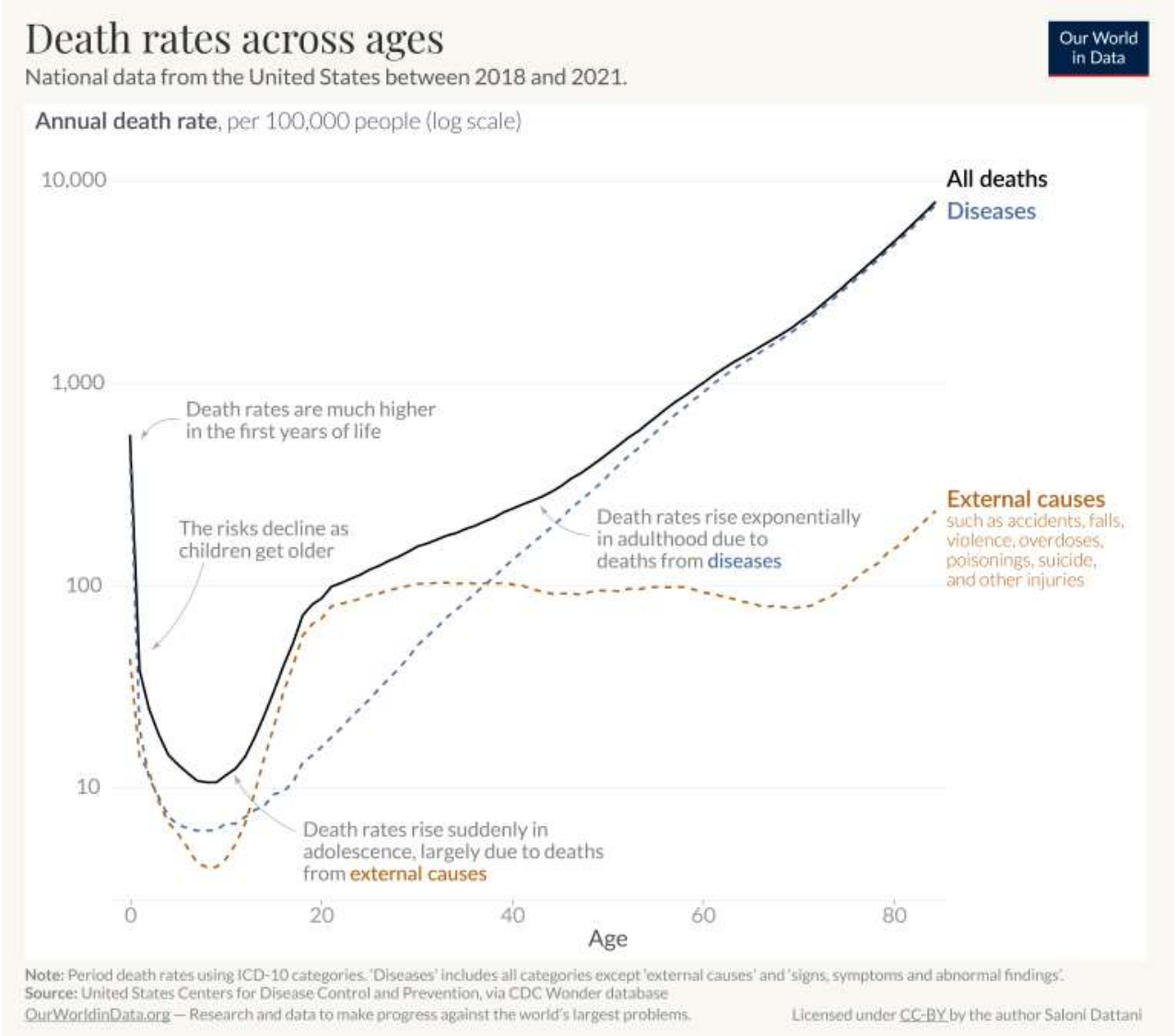
Biomarkers for Longevity

Alexander Lozano, MD, PhD

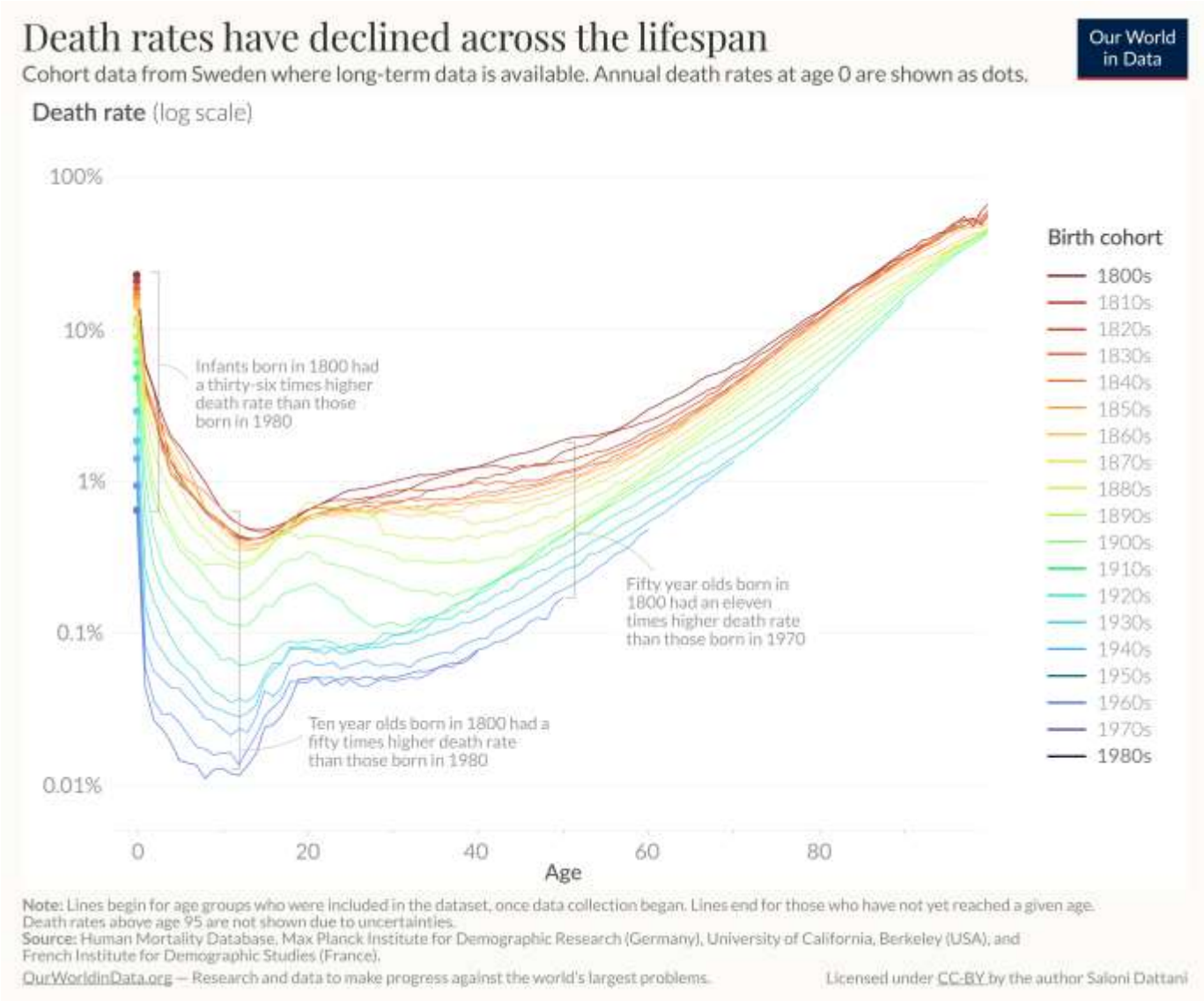
Disclosures

