From arteries to algorithms: Foundation models for coronary artery disease diagnosis and cardiovascular risk assessment

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Exploris Health

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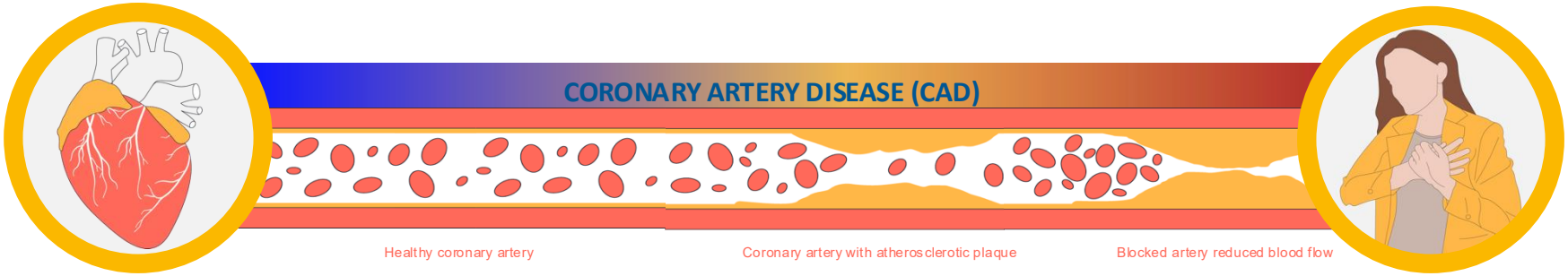
Coronary artery disease is present long before symptoms, but our tools detect it too late



Cardiovascular diseases leading cause of mortality

c.20M deaths p.a., claiming 1 out of every 3 lives[1]

CAD is highly complex and builds silently over decades

often from the teens to midlife – leaving a long window to act[2]

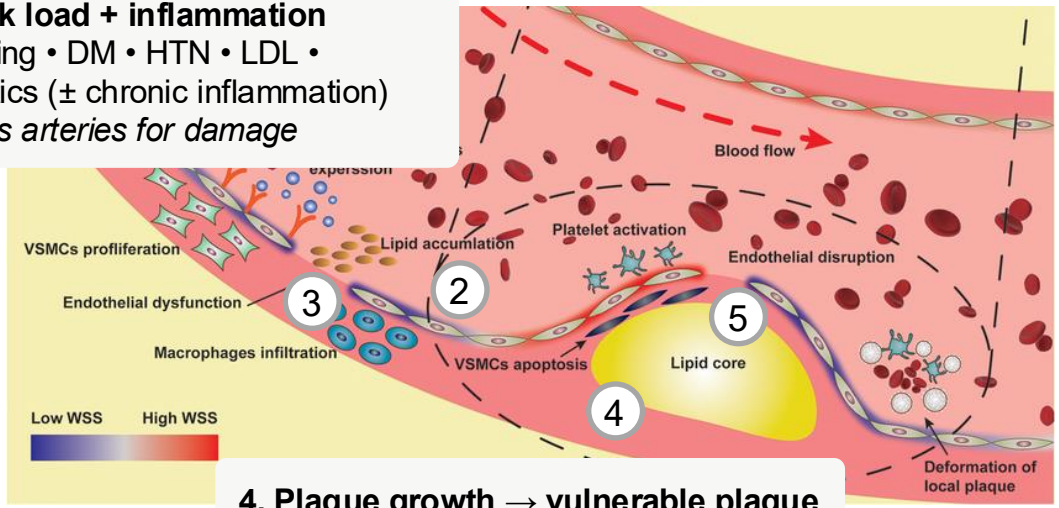
Myocardial infarction is the principal clinical consequence

and may be avoided with timely CAD detection

1. Source: WHO.
2. Source: heart.org, AHA, Mayo Clinic, NHLBI; Insull W. Am J Med 2009.

Where plaques form, why they become dangerous, and how events happen

1. Risk load + inflammation
Smoking • DM • HTN • LDL •
Genetics (± chronic inflammation)
Primes arteries for damage



2. Disturbed flow hotspots
Low/oscillatory shear at bends/branches
Endothelium activates + becomes leaky

3. LDL retention + immune entry
LDL gets trapped → monocytes/macrophages → foam cells
Plaque begins

4. Plaque growth → vulnerable plaque
Lipid core grows + cap weakens (SMC/VSMC dysfunction, inflammation)
Unstable structure

