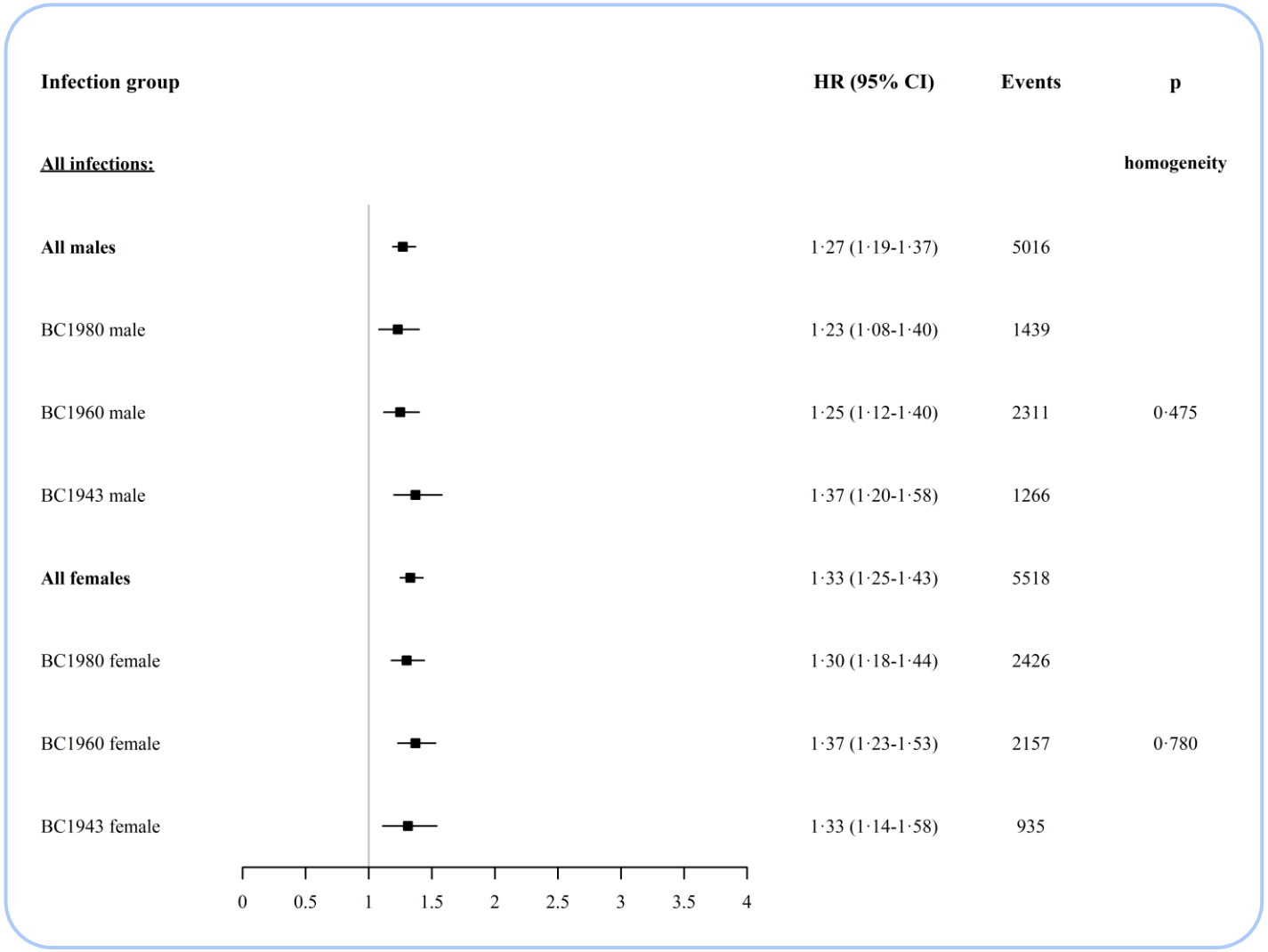
Cohort Profile: The Danish Blood Donor Study

Christian Erikstrup [1,2]* Erik Sørensen,[3] Kaspar R Nielsen,[4] Mie T Bruun,[5] Mikkel S Petersen,[1] Klaus Rostgaard,[6,7] Lise W Thørner,[3] Margit Larsen,[3] Susan Mikkelsen,[1] Khoa M Dinh [1] Michael Schwinn,[3] Andreas S Rigas,[3] Maria Didriksen [3] Joseph Dowsett,[3] Jakob H von Stemann,[3] Thorsten Brodersen,[8] Isabella W Paulsen,[8] Lotte Hindhede,[1] Susanne G Sækmose,[8] Kathrine A Kaspersen,[1,9] Jens K Boldsen,[1,9] Bertram Kjerulff,[1,9] Thomas Werge,[10,11,12,13] Søren Brunak [14] Karina Banasik [14] Thomas F Hansen,[14,15] Henrik Ullum [16] Henrik Hjalgrim,[6,7,13,17†] Sisse R Ostrowski[3,13†] and Ole B Pedersen[8,13†]

Bertram Kjerulff
Postdoc, PhD

Infections in smokers

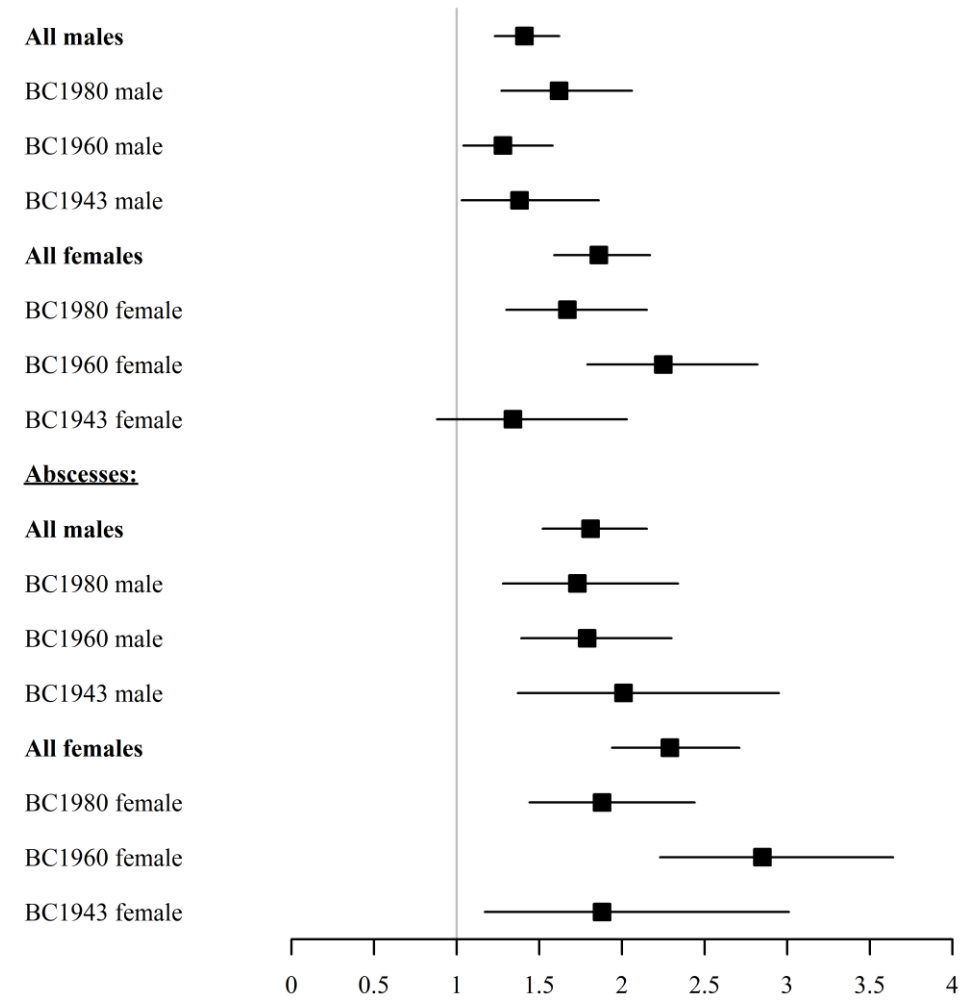
- Hospital contacts
- Follow-up for >110,000 participants
- Mean follow-up was 5 years
- Changing smoking status
- Split into three birth cohorts (BC)
- Increased risk for most infection types.



