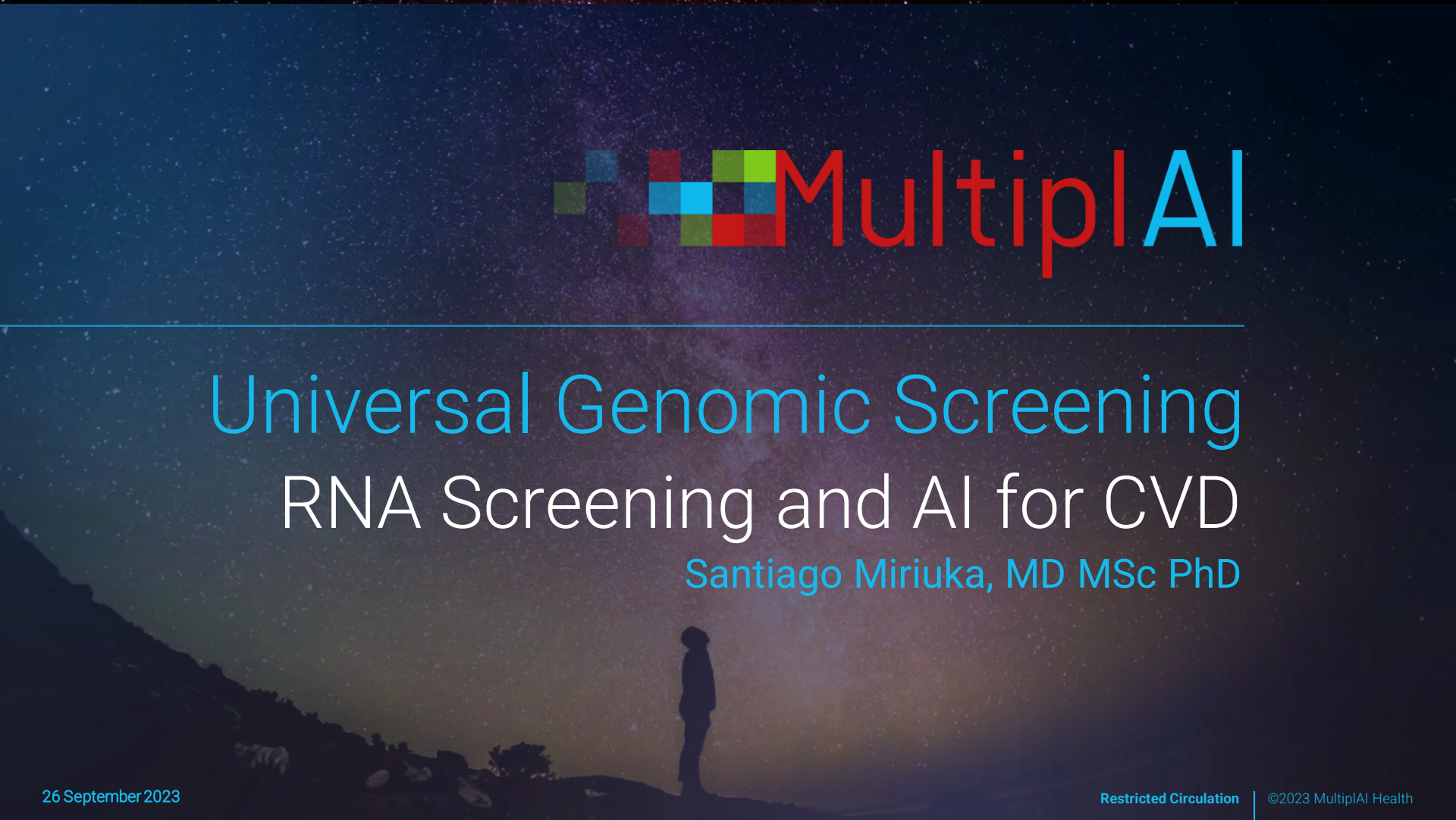


Universal Genomic Screening

RNA Screening and AI for CVD

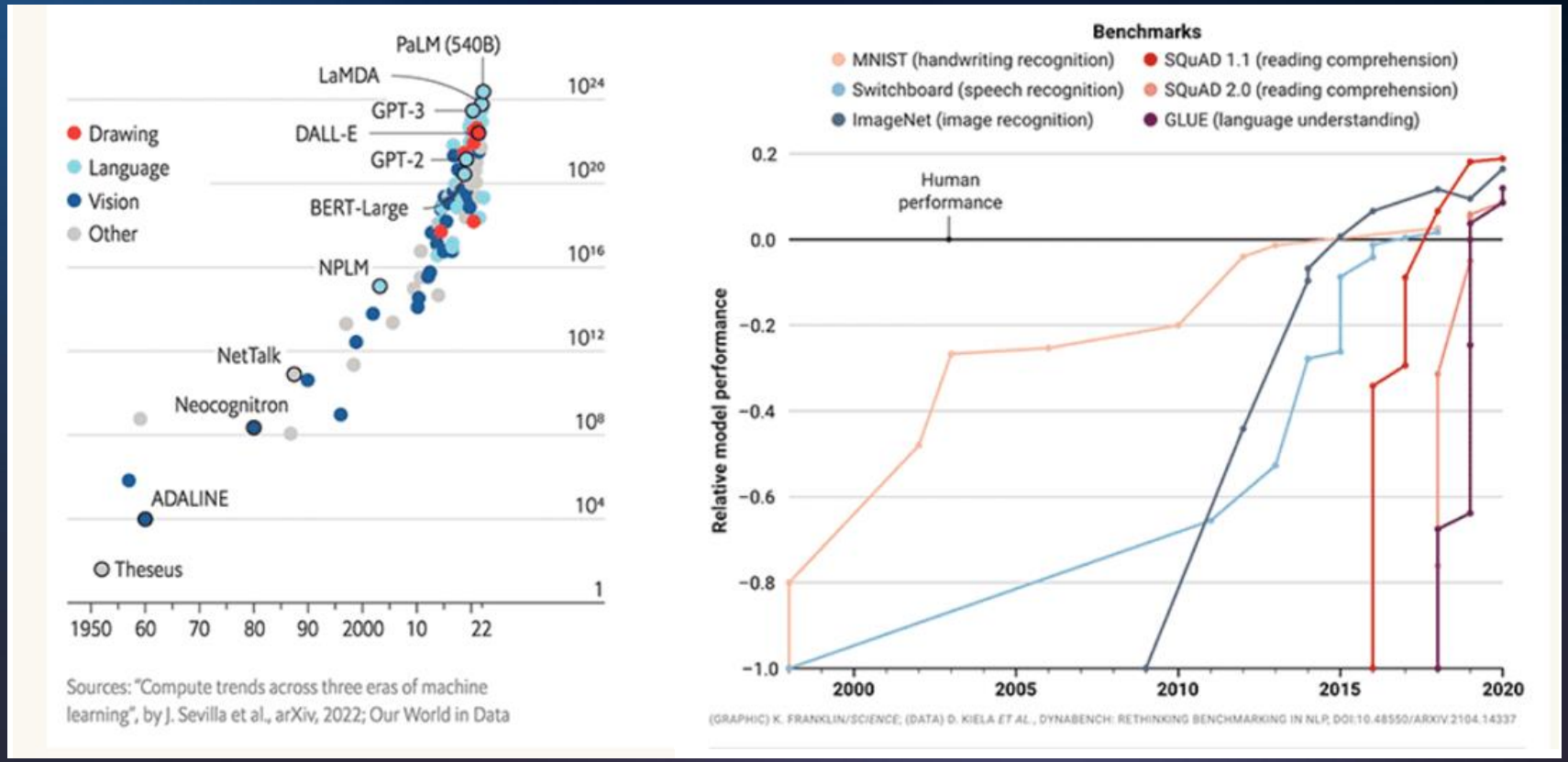
Santiago Miriuka, MD MSc PhD

26 September 2023

The future of disease detection and prevention is digital

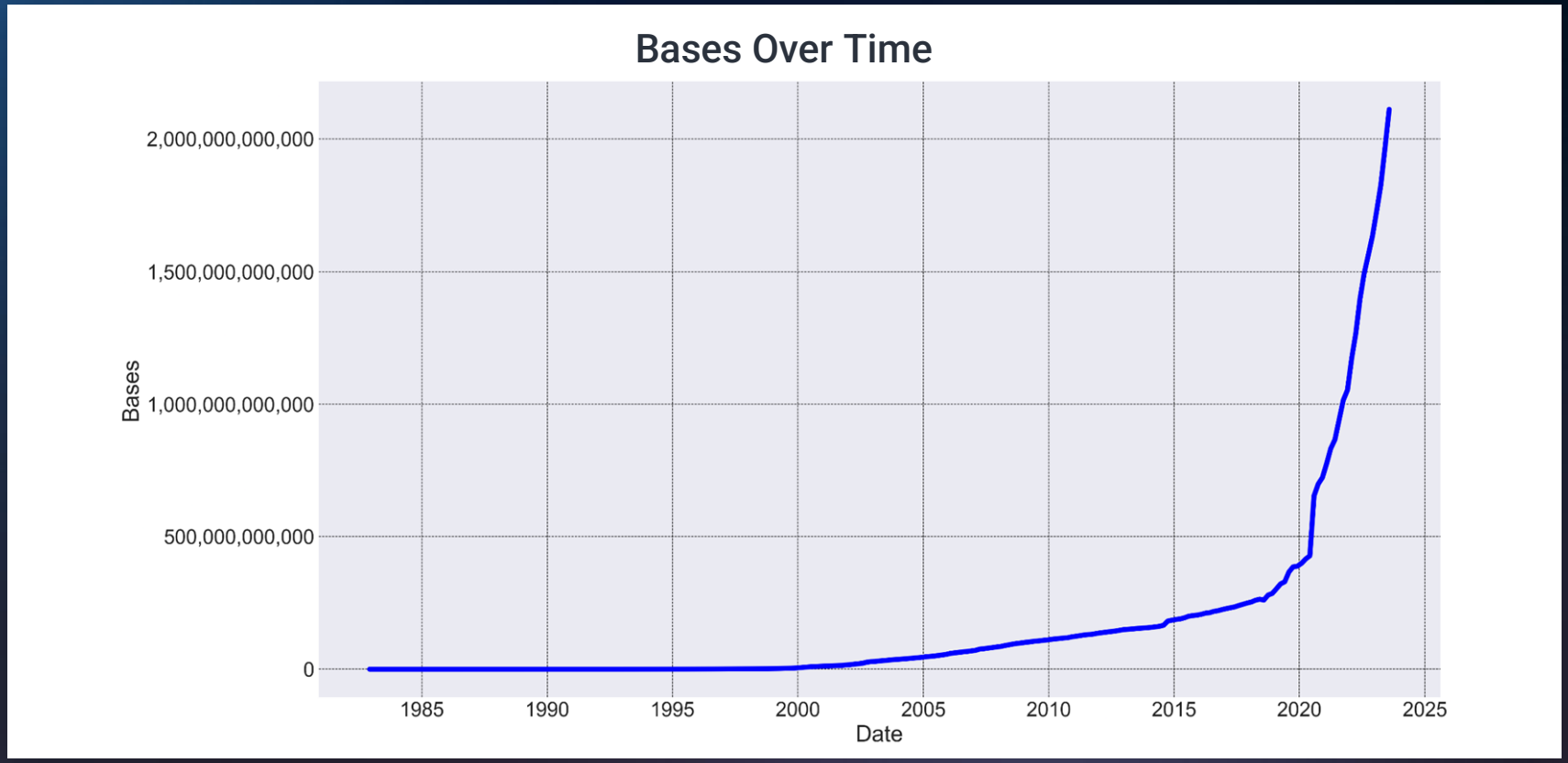
- **Artificial Intelligence -** Data transformation and analysis