- LiquidCell
  - Equity
- September VC
  - General Partner

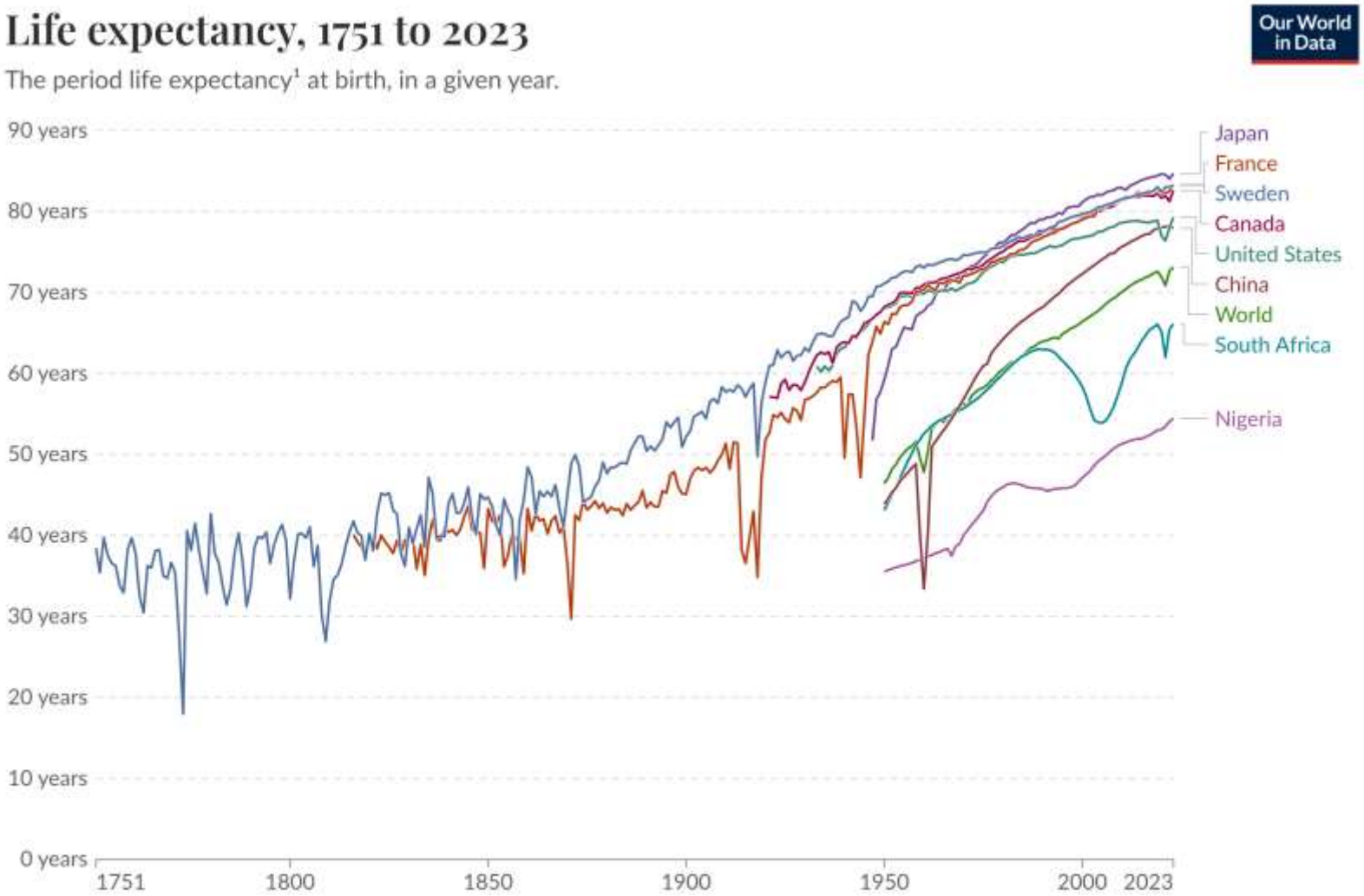
Age is perhaps the most important predictor of mortality