Kjerulff B et al. Smoking is associated with infection risk in healthy blood donors. Clin Microbiol Infect. 2023 Apr;29(4):506-514

Kaspersen K et al. Obesity and Risk of Infection: Results from the Danish Blood Donor Study. Epidemiology 26(4):p 580-589, July 2015.

Hospital contacts – skin infections

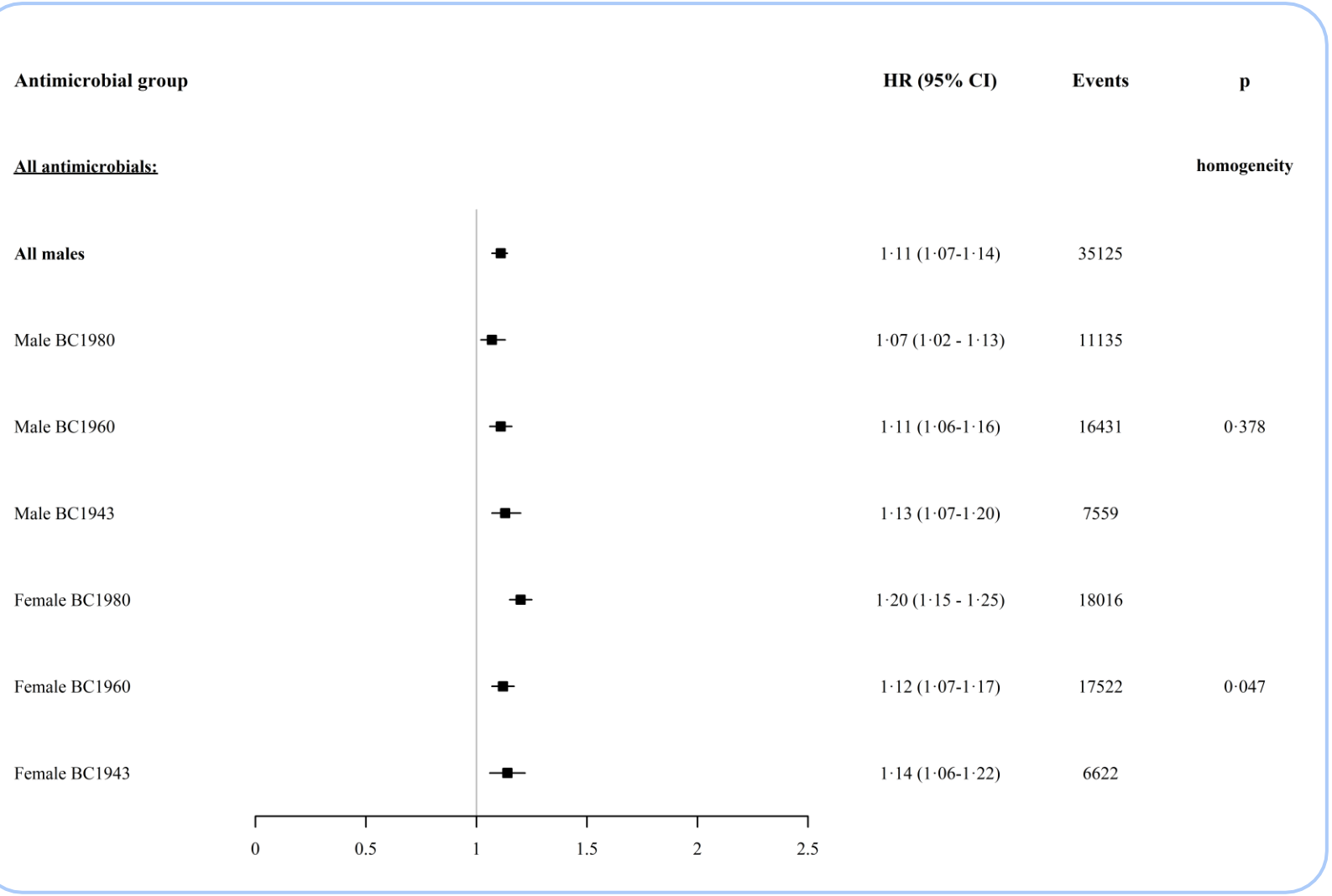


Infection group	HR (95% CI)	Events	p homogeneity
Skin and soft tissue infections:			
All males	1·41 (1·23-1·62)	1267	
BC1980 male	1·62 (1·27-2·06)	361	
BC1960 male	1·28 (1·04 -1·58)	624	0·357
BC1943 male	1·38 (1·03-1·86)	282	
All females	1·86 (1·59-2·17)	841	
BC1980 female	1·67 (1·30-2·15)	323	
BC1960 female	2·25 (1·79 -2·82)	367	0·053
BC1943 female	1·34 (0·88-2·03)	151	
Abscesses:			
All males	1·81 (1·52-2·15)	712	
BC1980 male	1·73 (1·28-2·34)	227	
BC1960 male	1·79 (1·39-2·30)	350	0·831
BC1943 male	2·01 (1·37-2·95)	135	
All females	2·29 (1·94-2·71)	666	
BC1980 female	1·88 (1·44-2·44)	279	
BC1960 female	2·85 (2·23-3·64)	290	0·053
BC1943 female	1·88 (1·17-3·01)	97	

Prescriptions in smokers

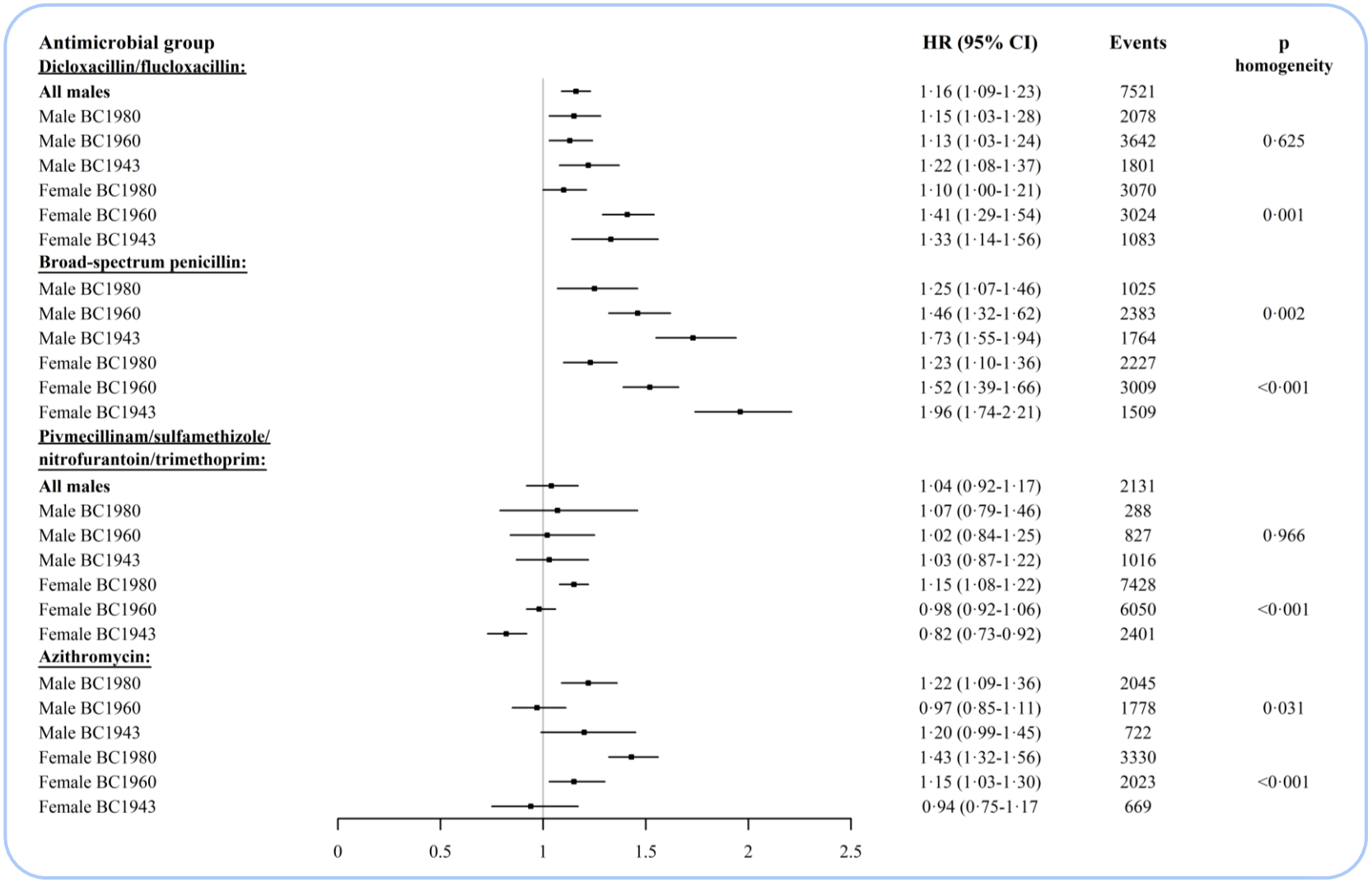
- Follow-up for >120,000 participants
- Mean follow-up 2.8 years