- **Genomic Sequencing -** Provides us with more data than ever before
- **Data management, processing and integration -** A vast amount of different sources of information providing insight on health and disease

The scaling up of Artificial Intelligence



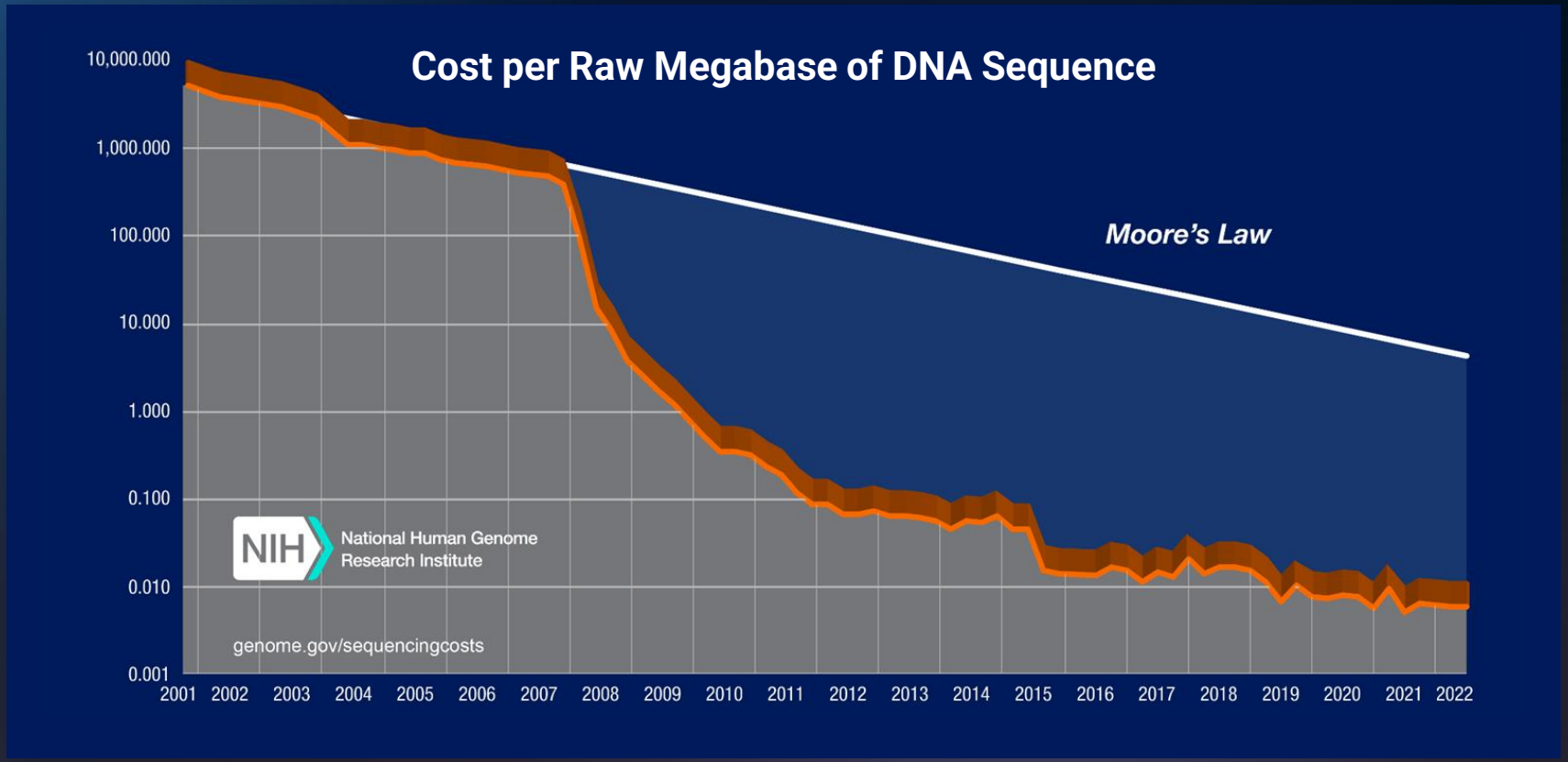
Source: https://cmte.ieee.org/futuredirections/2023/04/18/ai-flanking-business-consultants/