As time marched forward, mortality at a given **age** has decreased

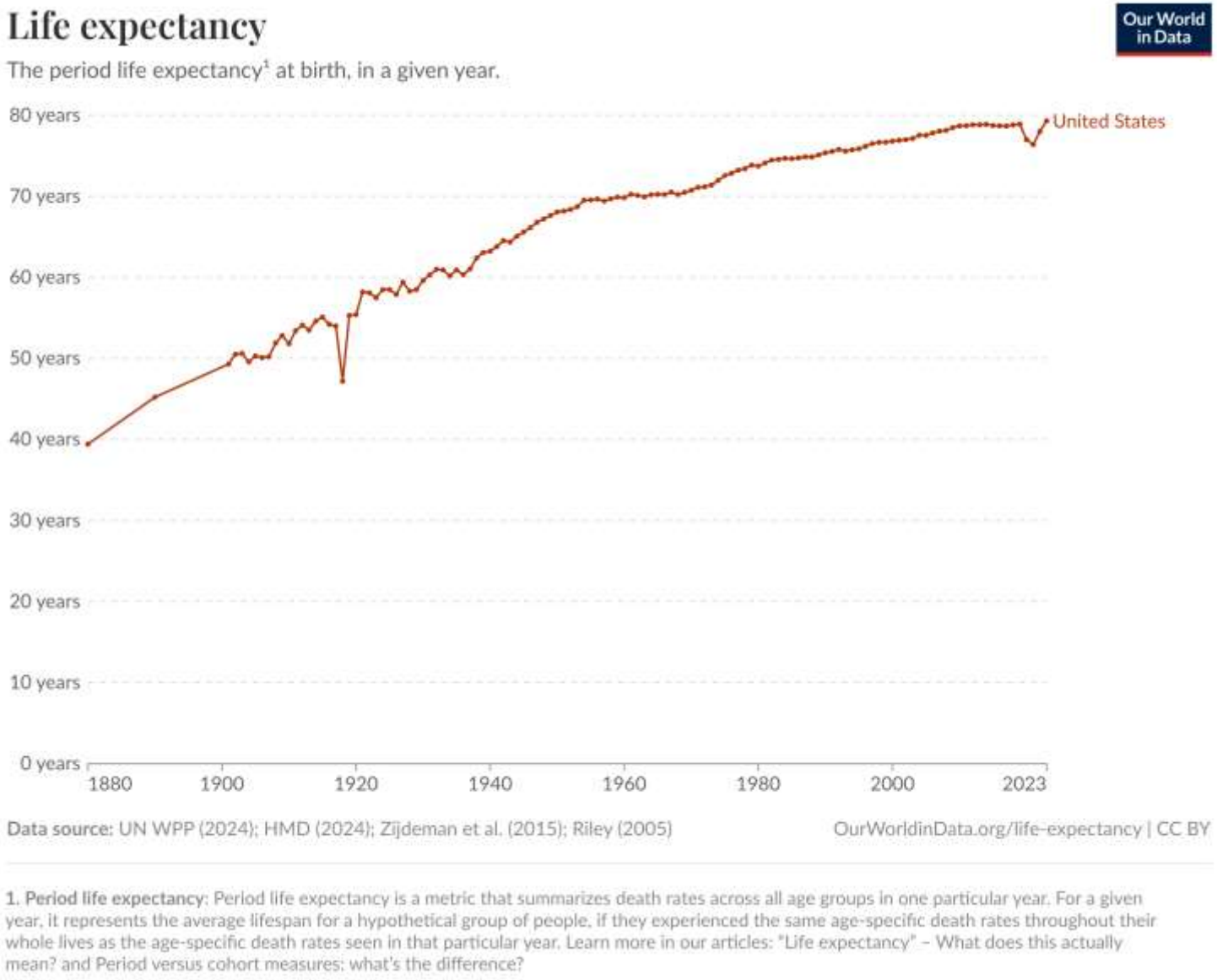


And **life expectancy** has increased



1. **Period life expectancy**: Period life expectancy is a metric that summarizes death rates across all age groups in one particular year. For a given year, it represents the average lifespan for a hypothetical group of people, if they