- Increased risk for most antimicrobials.



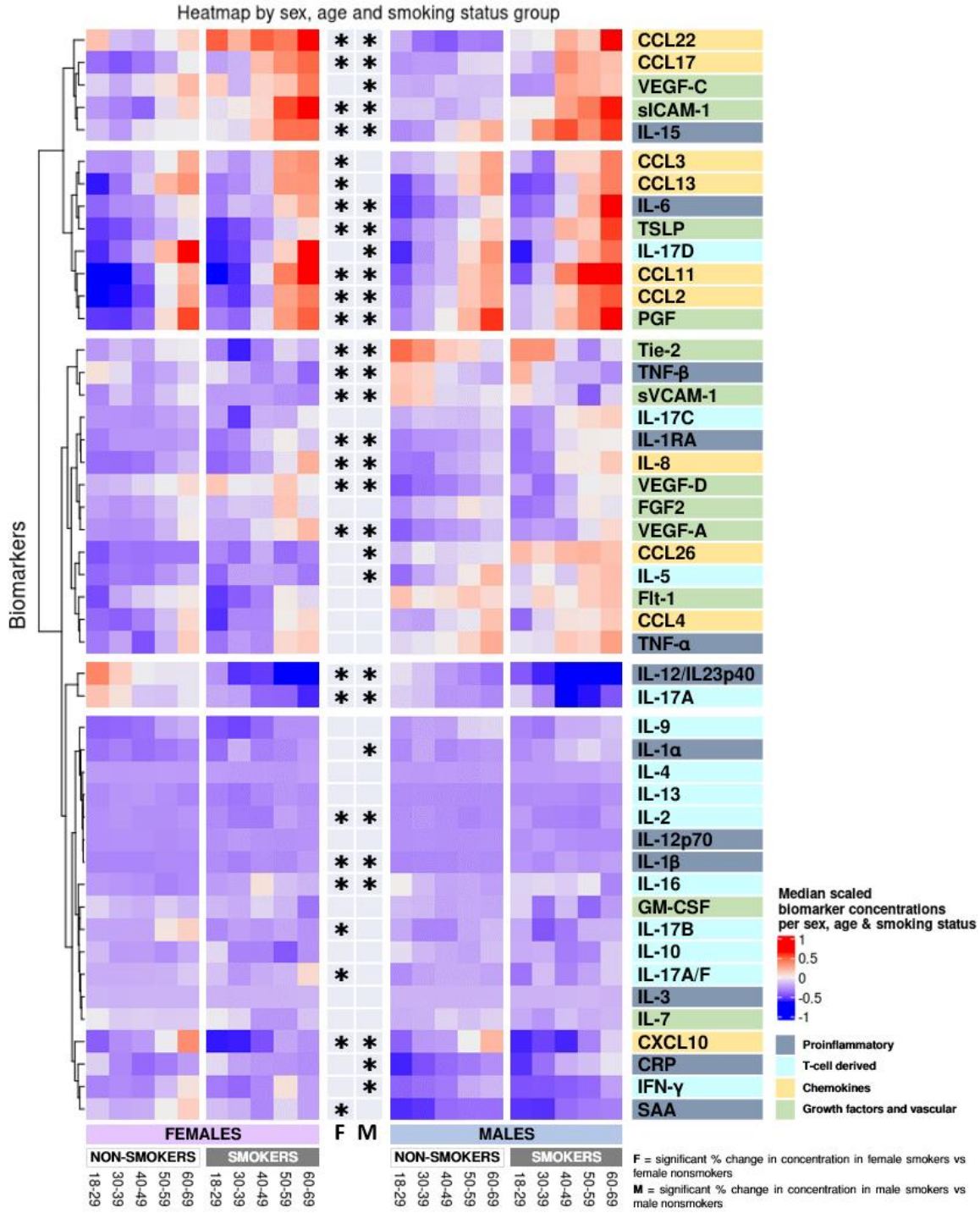
Prescriptions in smokers

- Follow-up for >120,000 participants
- Mean follow-up 2.8 years
- Increased risk for most antimicrobials.
- Notably increased broad-spectrum and dicloxacillin/flucloxacillin risk



Biomarkers

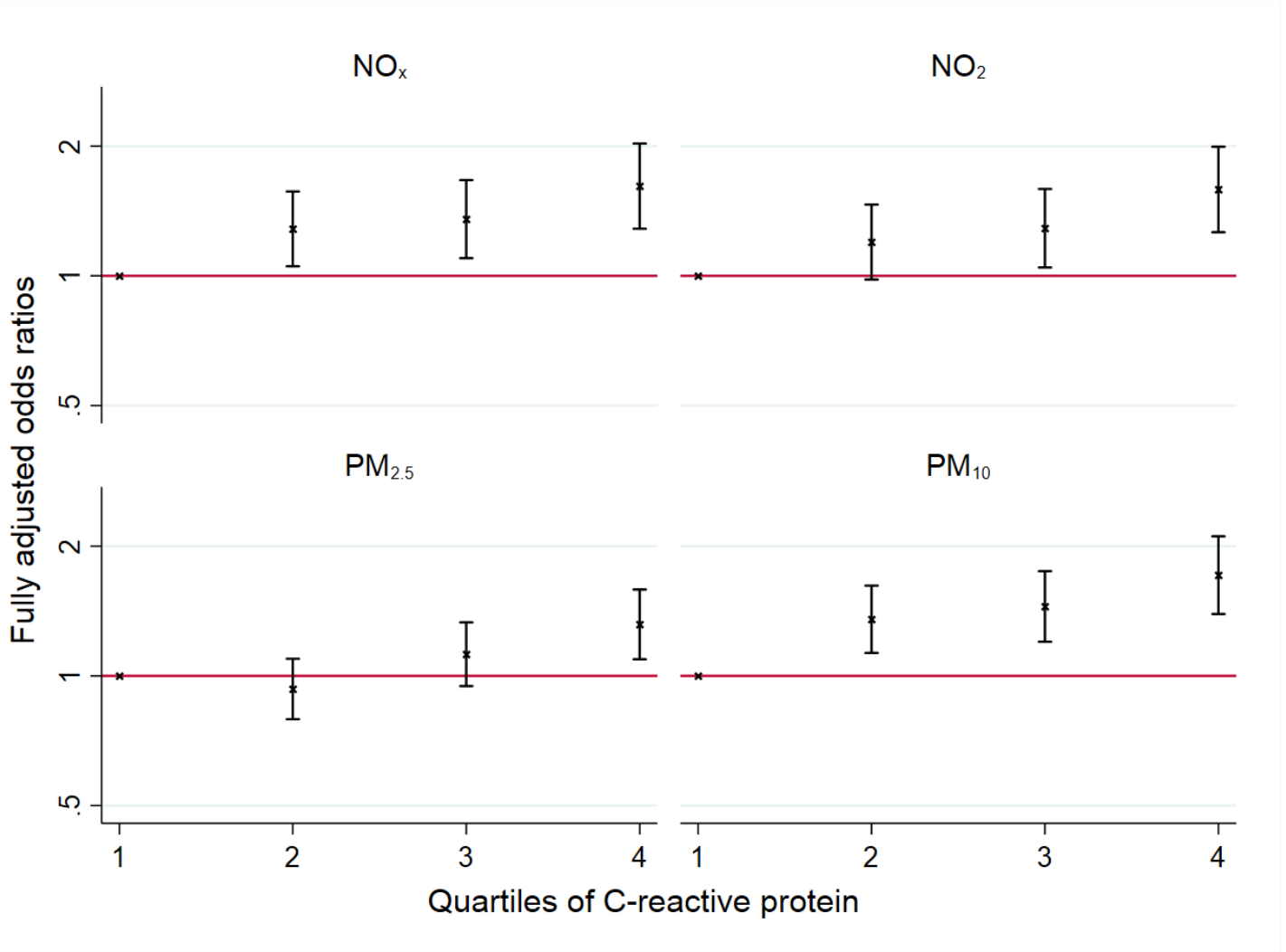
- Mesoscale measurements in ~10,000 donor samples
- What we find in registries reflects what we measure
- Same story for BMI