Genomic sequencing is exploding



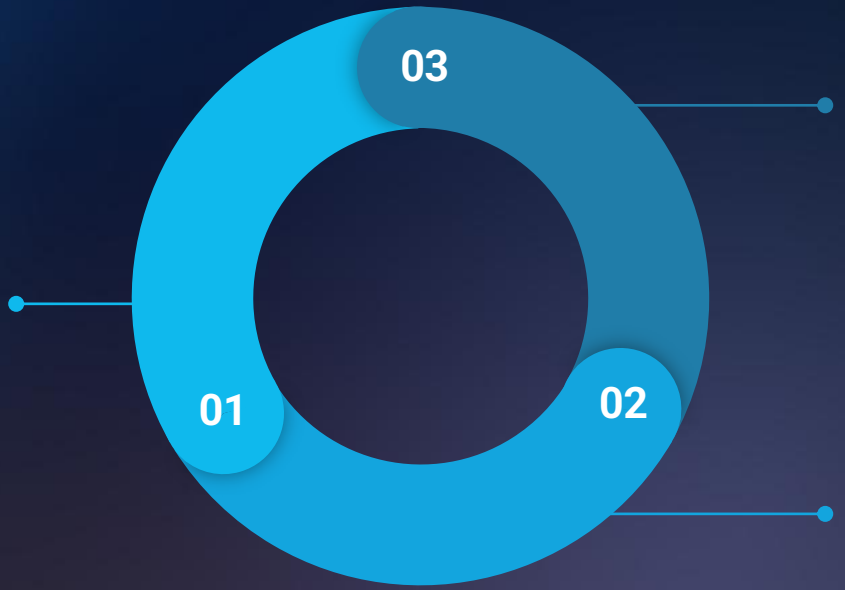
Source: NCBI

Cost of genomic sequencing



Source: NIH

The Virtuous Circle of AI Genomics



Costs

Less than U$100 whole genome sequencing

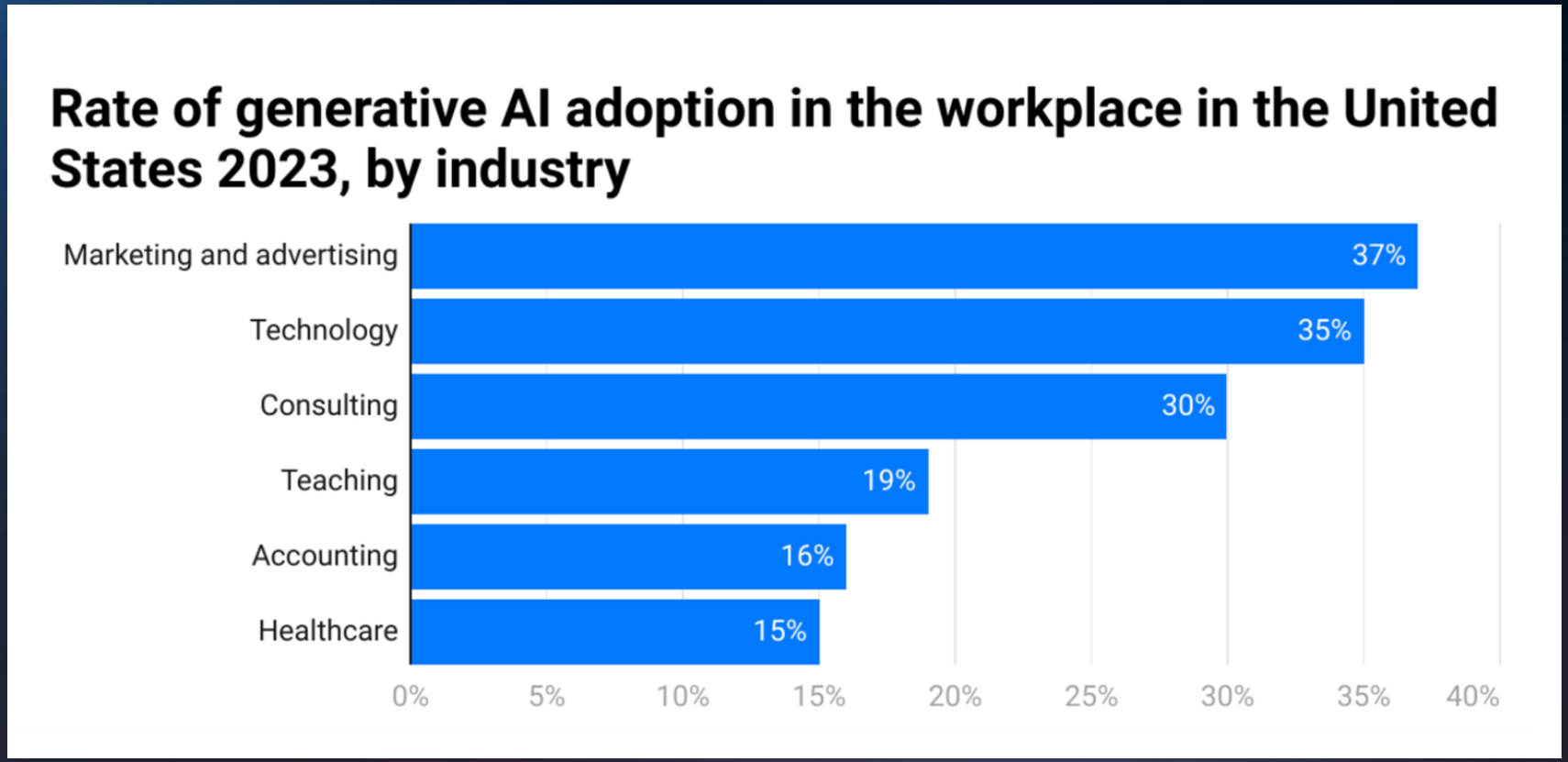
Computational Power

U$0.01/GFLOPS

Data availability

2,631,493,489 WGS uploaded to NCBI (Aug/2023)