5. Rupture/erosion → thrombosis → MI
Platelets + clot can block flow suddenly
Event risk ≠ stenosis alone

Events arise from plaque biology, not stenosis alone

CCTA has been shown to reduce MI and mortality from 8.2% to 6.6%[1], but it does not scale as a first-line test

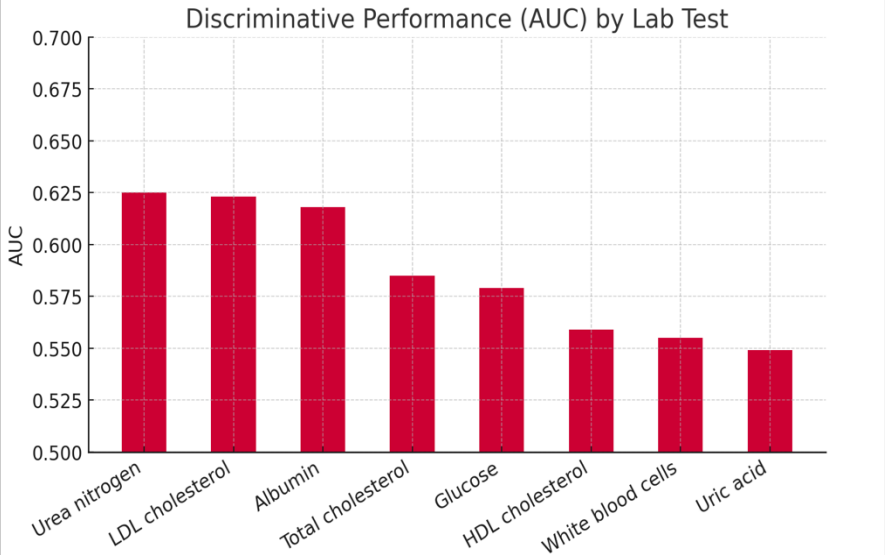
1. Not scalable as a first-line test
Requires CT capacity, contrast workflow, expert reading → limited throughput & access & high costs

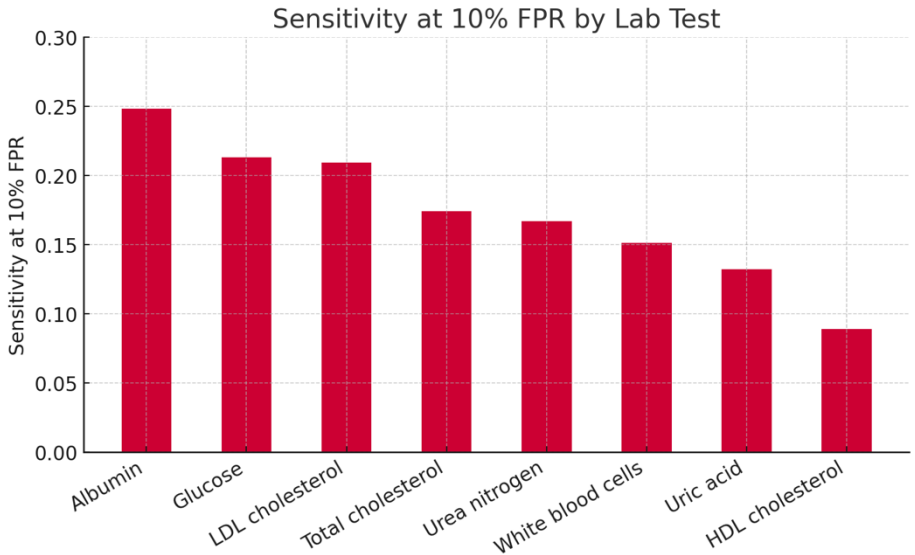
2. Patient burden & eligibility constraints
Radiation + iodinated contrast → exclusions (CKD/allergy)