experienced the same age-specific death rates throughout their whole lives as the age-specific death rates seen in that particular year. Learn more in our articles: "Life expectancy" – What does this actually mean? and Period versus cohort measures: what's the difference?

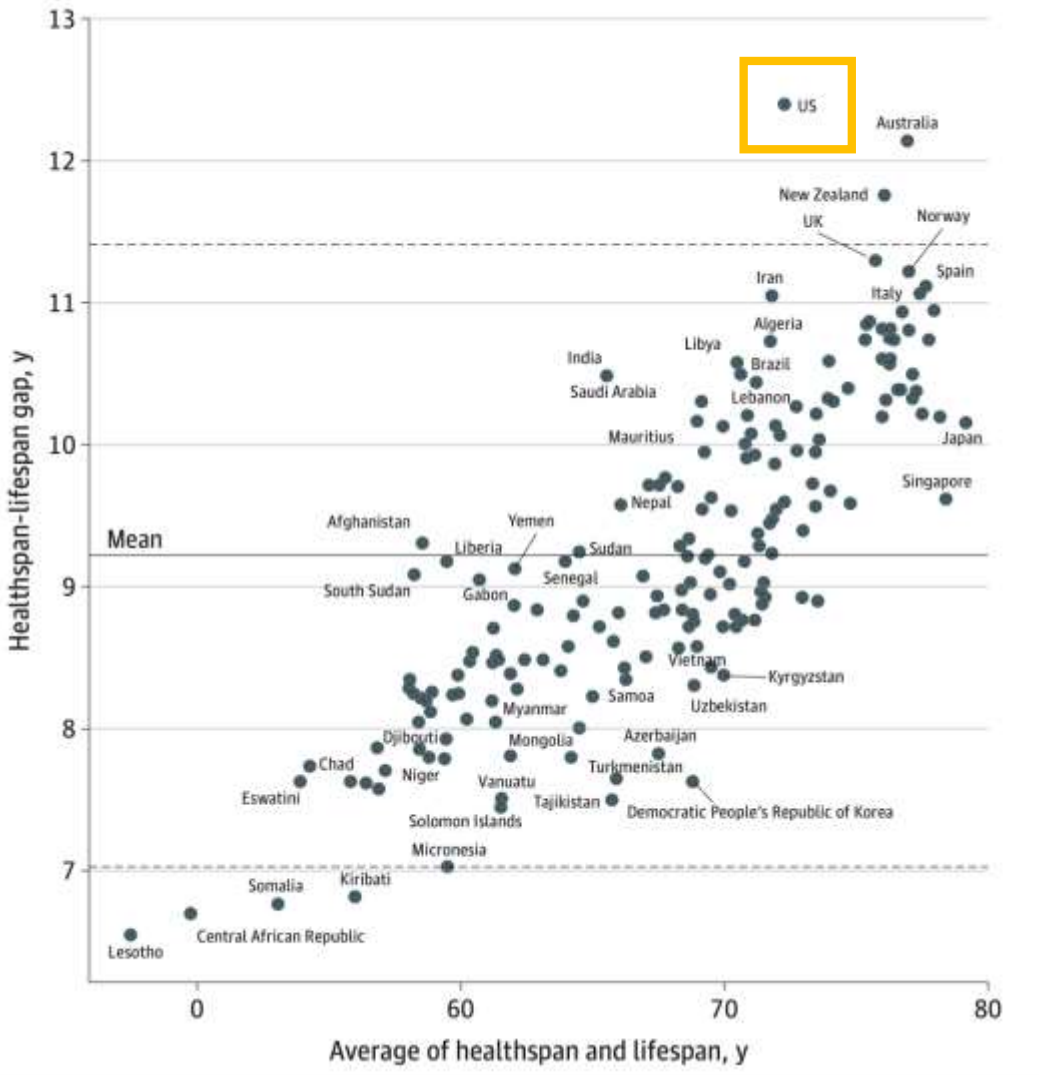
But recently American life expectancy has **plateaued** and even **decreased**