Adoption of AI in the healthcare industry



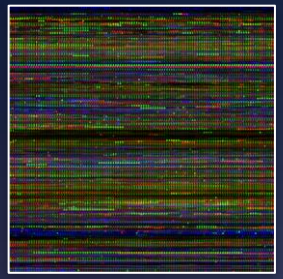
Source: statista.com

MultiplAI empowers anyone and their doctors to safely, privately, and accurately assess disease risk exceptionally early to proactively manage long-term health outcomes.

Next-gen genomic sequencing	Proprietary data transformation	AI neural networks

Digitizing the blood

Blood sample → **Blood RNA-Seq** → **Data Transformation** → **Super-biomarker** → **Neural Networks** → **Diagnosis**



DNA mainly offers insights into **hereditary** conditions
RNA also reflects **environmental factors**

We express the **complexity of RNA** in a format **ideal for algorithmic analysis**

MultiplAI: Current Results

More than 1,000 samples sequenced

~100m reads

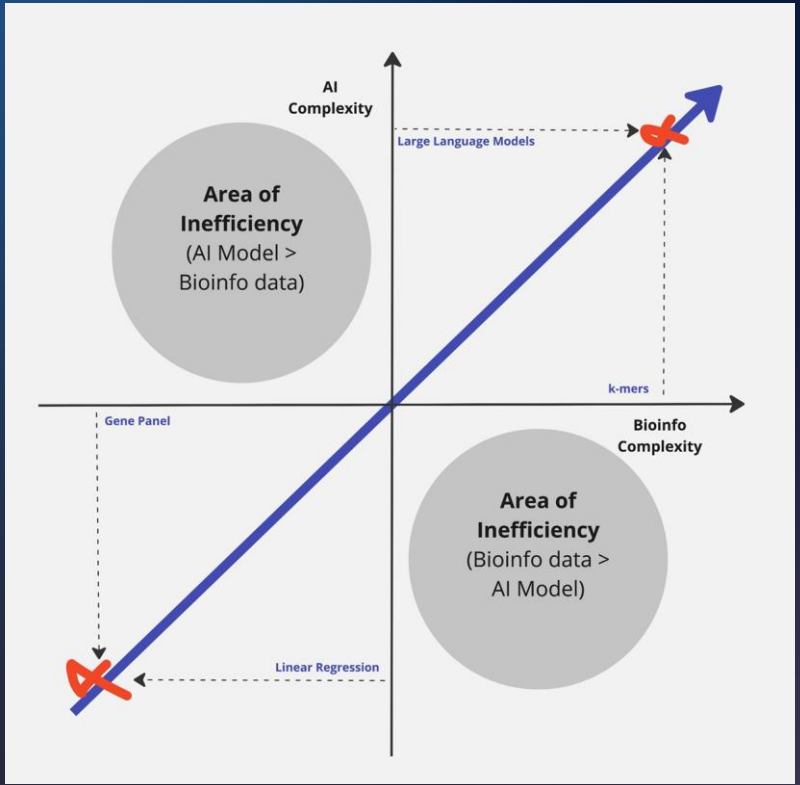
30-40k out of 65k genes detected

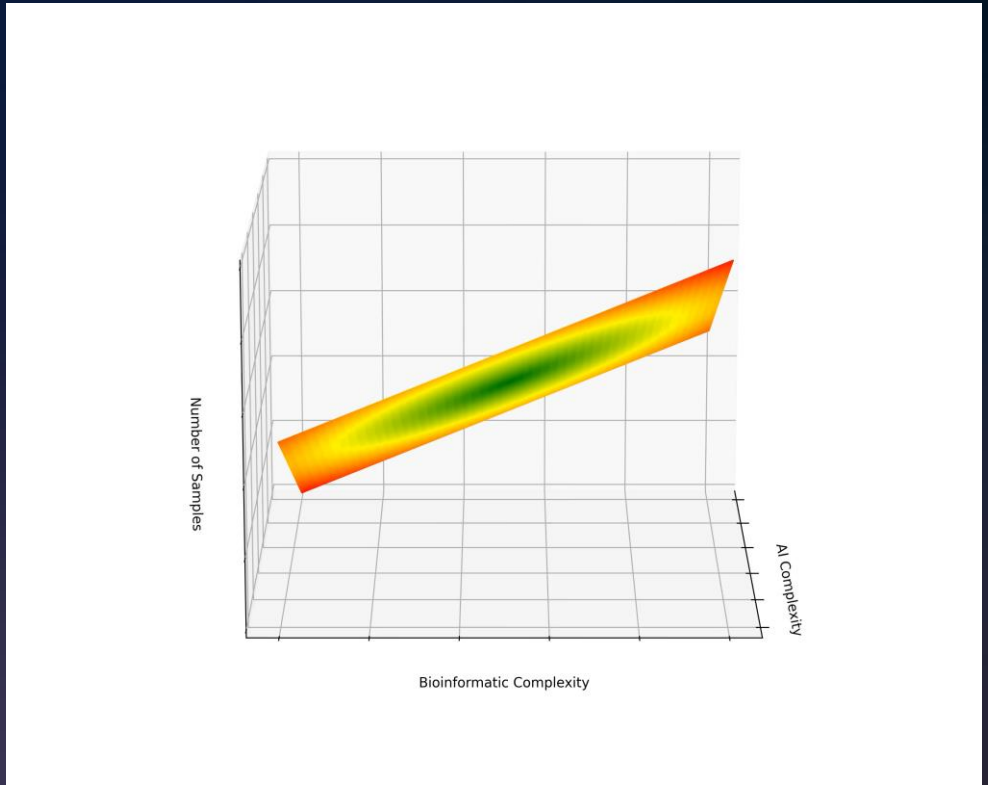
120k transcripts

7000 circRNAs

350k exons

The complex landscape of AI and Genomics





Cardiovascular disease (CVD) is the #1 cause of mortality globally

18m
deaths / year

15x
more women die of it than **breast cancer**

#1
reason for waste in healthcare spending

Almost **1 in 3 annual deaths globally** are caused by CVDs.