Kjerulff, B., Dowsett, J., Jacobsen, R.L. *et al.* Lifestyle and demographic associations with 47 inflammatory and vascular stress biomarkers in 9876 blood donors. *Commun Med* **4**, 50 (2024).

Air pollution and CRP

- Increased CRP for the most commonly examined pollutants
- CO, SO_2, mineral dust, organic carbon, primary particle matter, SO_4^{2-}, NH_4^+, and secondary inorganic aerosols reflected NO_x and PM

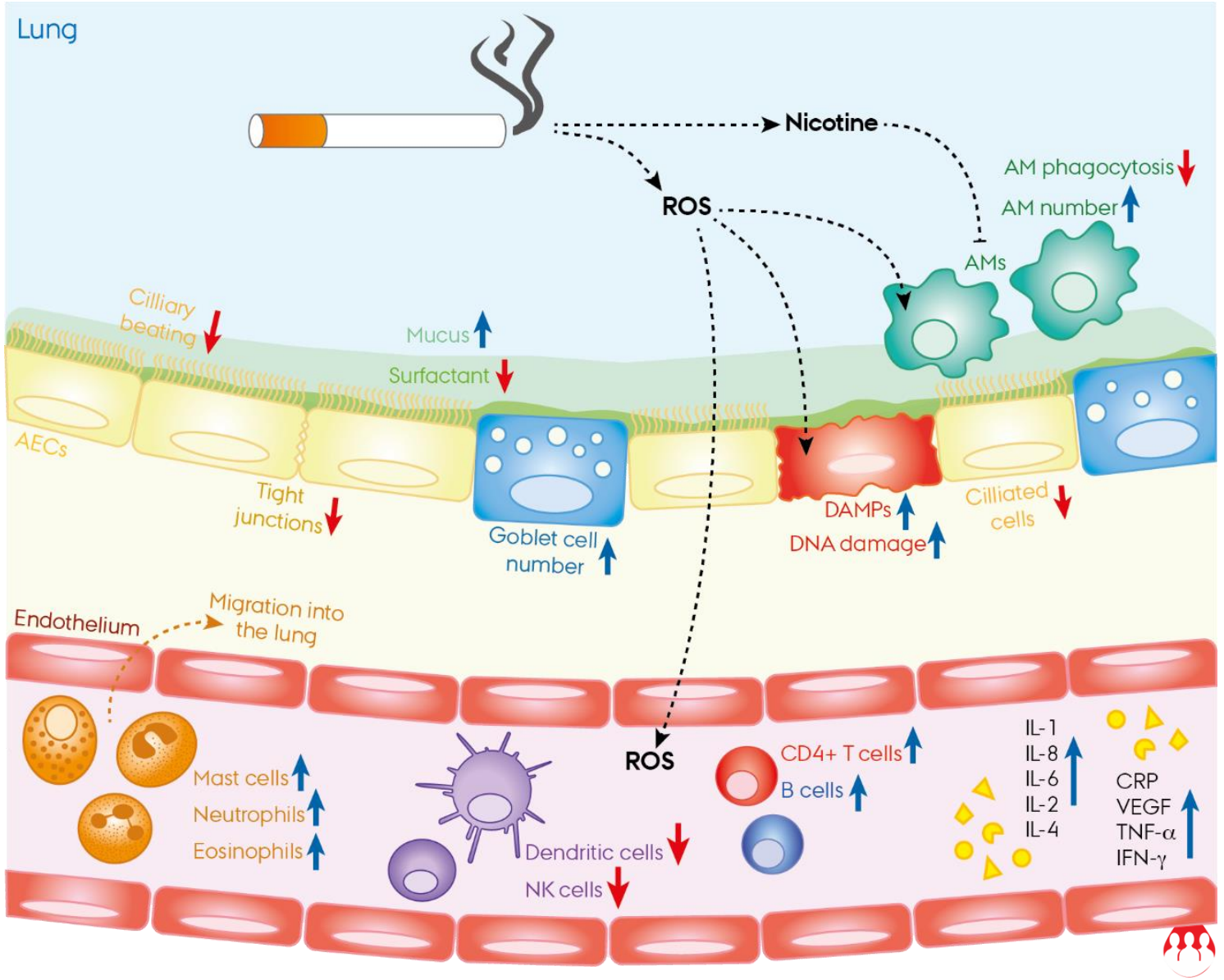


Kjerulff B, et al. Medium term moderate to low-level air pollution exposure is associated with higher C-reactive protein among healthy Danish blood donors. Environ Res. 2023 Sep 15;233:116426.

What is known

- Several known influences from BMI on biomarkers
- Wide range of inflammation and vascular stress markers increased in smokers
- Several inflammatory markers increased with air pollution exposure
- Effects on infections risk