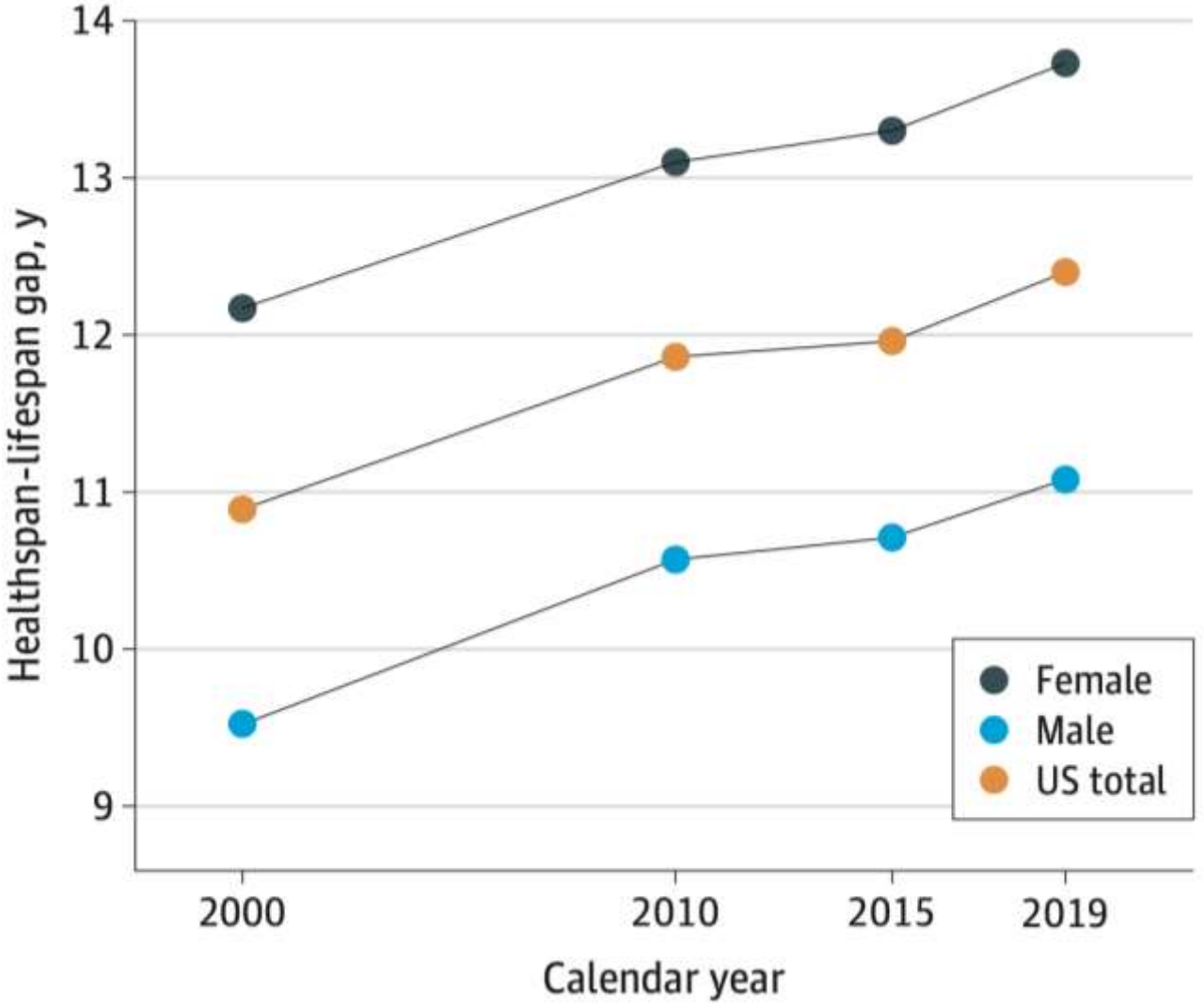
Healthspan is a measure that takes into account lifespan, and the years of life lived free from disease, disability, and suffering