Traditional risk stratification **does not accurately detect vascular disease early enough**

High Risk

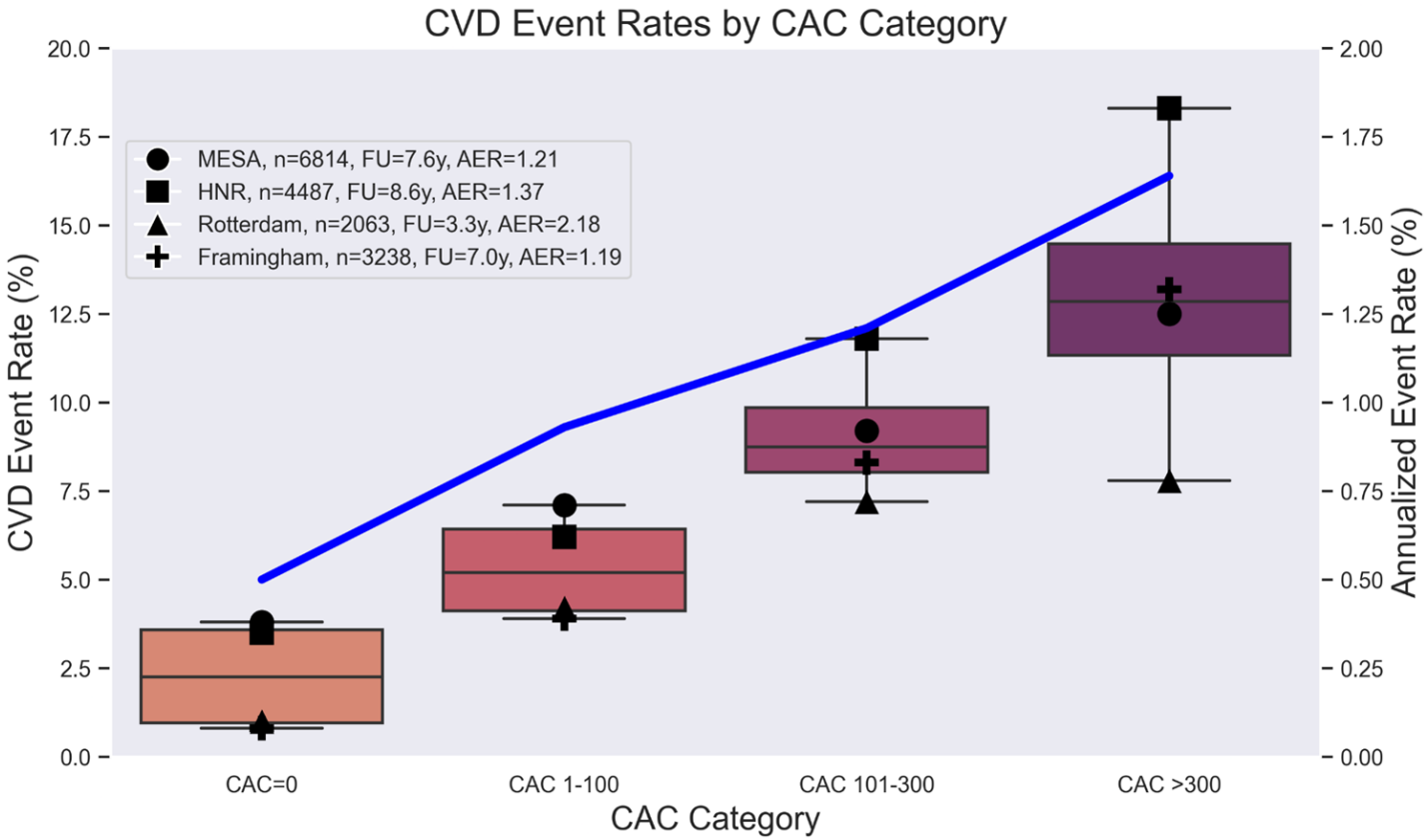
Died of stroke at 91

Low Risk

Heart Attack at 35

Millions of people are at risk without knowing it

Presence of **coronary calcium** according to **risk score category**



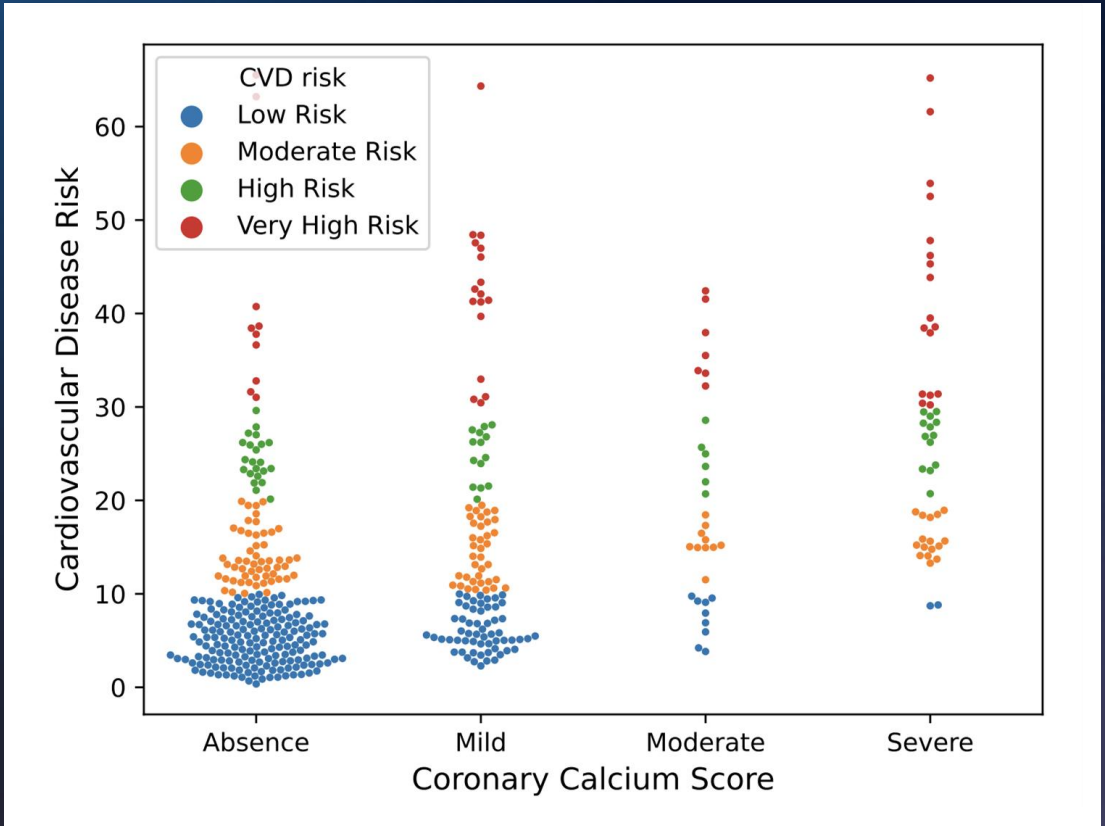
JACC 2018, Coronary Calcium Score and Cardiovascular Risk