3. Primarily anatomical signal and considerable inter-observer variability
Intermediate lesions often require functional assessment, interpretation physician dependent

1. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)02679-5/fulltext

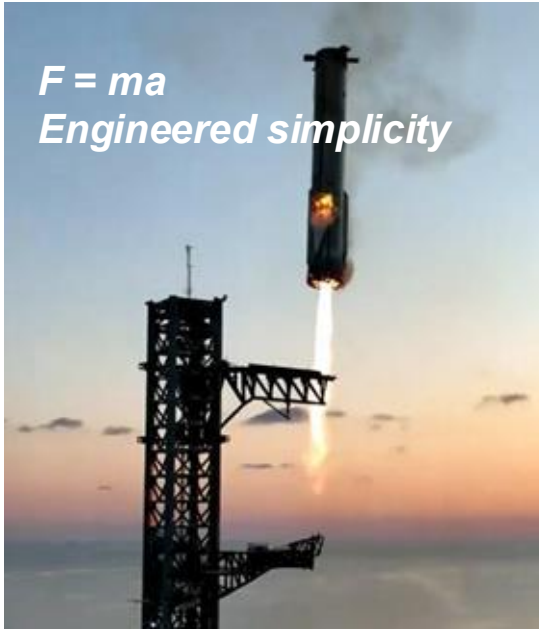
Routinely available single markers provide poor discriminative ability





1. Source: Data on file

We lack mechanistic equations that adequately capture CAD complexity



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ESC European Society of Cardiology
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ESC GUIDELINES

2024 ESC Guidelines for the management of chronic coronary syndromes

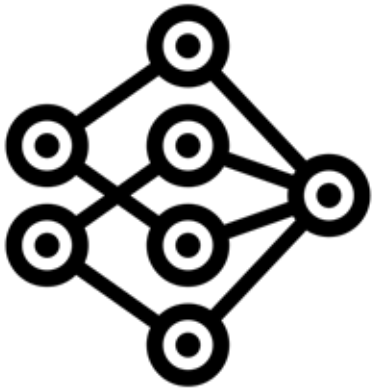
Developed by the task force for the management of chronic coronary syndromes of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Christiaan Vrints *†, (Chairperson) (Belgium), Felicita Andreotti *†, (Chairperson) (Italy), Konstantinos C. Koskinas‡, (Task Force Co-ordinator) (Switzerland), Xavier Rossello ‡, (Task Force Co-ordinator) (Spain), Marianna Adamo (Italy), James Ainslie (United Kingdom), Adrian Paul Banning (United Kingdom), Andrzej Budaj (Poland), Ronny R. Buechel (Switzerland), Giovanni Alfonso Chiariello (Italy), Alaide Chieffo (Italy), Ruxandra Maria Christodorescu (Romania), Christi Deaton (United Kingdom), Torsten Doenst [1] (Germany), Hywel W. Jones (United Kingdom), Vijay Kunadian (United Kingdom), Julinda Mehilli (Germany), Milan Milojevic [1] (Serbia), Jan J. Piek (Netherlands), Francesca Pugliese (United Kingdom), Andrea Rubboli (Italy), Anne Grete Semb (Norway), Roxy Senior (United Kingdom), Jurrien M. ten Berg (Netherlands), Eric Van Belle (France), Emeline M. Van Craenenbroeck (Belgium), Rafael Vidal-Perez (Spain), Simon Winther (Denmark), and ESC Scientific Document Group

Foundational models enable a shared representation accross different biological signals