- Microbiome

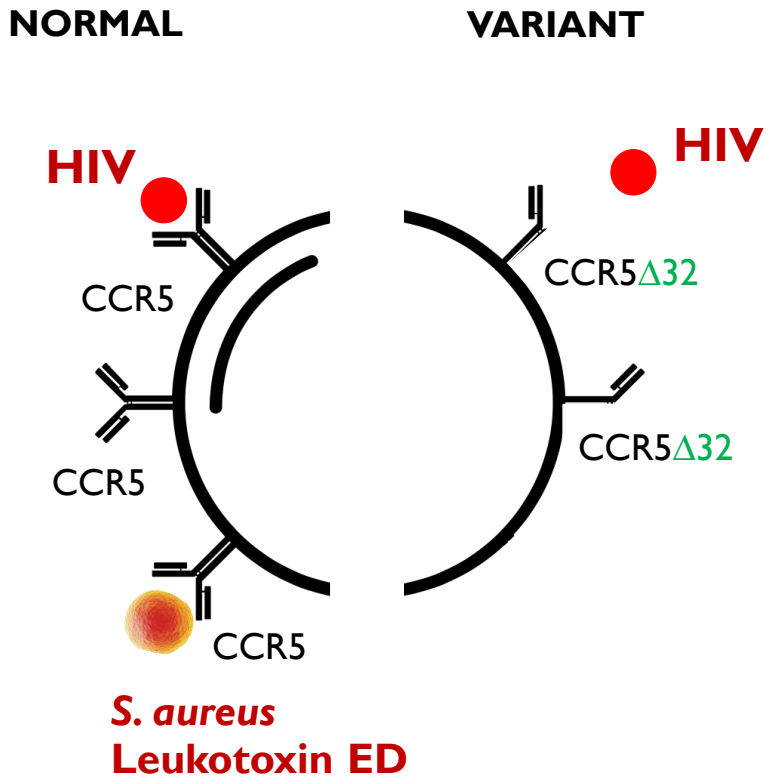


Khoa Manh Dinh

MD, Postdoc, PhD

CCR5 Δ32-DELETION AND *STAPHYLOCOCCUS AUREUS*
- A STUDY WITHIN THE STUDY

Question:
Study the impact of CCR5Δ32 on *S. aureus* carriage and infection



CCR5 Δ32-DELETION AND *STAPHYLOCOCCUS AUREUS*
- A STUDY WITHIN THE STUDY

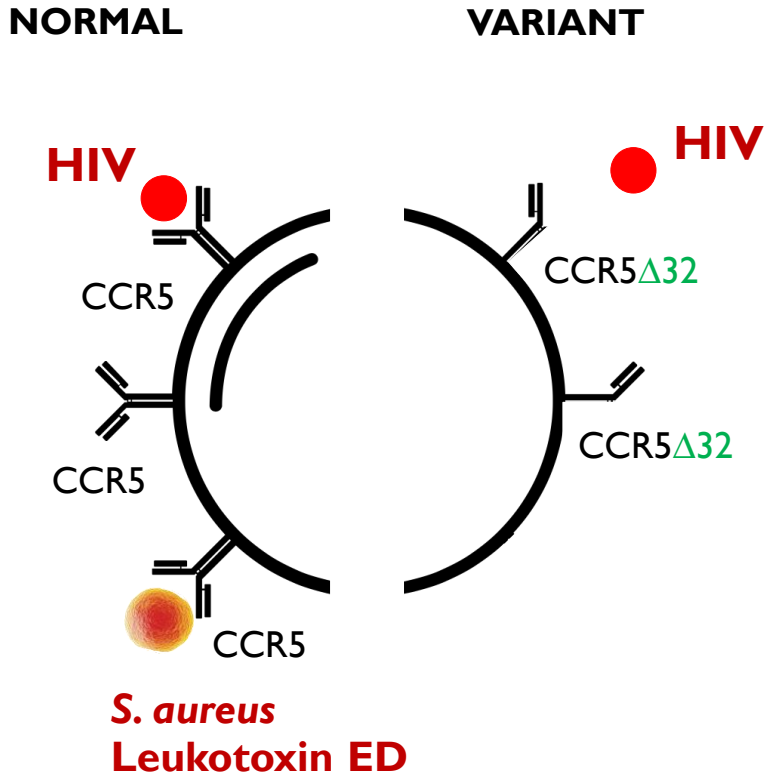
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95,000 participants from the DBDS genotyped with Illumina Global Screen Array (~650,000 SNPs)

The Danish Blood Donor *Staphylococcus aureus* Carriage Study
- **9,000 DBDS donors** included, **14,000 nasal swabs** collected

Exposure: **Δ32-deletion** in CCR5 (MAF: 0.12)

Outcome:
- *S. aureus* nasal carriage
- *S. aureus* infections and all-cause infections (prescription and diagnosis codes in health registers)





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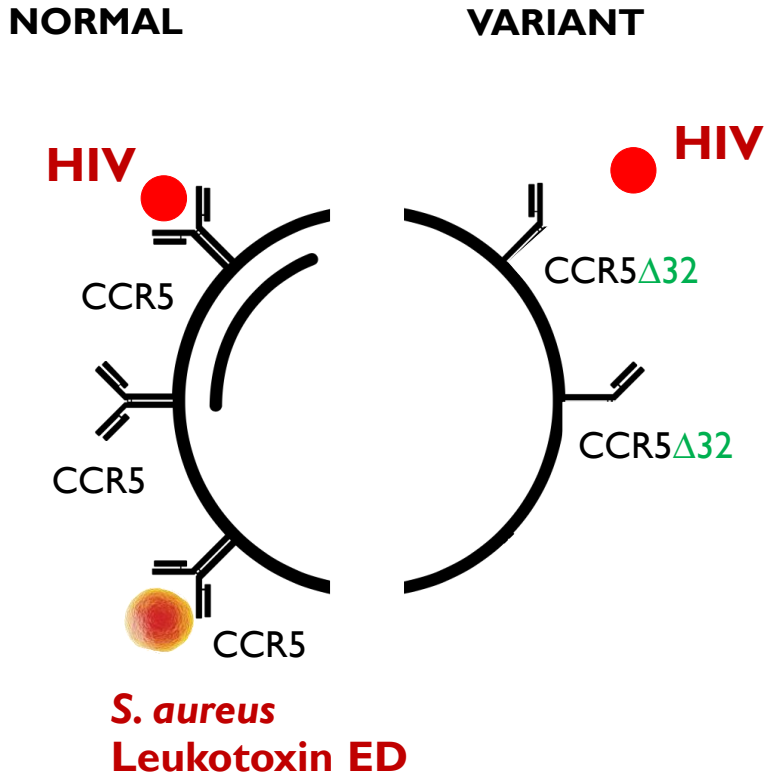
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Outcome:
- *S. aureus* nasal carriage
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Conclusion:
CCR5Δ32 does not affect the risk of nasal carriage, *S. aureus* infection or all-cause infection to any clinically relevant degree in Danes





S. AUREUS CARRIERSHIP AND RISK OF INFECTION

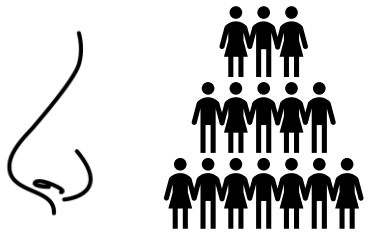
Question

Does *S. aureus* carriership affect the risk of infection among 9,000 healthy individuals?

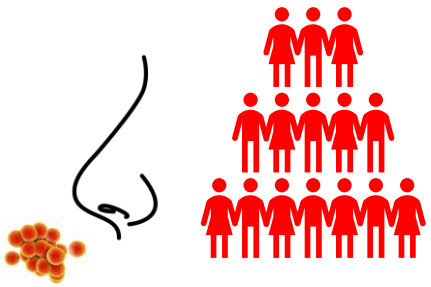
S. AUREUS CARRIERSHIP AND RISK OF INFECTION

Question

Does *S. aureus* carriership affect the risk of infection among 9,000 healthy individuals?



Non-carriers (60%)



Carriers (40%)



Pharmacy

Filled prescription of
- Dicloxacillin
- Fusidic acid

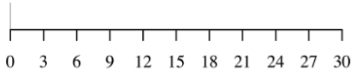


Hospital

ICD-10 diagnosis codes
- *S. aureus* infections

S. AUREUS CARRIERSHIP AND RISK OF INFECTION

Antibacterial agent groups	N	N of events	IR /100 person-years (95% CI)	IRR (95% CI)	P
Dicloxacillin:					
Non-carriers	5,235	572	2.71 (2.49–2.94)	1 (reference)	
Carriers	3,503	538	3.77 (3.46–4.10)	1.40 (1.24–1.58)	<0.001
Fusidic acid agents:					
Non-carriers	5,235	781	3.70 (3.44–3.96)	1 (reference)	
Carriers	3,503	631	4.42 (4.08–4.78)	1.22 (1.10–1.36)	<0.001
1st Dicloxacillin --> 2nd Dicloxacillin:					
Non-carriers	403	169	17.0 (14.5–19.6)	1 (reference)	
Carriers	348	190	22.8 (20.0–26.2)	1.41 (1.14–1.75)	0.001

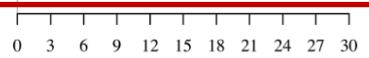


Conclusion:

S. aureus nasal carriage is associated with higher risk of filled dicloxacillin and fusidic acid agents.

S. AUREUS CARRIERSHIP AND RISK OF INFECTION

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Conclusion:

S. aureus nasal carriage is associated with higher risk of filled dicloxacillin and fusidic acid agents.

Participants who initially redeemed a prescription for dicloxacillin or fusidic acid were at higher risk of needing a new prescription for dicloxacillin during subsequent two years — incidence rates increased six-fold, carriers higher risk!

