20 I 23 JUNE 2022

Liège I Théâtre de Liège I Belgium

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70th ESCVS

International congress of the European Society for Cardiovascular and Endovascular Surgery

7th IMAD meeting

European Reference Network

for rare or low prevalence complex diseases

Network Vascular Diseases (VASCERN)

Member UZ Gent – België

Interpretation and clinical implications of population based genetics for TAAD

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Conflict of Interest: none

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Timeline

Sanger and Gilbert develop DNA sequencing method

End Human Genome project

1955 Watson, Crick and Franklin describe the dsDNA helix

1977

1990 Start Human Genome project

2003

2015 1000 Genome project complete

https://poweredtemplate.com/dna-timeline-infographic-75769/

How population based genetics will change clinical practice

- Genotype first approach
- Deep learning – Polygenic Risk Scores

Genotype First Approach

WES + Pheno data

Bio*Me* (N= 32,344)

+

UKBB (N=49,960)

41 P/LP *FBN1* variants

- 22% MFS dx
- 12% phenotypic features – no dx
- 5/15 with echo data had TAA

Caveats:

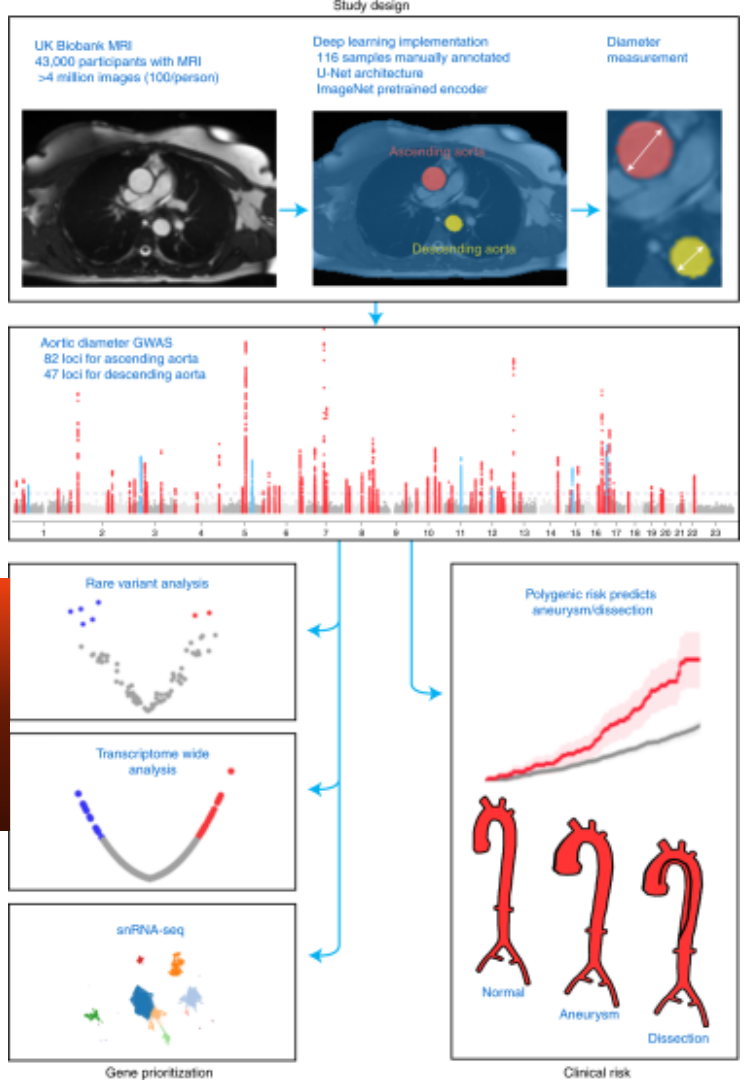
1. **Phenotypic data**
2. **Variant curation**

Routine population genotyping may enable multidisciplinary care and avoid life-threatening events.

Wenger BM, … De Backer J, … Gelb B. et al.. Genet Med. 2020

DL - GWAS - PRS

DL to assess size of the AA & DA - MRI data on 43,243 UK BB participants (4.4 mln images)



Previously unreported genetic loci:

82 in AA - 47 in DA

PRS for AA size : independent RF for TAAD

PRS + clinical RF: ID asymptomatic individuals at high risk of TAA who would benefit from thoracic imaging

*Pirruccello, J.P.,. et al. Deep learning enables genetic analysis of the human thoracic aorta. Nat Genet **54,** 40–51 (2022).*

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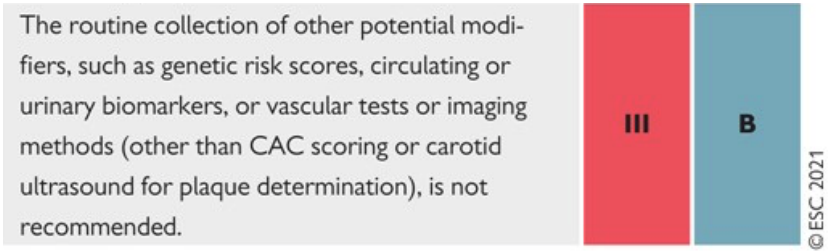
Polygenic Risk Scores for better (personalized) risk prediction

1. **Clinical populations may differ** from research samples in disease severity, ancestral diversity, and exposure to environmental risk
2. **Incremental** prediction accuracy is relatively modest
3. Engagement of clinicians and service users, to ensure that any application of PRSs **avoids deterministic interpretations** and is based on the understanding that PRS is an **indicator, not a precise measure**



Visseren F, Mach F, et al. EHJ 2021

How will genomics change the way we practice?

Genomics have entered **mainstream medicine** (and are here to stay!) - making it possible to predict, diagnose, and treat diseases **more precisely and personally** than ever

Genomics are **complex but not scary**!

Integrate genetics into your daily practice

Basic knowledge

Work together!

Thank you!

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