Modern AI



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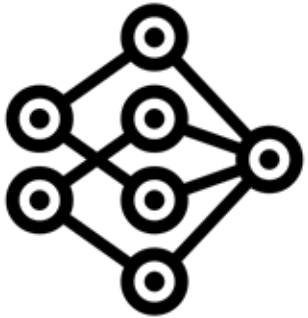
Foundation Model



Large model
*Trained **without** annotations*
Shared across tasks

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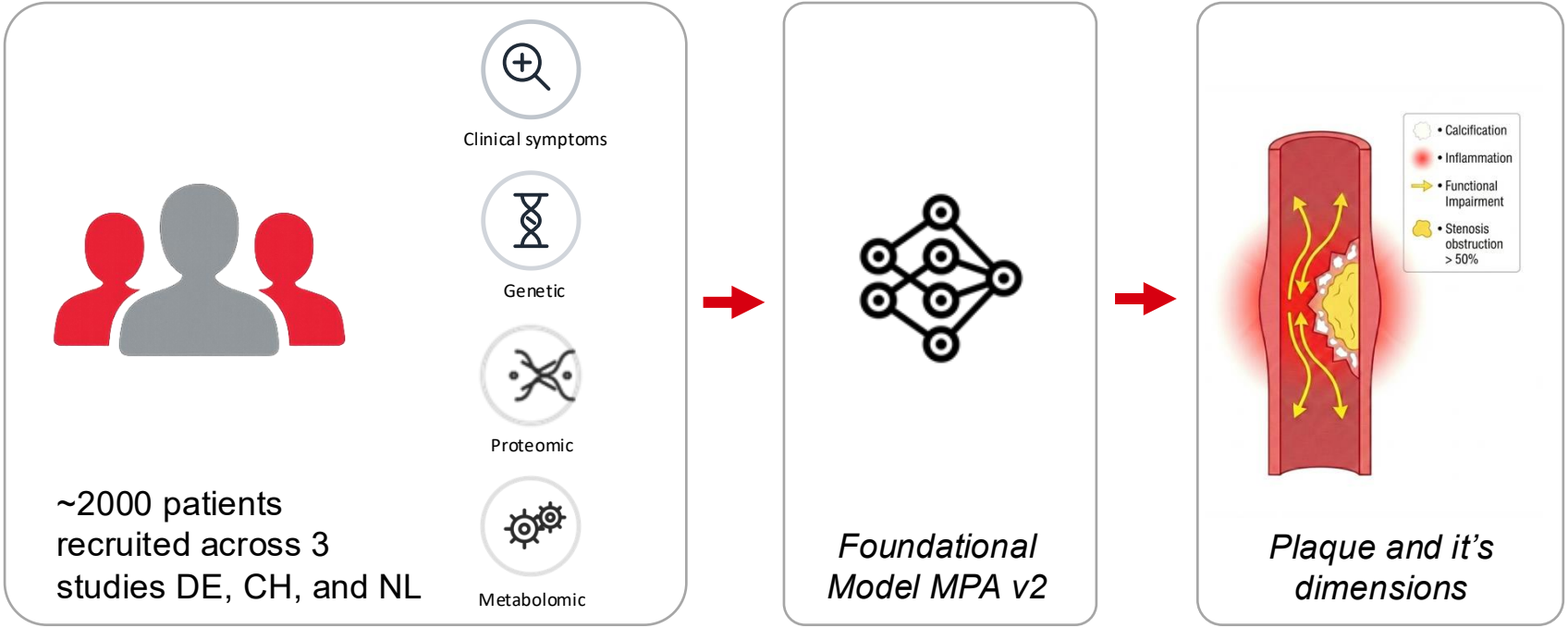
Traditional AI