COVID-19 LOCKDOWN AND COMMON RESPIRATORY VIRUS PREVALENCE

Question

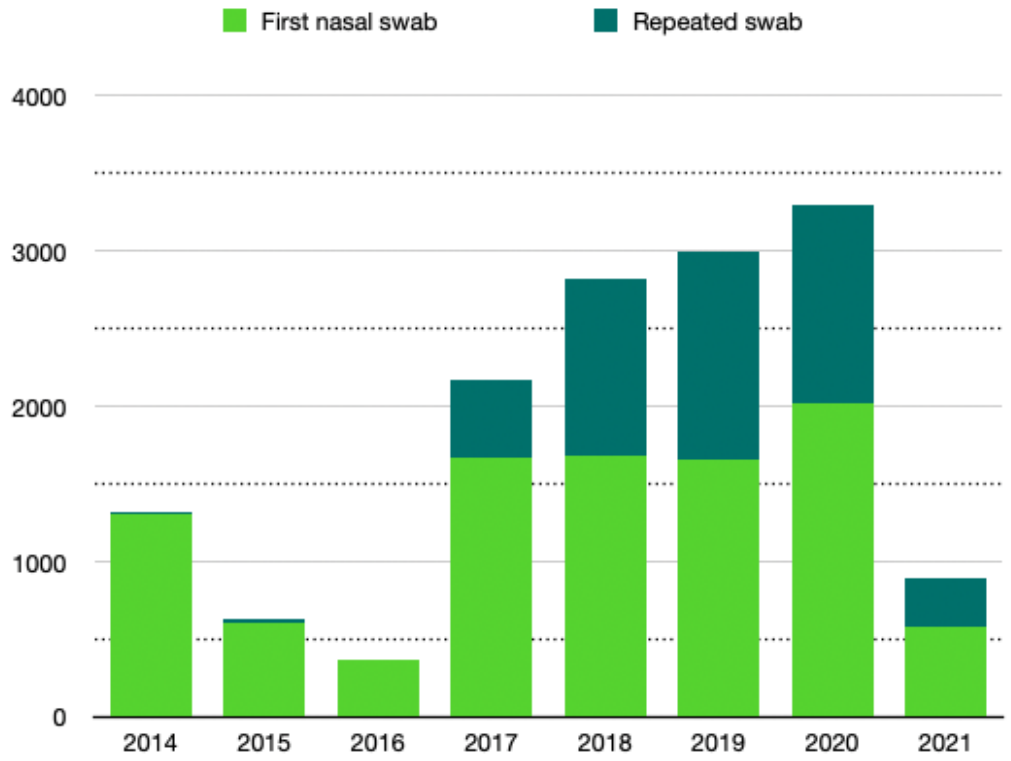
How nationwide lockdowns impact on common respiratory virus transmission among donors in bleeding facility setting.

Exposure: **Two national lockdown periods**

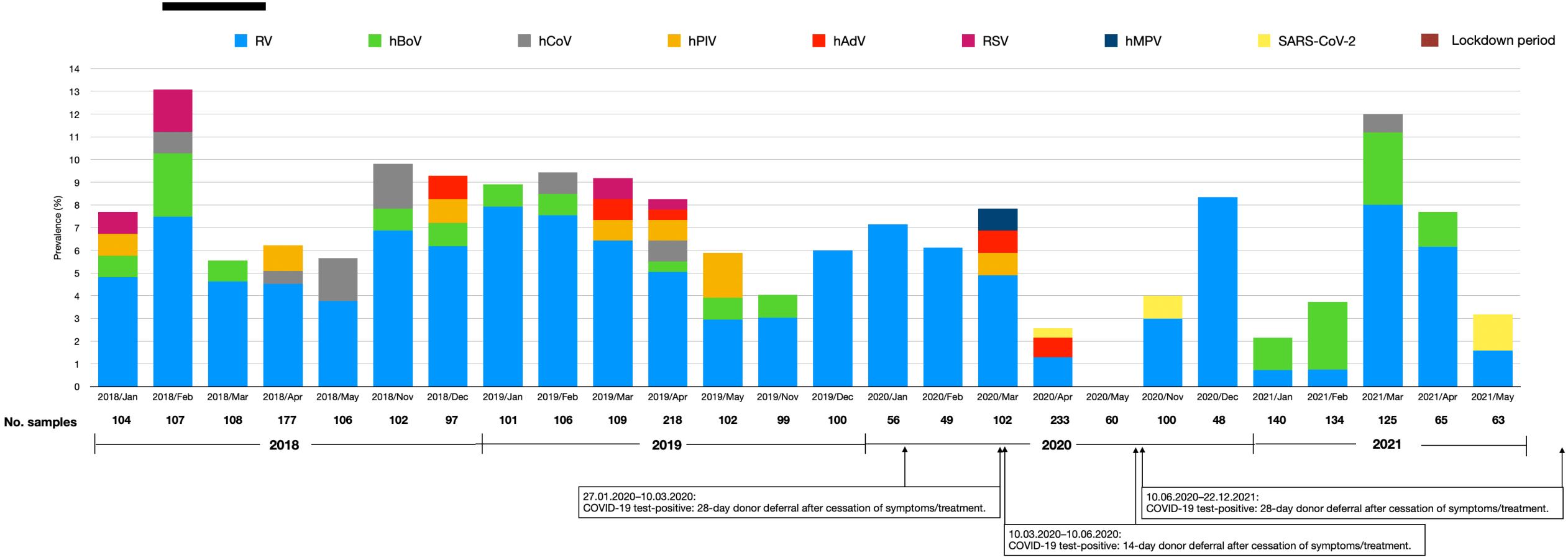
- 11 Mar 2020 – 15 Apr 2020
- 08 Dec 2020 – 05 Feb 2021

Outcome:

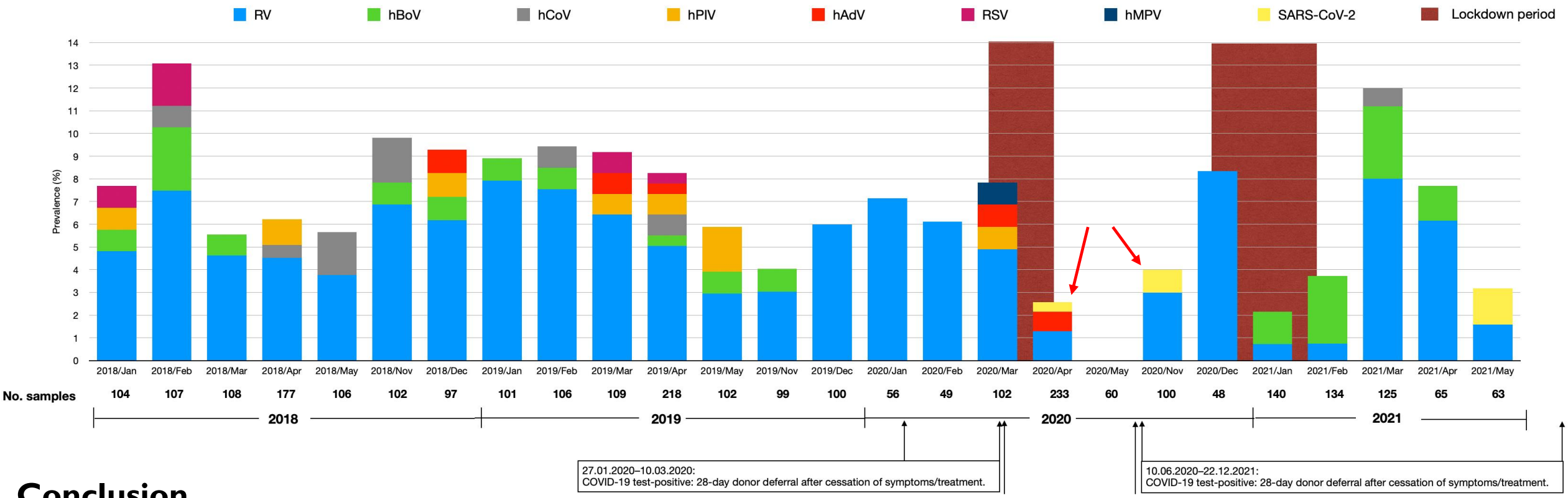
- PCR analysis of 24 virus sequences from 11 viruses



COVID-19 LOCKDOWN AND COMMON RESPIRATORY VIRUS PREVALENCE



COVID-19 LOCKDOWN AND COMMON RESPIRATORY VIRUS PREVALENCE



Conclusion

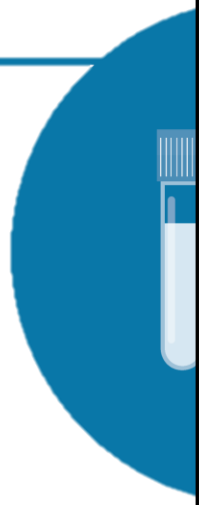
We observed a drop in virus prevalence in the subsequent month after lockdown implementation, and reverse effect after lifting lockdown.