America leads the world in the **gap** between **Health** and **Lifespan**

Healthspan-adjusted Life Expectancy



US Healthspan-lifespan gap is increasing over time



Garmany, Armin, and Andre Terzic. "Global healthspan-lifespan gaps among 183 World Health Organization member states." *JAMA Network Open* 7.12 (2024): e2450241-e2450241.

Scratching the surface of longevity, how can we figure out someone’s health?

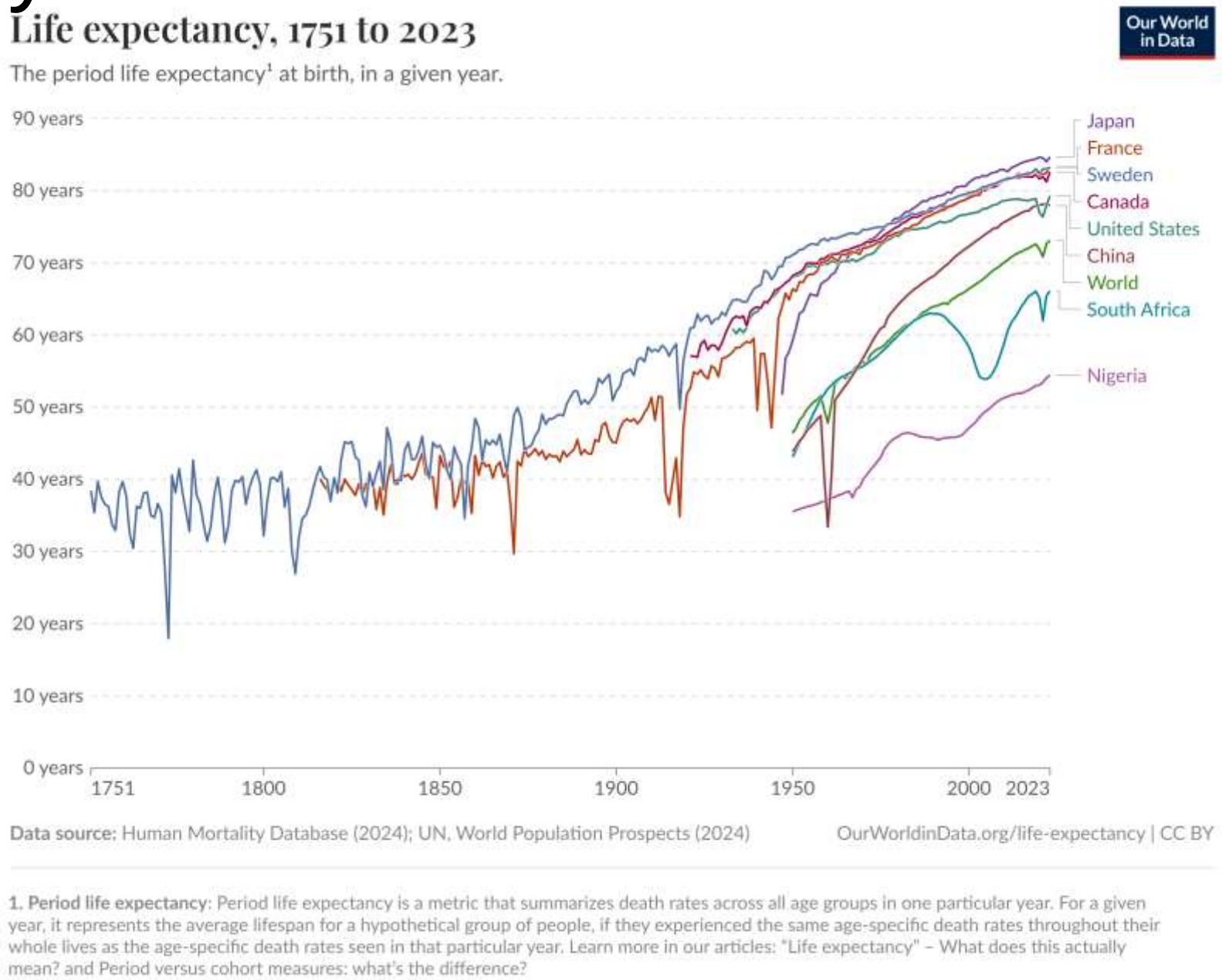
Lets go back in time

Life expectancy in ancient times

1600,
~33 years

400 BC,
~25 years

400 BC — 1600



400 BC
Life expectancy
~25 years

Aphorisms
Hippocrates

44. Persons who are naturally very fat are apt to **die earlier** than those who are slender.

Aphorisms, By Hippocrates, Written 400 B.C.E, Translated by Francis Adams

Life expectancy, Cambridge University press

You can tell a lot about **health** even before you do invasive tests

Discobolus by Myron, ~450 BC

Discobolus by Myron, ~450 BC

Woman on Her Deathbed, anonyme, école flamande, 1621