Gold standard of diagnosis has its challenges

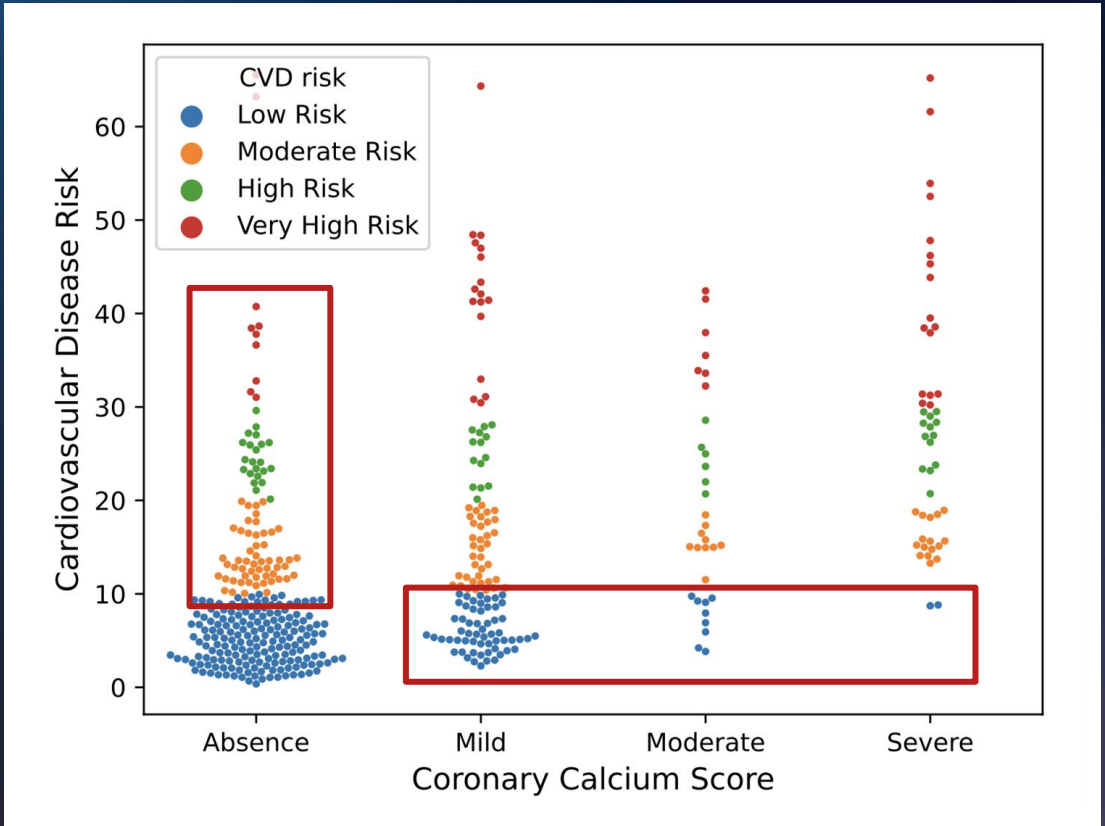
CT Scans not recommended
in low risk classification

Only **30% of countries** have at least
one CT scanner per million people

CAC by Risk score (Framingham)



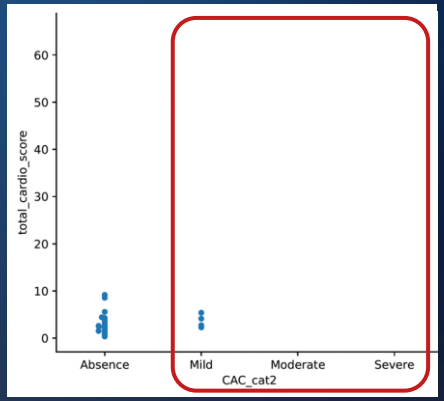
CAC by Risk score (Framingham)



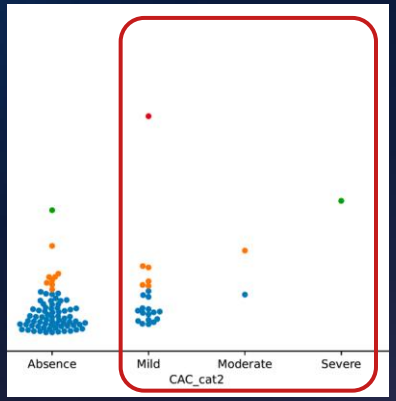
- Prevalence of CAC>0 → 45 %
- Risk equations are not reliable for determining the presence or absence of coronary artery calcification (CAC)
- Misclassification rate = 33%

CAC by Risk score (Framingham) - By Age

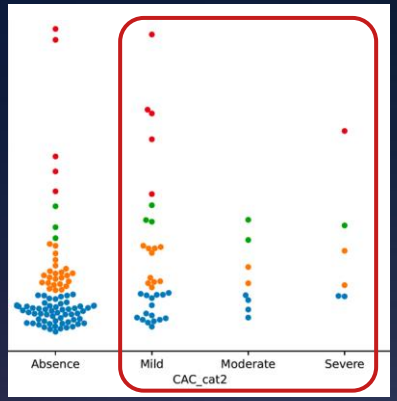
Age_cat2 = 30-39



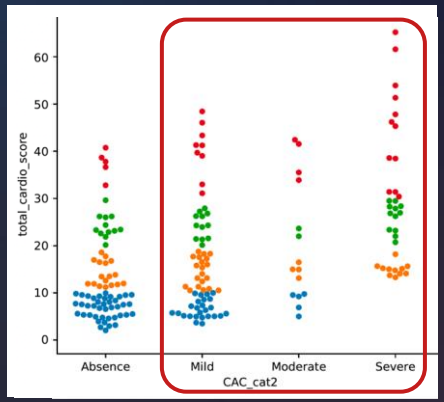
Age_cat2 = 40-49



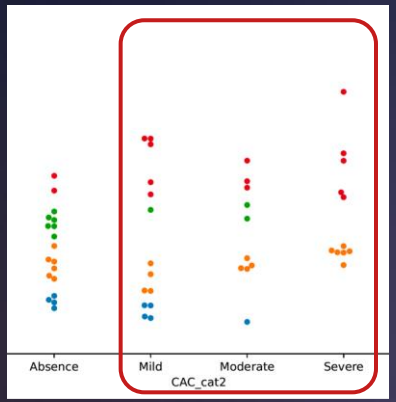
Age_cat2 = 50-59



Age_cat2 = 60-69



Age_cat2 = 70-79



- Most patients were classified as low risk (mainly due to Age)
- Failure to identify patients who would benefit from early prevention

MultiplAI
Universal genomic screening

Determination of the presence and extent of coronary calcifications by transcriptomic analysis of whole blood assisted by artificial intelligence: pilot study

The CCT-1 study

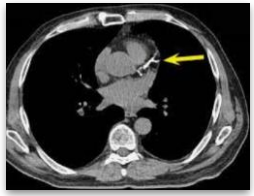
The CCT-1 Study: Study design & Data collection

Baseline | **5 Year follow up**

Participants

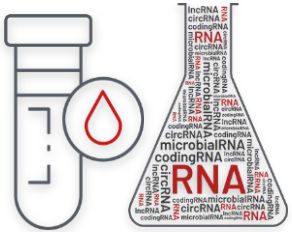
- Non prior CVD
- Men 40-70 years
- Women 50-70 years