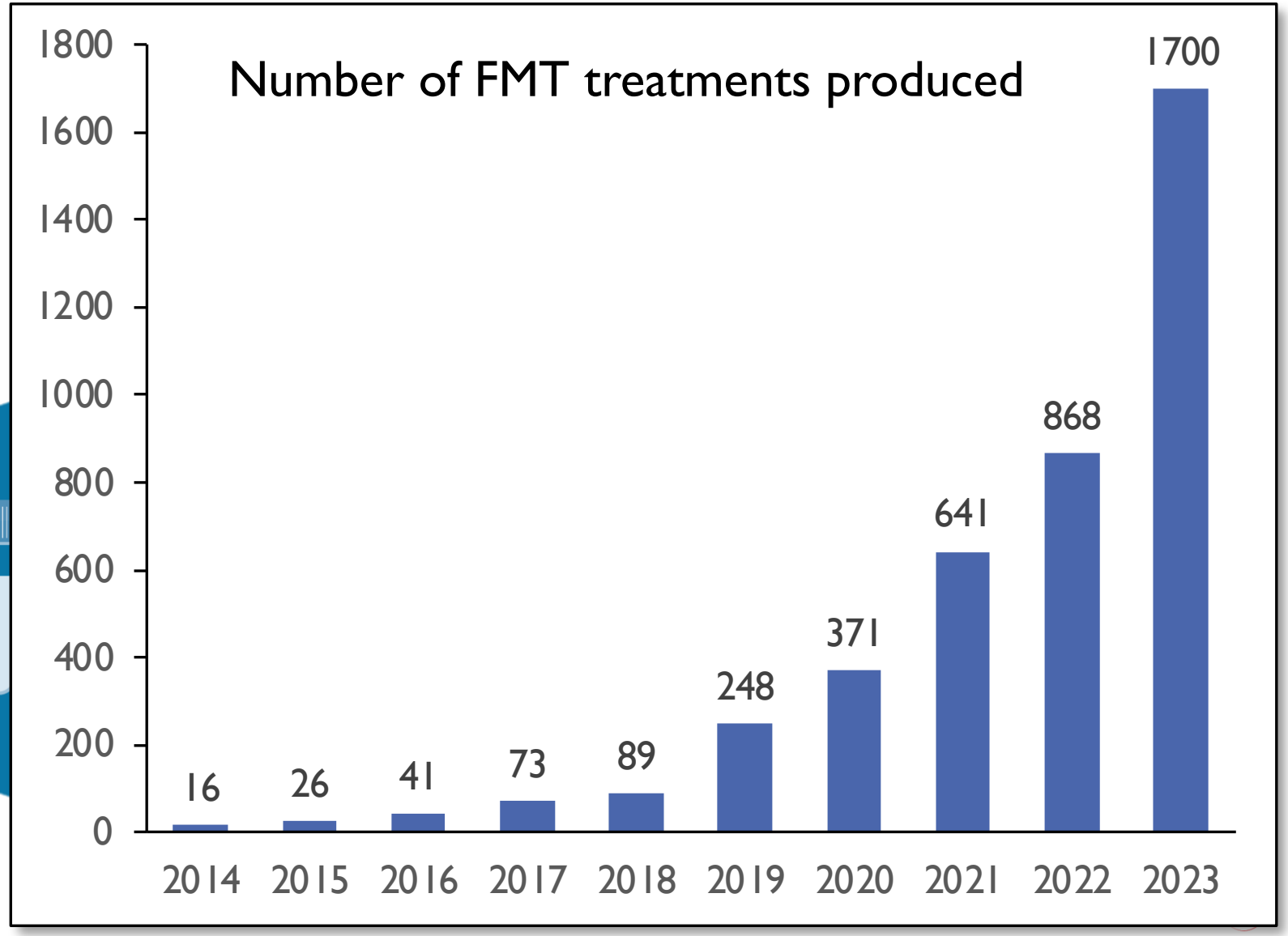
Only two cases of SARS-CoV-2 was detected during two COVID-19 waves/lockdowns among blood donors.

R&D – other SoHOs
FAECAL MICROBIOTA TRANSPLANTATION

Blood Service: Processing

Processing, release, storage, delivery





Fecal Microbiota Transplantation Is Superior to Fidaxomicin for Treatment of Recurrent *Clostridium difficile* Infection

Christian Lodberg Hvas,[1] Simon Mark Dahl Jørgensen,[1] Søren Peter Jørgensen,[1] Merete Storgaard,[2] Lars Lemming,[3] Mette Mejlby Hansen,[1] Christian Erikstrup,[4] and Jens Frederik Dahlerup[1]

2020

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark; [2]Department of Infectious

Faecal mi
Clostridioi
double-bl

Simon Mark Dahl Baun
Lotte Lindgreen Eriksen
Christian Lodberg Hvas

Summary

Background *Clostridioides difficile* infec
Microbiota restoration with faecal r

Vancomycin

We are assessing donor factors affecting FMT treatment success.

Gastroenterology, April 201

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Research note

Risk of *Helicobacter pylori* transmission by faecal microbiota transplantation via oral capsules

Anne Karmisholt Grosen [1, 2, *], Susan Mikkelsen [1], Simon Mark Dahl Baunwall [2, 3], Jens Frederik Dahlerup [2, 3], Lise Tornvig Erikstrup [4], Christian Lodberg Hvas [2, 3], Christian Erikstrup [1, 2]