Small model
*Trained **with** annotations*
Task-specific

Slide inspired by Jean-Philippe Vert

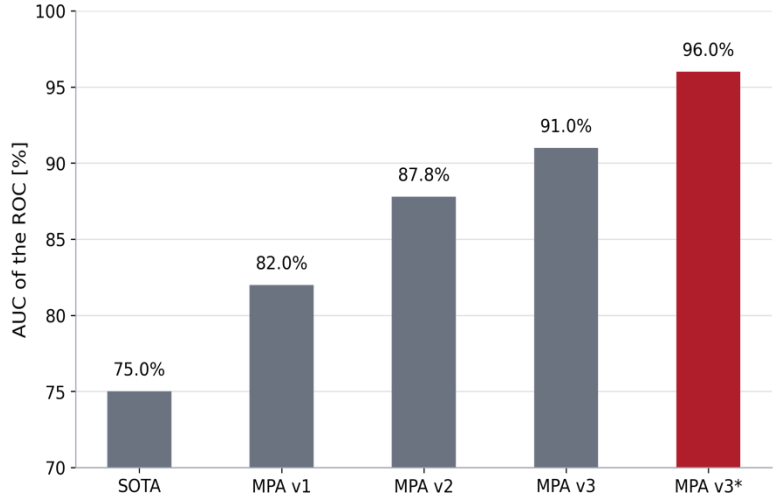
Modern AI for in-vitro diagnosis of Coronary Artery Disease



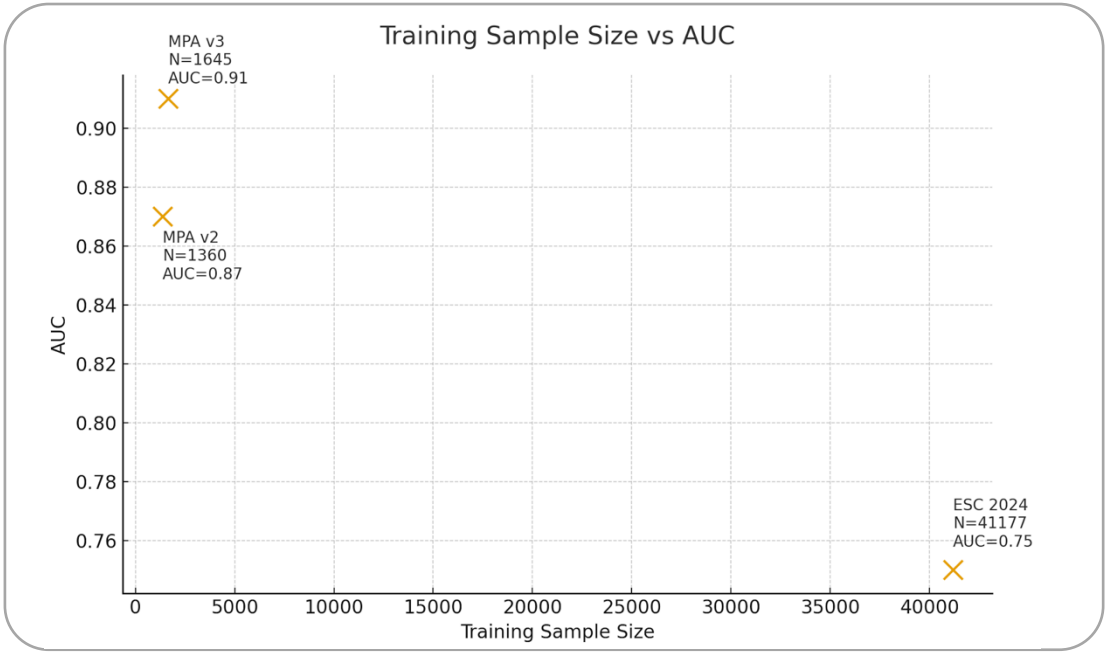
Strong predicitve performance in identifying stenosis

Key points:

- State of the art: Algorithm recommended by the ESC 2024 guidelines
- Performance gains: Driven by increased data availability (additional studies) and greater data variance
- Clinical performance: AUC of 96% achieved in a subpopulation within the low-risk and very high-risk strata. **Relevance:** These strata correspond to the algorithm's clinical decision boundaries