Chest CT Comparator



CT-Baseline/Outcomes
- Coronary artery calcium (CAC)
- Aortic calcium
- Steatosis
- Epicardial fat

Whole blood RNA



Clinical data

- Sex-Age
- Blood Pressure
- Body weight/ Height
- Drug treatments

Incident events

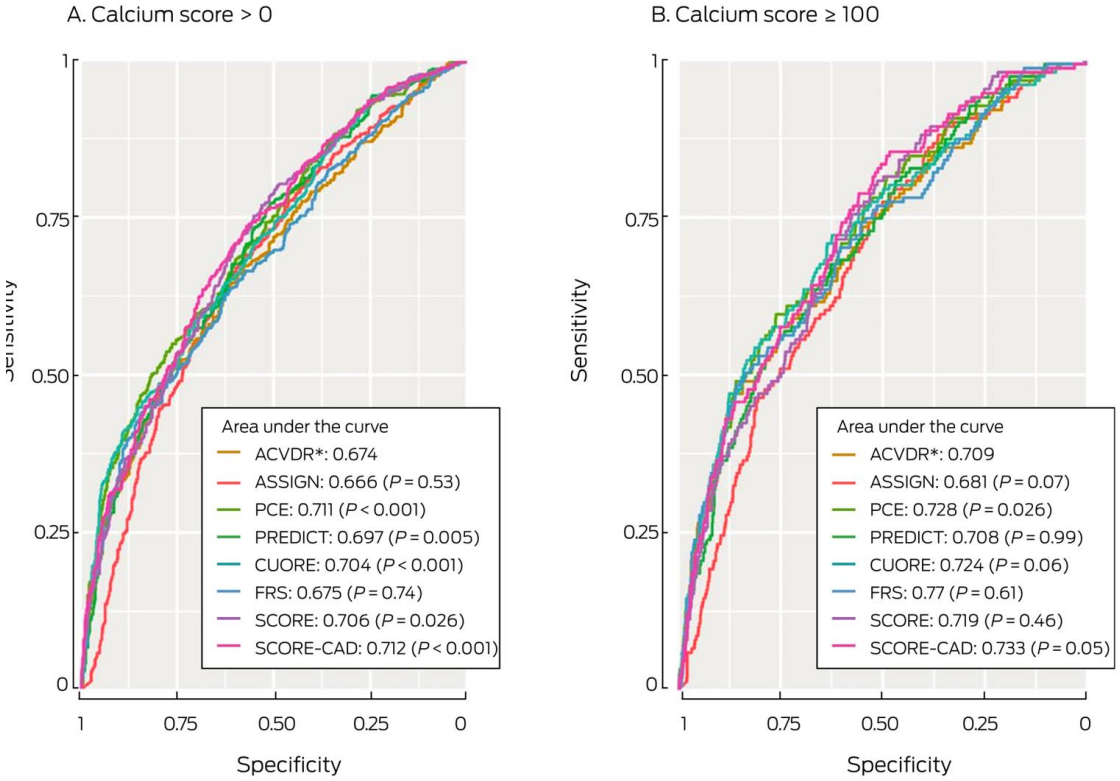
- Death from any cause
- AMI, angina
- Stroke or transient ischemic attack
- Hospitalized Heart failure
- Vascular revascularization
- Cancer

Diagnostic results
Precision for CAC detection

Prognostic results
Precision for predicting incident events

CCT1 study results. Area Under the Curve (AUC)

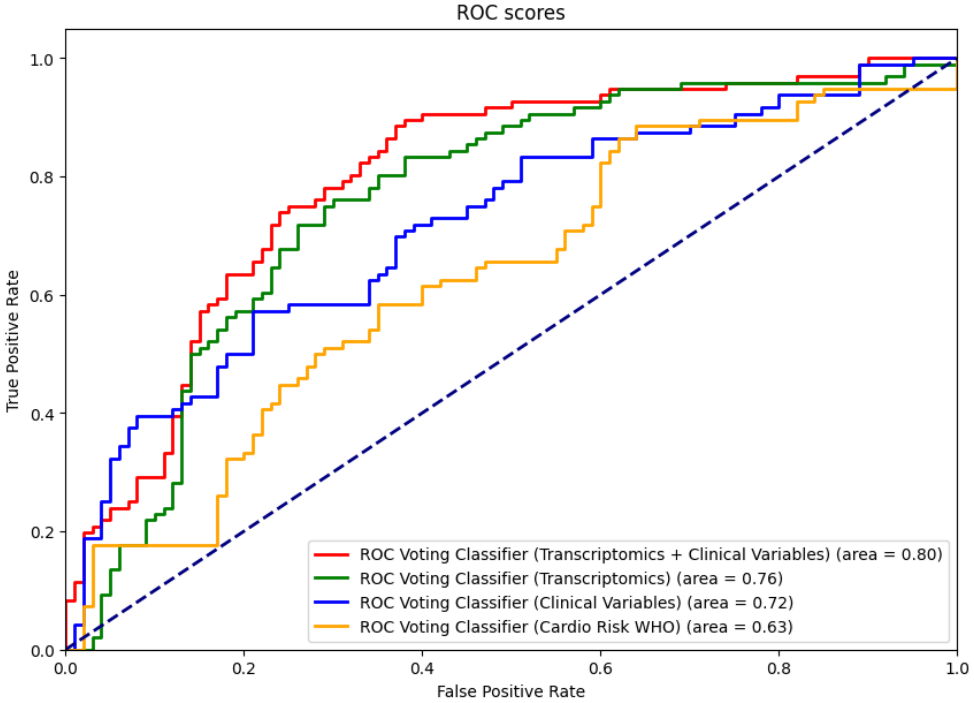
Prediction of coronary calcium compared to the traditional approach



Source: https://doi.org/10.5694/mja2.50702

CCT1 study results. Area Under the Curve (AUC)