USING BLOOD DONORS TO ASSESS TRAIT NORMALITY

Predictors of bowel symptom phenotypes - adjusted analysis

Predictor	1-2 symptoms: Acid regurgitation and/or heart burn RRR (95% CI)	1-2 symptoms: Bloating and/or rumbling RRR (95% CI)	1-2 symptoms: Others RRR (95% CI)	3-4 symptoms RRR (95% CI)	5-6 symptoms RRR (95% CI)	≥ 7 symptoms RRR (95% CI)
Demographics						
Female sex	0.86 (0.75 - 0.99)	1.38 (1.27 - 1.51)	1.46 (1.32 - 1.63)	1.70 (1.53 - 1.89)	2.75 (2.25 - 3.38)	3.49 (2.34 - 5.20)
Premenopausal (female of age < 50)	0.72 (0.59 - 0.88)	1.25 (1.13 - 1.39)	1.29 (1.14 - 1.47)	1.69 (1.49 - 1.92)	1.88 (1.50 - 2.36)	2.87 (1.85 - 4.45)
Age < 50	0.88 (0.78 - 0.99)	1.27 (1.18 - 1.36)	1.81 (1.66 - 1.98)	1.85 (1.69 - 2.03)	2.66 (2.21 - 3.20)	2.82 (1.94 - 4.10)
Obesity	2.59 (2.33 - 2.89)	1.08 (1.01 - 1.17)	1.32 (1.22 - 1.44)	1.51 (1.40 - 1.63)	1.55 (1.40 - 1.73)	1.86 (1.61 - 2.16)
Smoker	1.43 (1.24 - 1.65)	1.13 (1.03 - 1.23)	1.34 (1.22 - 1.47)	1.38 (1.27 - 1.51)	1.57 (1.40 - 1.77)	1.80 (1.52 - 2.12)
Clinical characteristics						
IBS	1.52 (1.20 - 1.91)	2.25 (1.98 - 2.54)	2.40 (2.09 - 2.76)	4.99 (4.42 - 5.62)	11.82 (10.29 - 13.57)	21.81 (18.34 - 25.94)
Lacto- or gluten-intolerance	1.09 (0.77 - 1.54)	1.78 (1.50 - 2.09)	2.08 (1.75 - 2.49)	3.30 (2.82 - 3.87)	5.31 (4.42 - 6.39)	7.87 (6.26 - 9.90)
Bowel habits						
Irregular defecation	1.49 (1.15 - 1.93)	2.35 (2.06 - 2.69)	6.09 (5.37 - 6.91)	10.83 (9.63 - 12.19)	26.04 (22.86 - 29.66)	65.95 (56.19 - 77.39)
Frequency						
1 - 3 a day	REF	REF	REF	REF	REF	REF
< 1 a day	1.03 (0.87 - 1.22)	1.06 (0.97 - 1.15)	1.24 (1.12 - 1.36)	1.25 (1.14 - 1.38)	1.37 (1.19 - 1.57)	1.71 (1.36 - 2.15)
> 3 a day	0.76 (0.50 - 1.15)	1.24 (1.00 - 1.52)	1.78 (1.43 - 2.21)	2.22 (1.80 - 2.72)	3.31 (2.48 - 4.42)	5.77 (3.78 - 8.79)
< every third day	1.22 (0.47 - 3.14)	1.32 (0.79 - 2.19)	1.38 (0.77 - 2.47)	2.38 (1.46 - 3.87)	4.37 (2.46 - 7.74)	9.68 (4.91 - 19.06)
1 - 3 a day - > 3 a day	1.34 (0.70 - 2.55)	2.51 (1.80 - 3.51)	6.61 (4.86 - 9.00)	12.06 (9.05 - 16.08)	29.67 (21.78 - 40.43)	65.55 (45.76 - 93.90)
< 1 a day - 1 - 3 a day	1.77 (1.14 - 2.73)	2.66 (2.11 - 3.35)	6.65 (5.36 - 8.24)	12.00 (9.81 - 14.68)	29.16 (23.59 - 36.04)	64.38 (50.65 - 81.84)
< every third day - < 1 a day	-	1.91 (0.88 - 4.17)	7.16 (3.62 - 14.18)	8.54 (4.41 - 16.53)	28.21 (14.56 - 54.66)	70.83 (35.50 - 141.31)
Large variation	1.67 (0.64 - 4.38)	2.52 (1.53 - 4.13)	8.29 (5.30 - 12.97)	19.71 (13.00 - 29.88)	53.18 (34.80 - 81.27)	165.46 (106.75 - 256.44)
Consistency						
Bristol 4	REF	REF	REF	REF	REF	REF
Bristol 3	1.10 (0.97 - 1.26)	1.09 (1.02 - 1.17)	1.44 (1.33 - 1.56)	1.50 (1.39 - 1.62)	1.88 (1.66 - 2.13)	2.29 (1.84 - 2.85)
Bristol 5	1.07 (0.90 - 1.28)	1.36 (1.23 - 1.49)	1.72 (1.54 - 1.92)	2.22 (2.00 - 2.46)	3.11 (2.66 - 3.62)	4.63 (3.59 - 5.98)
Bristol 1-2	1.19 (0.94 - 1.50)	1.22 (1.07 - 1.38)	1.68 (1.46 - 1.93)	2.09 (1.83 - 2.38)	3.03 (2.52 - 3.65)	5.18 (3.91 - 6.85)
Bristol 6-7	1.22 (0.89 - 1.67)	1.57 (1.31 - 1.88)	2.42 (1.99 - 2.94)	3.87 (3.25 - 4.61)	8.02 (6.38 - 10.09)	16.82 (12.15 - 23.28)
Bristol 3–4, Bristol 3–5, Bristol 4–5	1.57 (0.95 - 2.60)	2.16 (1.65 - 2.83)	5.86 (4.56 - 7.52)	10.89 (8.64 - 13.72)	25.75 (19.94 - 33.25)	58.16 (42.73 - 79.16)
Bristol 4–6, Bristol 5–6, Bristol 5–7	-	1.73 (0.86 - 3.51)	7.96 (4.42 - 14.33)	16.43 (9.52 - 28.35)	47.58 (26.70 - 84.78)	170.20 (92.09 - 314.53)
Bristol 1–3, Bristol 2–3, Bristol 2–4	-	3.03 (1.36 - 6.76)	10.46 (5.02 - 21.77)	19.97 (9.95 - 40.07)	70.66 (34.98 - 142.74)	135.26 (63.75 - 286.97)
Large variation	1.64 (1.06 - 2.53)	2.98 (2.38 - 3.73)	9.05 (7.35 - 11.16)	18.05 (14.83 - 21.97)	53.17 (43.07 - 65.63)	135.25 (105.31 - 173.70)

Results are presented as adjusted relative risk ratios (RRR) with 95% confidence intervals (CI). Participants with no symptoms serve as base reference.



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TRANSLATIONAL RESEARCH
Genetics

Dyslipidemia, inflammation, calcification, and adiposity in aortic stenosis: a genome-wide study

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nature structural & molecular biology

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Variant in the synaptonemal complex protein SYCE2 associates with pregnan… loss through effect on recombination

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Valgerdur Steinthorsdottir[1], Bjarni V. Halldorsson[1,2], Ha…, Gunnar Palsson[1], Asmundur Oddsson[1], David Westergaa…, Gudny A. Arnadottir[1], Lilja Stefansdottir[1], Karina Banasik[3], Thomas Folkmann Hansen[3,6], Søren Brunak[3], Mette Nyeg…, Sisse Rye Ostrowski[8,9], Ole Birger Vesterager Pedersen[9,1…], Christian Erikstrup[11,12], DBDS genomics consortium*, Gudmar Thorleifsson[1], Lincoln D. Nadauld[13], Asgeir Haralds…, Thora Steingrimsdottir[14,16], Laufey Tryggvadottir[14,17], Ingileif…, Daniel F. Gudbjartsson[1,18], Eva R. Hoffmann[19], Patrick Sule…, Hilma Holm[1], Henriette Svarre Nielsen[4,9] & Kari Stefansso…

nature genetics

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Integrative common and rare variant analyses provide insights into the genetic architecture of liver cirrhosis

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Genome-wide analysis of 102,084 migraine cases identifies 123 risk loci and subtype-specific

nature COMMUNICATIONS

ARTICLE
https://doi.org/10.1038/s41467-022-29133-7 OPEN

A genome-wide meta-… loci associated with ca…

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equivalent to m… thromboembol…

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We report a genome-wide association study of venous thromboembolism (VTE) incorporating 81,190 cases and 1,419,671 controls sampled from six…

Research

JAMA Cardiology | Original Investigation

Variants at the Interleukin 1 Gene Locus and Pericarditis

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https://doi.org/10.1038/s41588-022-01199-5

…holic fatty liver

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ENHANCING DISEASE PREDICTION

JAMA | Original Investigation

Aug 2023

Evaluation of Large-Scale Proteomics for Prediction of Cardiovascular Events

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Clinical evaluation, genetic and proteome risk scores: All significantly enhanced disease prediction.

Current study limitation: Only one plasma sample collected, median time from sample to event was 8.5 years.

Potential of Blood Donor study samples:

Can provide sequential samples, reducing time from sample to event.

Enables assessment of biomarker trajectories, minimizing inter-individual variation impact.

32,000 Blood Donor Study samples have been analysed for 3000 biomarkers

CONCLUSION - INNOVATING THROUGH RESEARCH

We have obligations:

We documented effects of whole blood donations.

We need to document safety and health effects of plasma donation.



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COMMENTARY

TRANSFUSION

Very-high frequency plasmapheresis and donor health –absence of evidence is not equal to evidence of absence

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Unlocking new frontiers in donor research

- Sequential samples and responses
- Health registers
- Cost-efficiency

We have yet to fully realize the extensive capabilities donor studies.

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Ingileif Jónsdóttir



Thanks to our blood donors!