Discobolus by Myron, ~450 BC

Woman on Her Deathbed, anonyme, école flamande, 1621

“LGFD”

In other words, it’s a **vibe**

But how can we quantify this **~vibe~**

1614
Life expectancy: ~33

De Statica Medicina

Santorio Santorio

“He only who knows how much and when the body does more or less insensibly perspire, will be able to discern when and how much is to be added or taken away, either for the recovery or preservation of health”

Bigotti, Fabrizio. "Mathematica Medica. Santorio and the Quest for Certainty in Medicine." *Journal of Healthcare Communications* 1.4 (2016): 39-46.

https://www.verywellhealth.com/longevity-throughout-history-2224054

1832 The Quetlet Index
Life expectancy ~40

Renamed the Body Mass Index by Ancel Keys in 1972
Life expectancy 71.2

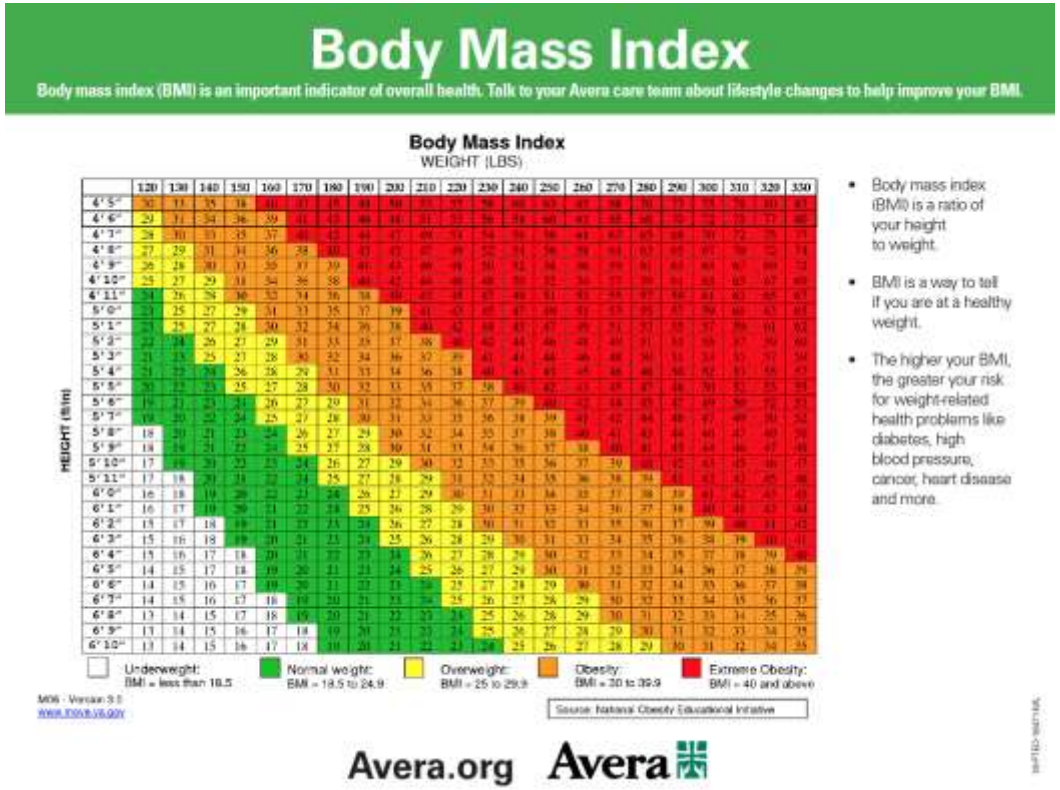


Image avera.org

Eknoyan, Garabed. "Adolphe Quetelet (1796–1874)—the average man and indices of obesity." *Nephrology Dialysis Transplantation* 23.1 (2008): 47-51.