Prediction of ANY coronary calcium compared to the traditional approach

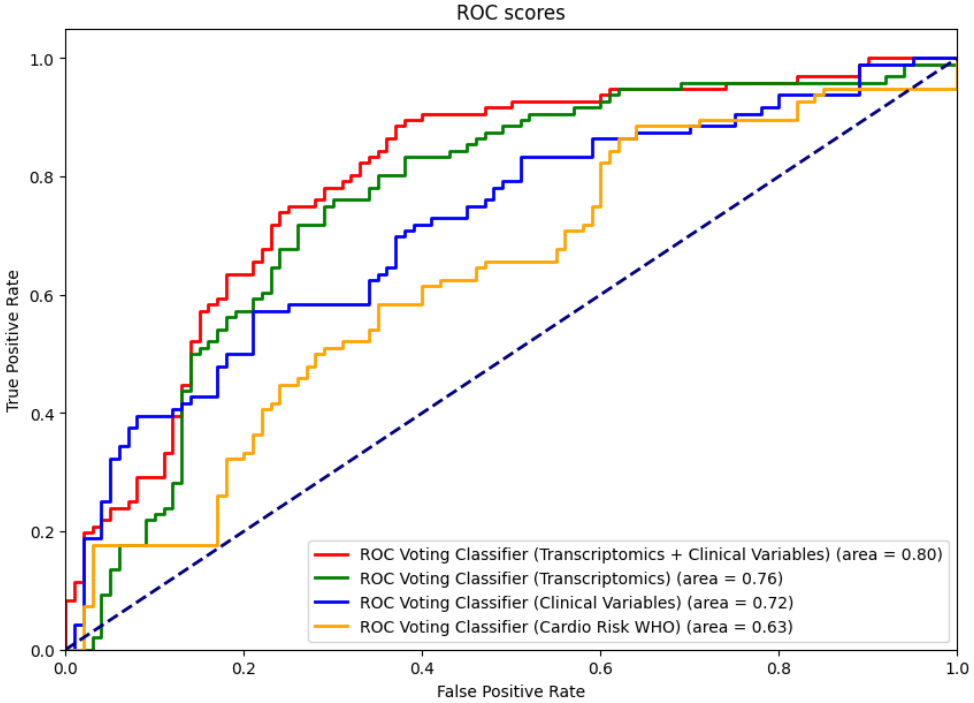


- CardioRisk WHO 0.63
- Clinical Variable 0.72
- Transcriptomics 0.76
- **Clinical Variables + Transcriptomics 0.80**

Outcome: Presence of coronary atherosclerosis (CT- Coronary Agatston units > 0)
Covariates: sex, age, smoker status, BMI

CCT1 study results. Area Under the Curve (AUC)

Prediction of ANY coronary calcium compared to the traditional approach



Variables Included in the model:

- Age and Sex
- Linear RNA
- transcripts
- circRNA
- Blood microbiome.

Outcome: Presence of coronary atherosclerosis (CT- Coronary Agatston units > 0)
Covariates: sex, age, smoker status, BMI

MultiplAI

Universal genomic screening

Early detection of subclinical CAC in asymptomatic individuals

The CAC-TRAIT study

clinicaltrials.gov ID NCT05619042

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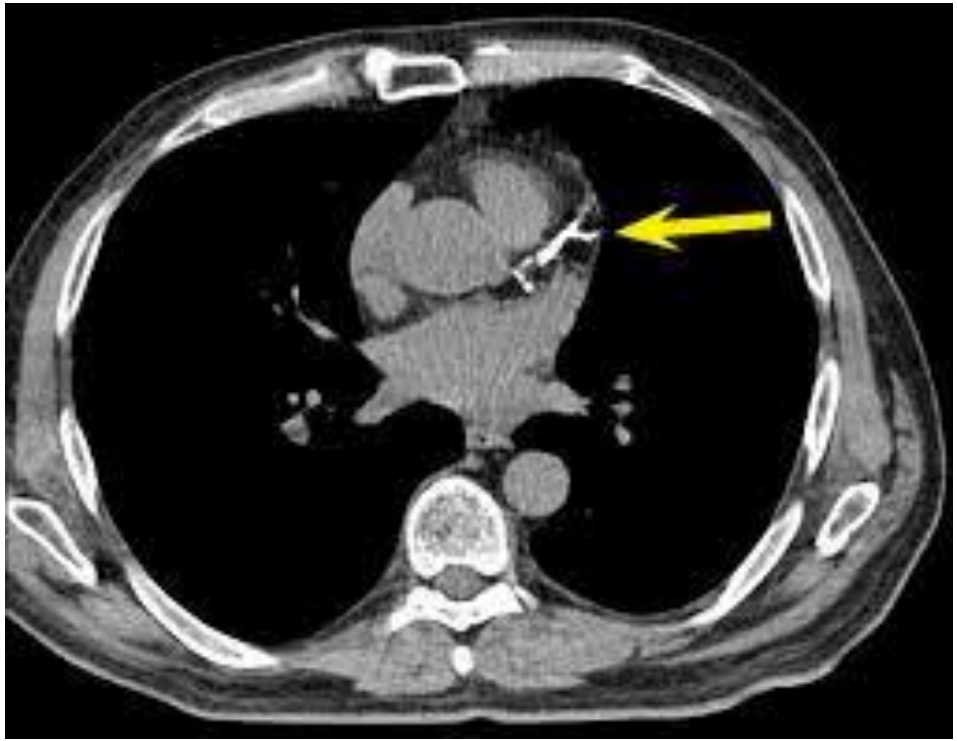
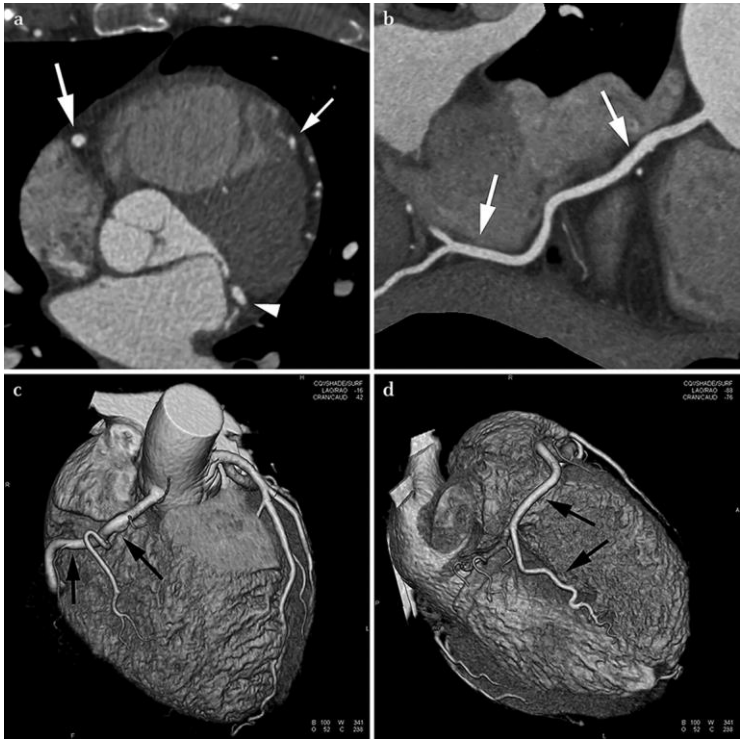
Universal genomic screening

Whole Blood Transcriptome Patterns according to the Coronary Atherosclerotic Plaque Burden determined by CT Angiography

The CORPLAQ-TRAIT pilot study

CT Scan versus angioCT Scan





Universal Genomic Screening for multiple pathologies

Artificial Intelligence and **Genomic Sequencing** allows us to face the challenges of complex diseases like CVD and make them available to anyone on the planet.

Universal **Accessibility**

- Anytime
- Anywhere
- Scalable

Universal **Affordability**

Today		Universal
$1000	Unit Price →	$10
10,000	Volume →	100,000,000
$10M	Revenue →	$1B

Universal **Sustainability**

- Low carbon blood collection
- Virtual medicine
- Sustainable Sequencing

"The future of cardiology is personalized medicine, and AI is essential to making that happen."

– Eric Topol

MultiplAI
Universal genomic screening

Thank You

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