Availability of data not the sole predictor of model performance



Algorithms Follow the Same Commercial Path as Medications and Diagnostics

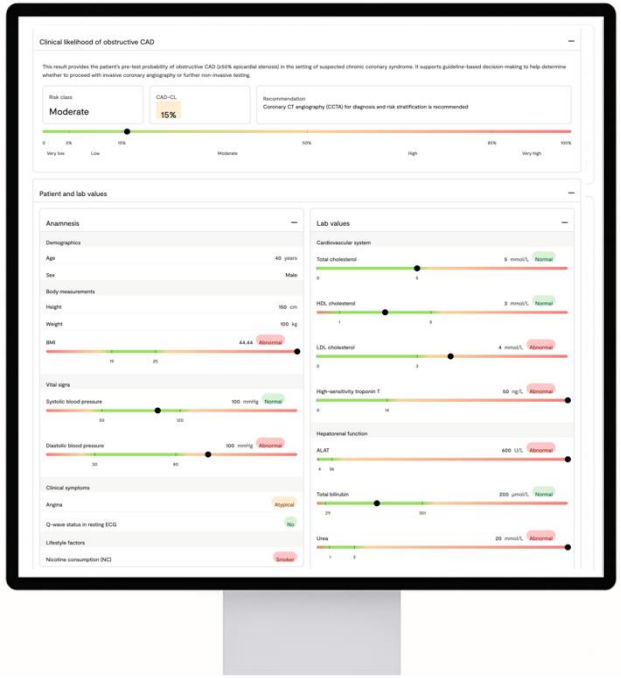
3 studies with renowned research institutions incl. > 2000 patients	Universitätsspital Basel; Maastricht UMC+	Confirmation of effectiveness vs. established gold standards (e.g. CT/MRI/Cath)
CE-certification (IVDR Class B) as SaMD, C5, ISO 27001, EU AI Act		CE SaMD
Proven enormous health economic benefits by renowned institutions	iGES; HARVARD MEDICAL SCHOOL; Brigham and Women's Hospital Founding Member, Mass General Brigham; Maastricht UMC+	Savings Primary Care EUR 200+ M; ED USD 1+ B
Selective reimbursement		Largest payers targeted; AOK Niedersachsen Die Gesundheitskasse.
Global, non-exclusive distribution partner + live pilots		Roche

EPFL AMLD

Cardio Explorer the non-invasive, IVDD-cleared test for obstructive Coronary Artery Disease

Approved for patients presenting with stable symptoms or risk factors suggestive of Chronic Coronary Syndrome (CCS)

Cardio Explorer® is trusted by clinical institutions



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CE bsi ISO 13485 Universitätsspital Basel Maastricht UMC+ HGZ Herz- und Gefässzentrum Bad Bevensen

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Conclusion & Thoughts

1. Foundation models enable scalable and accurate diagnostic of coronary artery disease from heterogeneous clinical data
2. Cardio Explorer can stratify patients biologically rather than anatomically
3. This may lead to potential interesting applications in optimizing patient enrolment, target validation and companion diagnostic

Appendix

Therapies vs Gaps

Main contributor	Guideline therapy	Gap
High LDL + high BP	LDL: statin; BP: treat-to-target (± ACEi/ARB if indicated).	No major gap
Disturbed flow → endothelial dysfunction	Indirect only: optimize risk factors (LDL/BP, etc.).	Considerable gap
Chronic plaque inflammation	Anti-inflammatory add-on: low-dose colchicine	Considerable gap
Angina + ACS risk (thrombosis)	Symptoms: antianginal meds. Events: antiplatelet strategy (mono/DAPT by risk).	No major gap *(personalization challenge)*

MPA runs automatically for every patient and does not require physician initiation

Chest Pain Unit Bad Bevensen Germany

Clinical Integration