https://www.verywellhealth.com/longevity-throughout-history-2224054

1969
Life expectancy 70.6

THE LANCET, DECEMBER 27, 1969

Occasional Survey

TEST-BATTERY TO MEASURE AGEING-RATE IN MAN

ALEX COMFORT
Medical Research Group on Ageing,
University College, London W.C.1

(*a*)	Hand-grip strength	1	−0·323
(*a, b*)	Systolic blood-pressure	1	0·519
(*b*)	Diastolic blood-pressure	1	0·409
(*a, b*)	Serum-cholesterol	1, 31, 32	0·234
(*a*)	Vibrometer	1	0·537

DRAFT TEST BATTERY FOR PHYSIOLOGICAL AGE IN MAN

	Test	Reference	*r*
	Hair-greying score	1	0·717
(*a*)	Skin elasticity	1	0·604
(*a, b*)	Systolic blood-pressure	1	0·519
(*b*)	Diastolic blood-pressure	1	0·409
(*b*)	Heart size	1	0·294
(*b*)	Thorax size	1	−0·124
(*a, b*)	Total vital capacity	1	−0·402
(*b*)	Tidal volume	1	..
(*b*)	One-second expiratory volume ..	1	−0·126
(*a*)	Hand-grip strength	1	−0·323
(*a*)	Light extinction test	1	0·488
(*a*)	Vibrometer	1	0·537
(*a, b*)	Visual acuity	1	−0·423
(*b*)	Audiometry (200 c.p.s.)	1, 35	0·445
(*a, b*)	Audiometry (4000 c.p.s.)	1, 35	0·596
(*a, b*)	Serum-cholesterol	1, 31, 32	0·234
(*b*)	Total serum-albumin	1	−0·267
(*b*)	Albumin/globulin ratio	16	..
	Plasma water	36	..
(*b*)	Mean venous pressure	16	..
(*b*)	Protein-bound iodine	31	−0·33
	Serum-copper	17	..
	Serum-elastase	37	..
	Serum-R.N.A.ase	38	..
	Nail calcium content	15	..
(*b*)	Stature	21, 39	−0·532
(*b*)	Seated stature	21	−0·53
(*b*)	Trunk height	21	−0·34
	Biacromial diameter	21	−0·40
	Metacarpal osteoporotic index ..	39	−0·786
	Lymphocyte R.N.A./D.N.A. ratio ..	10	..
•	Explant latency	40, 41	..
	Serum growth-promotion (tissue-culture)	42–45	..
•	Biopsy healing/contraction	46–48	..
•	Clonal further viability	49–51	..
	Leucocyte aneuploidy	52	..
	Autoantibody titres	18–20	..
•	Skin melanocyte-count	13, 14	..
	W.A.I.S. tests (automated set)	9, 22, 31, 35	
	Similarities		..
	Digit span		..
	Vocabulary		..
	Digit symbol		..
	Block design		..
	Digit copying		..
	Tapping test	35	−0·44
	Reaction-time, ruler test	35	0·48
	Reaction-time, light	35	0·35
	Flicker-fusion frequency	35	−0·48
	Taste sensitivity	53	..
†	Total 5-year mortality		..
†	Organ weights	54	..
†	Disease-specific mortalities		..
(*b*)	Tumour incidence, living		..
†	Tumour incidence, necropsy		..
†	Amyloidosis, stainable		..
†	Lipofuscin accumulation	55	..
†	Aortic calcium	16, 56	..
†	Collagen contractility		..
	Collagen fluorescence	57	..

(*a*) Selected for Hollingsworth battery.
(*b*) Included in or derivable from Gitman inventory.
• Biopsy dependent.
† Necropsy dependent.

Vibes, visible and invisible are quantified by biomarkers

Biomarkers measurable indicators of a biological state.
They can help us to understand and measure
Age, **health**, and **longevity**

You have years ahead of you, and I want those years to be filled with ***health*** *and* ***happiness***

Age

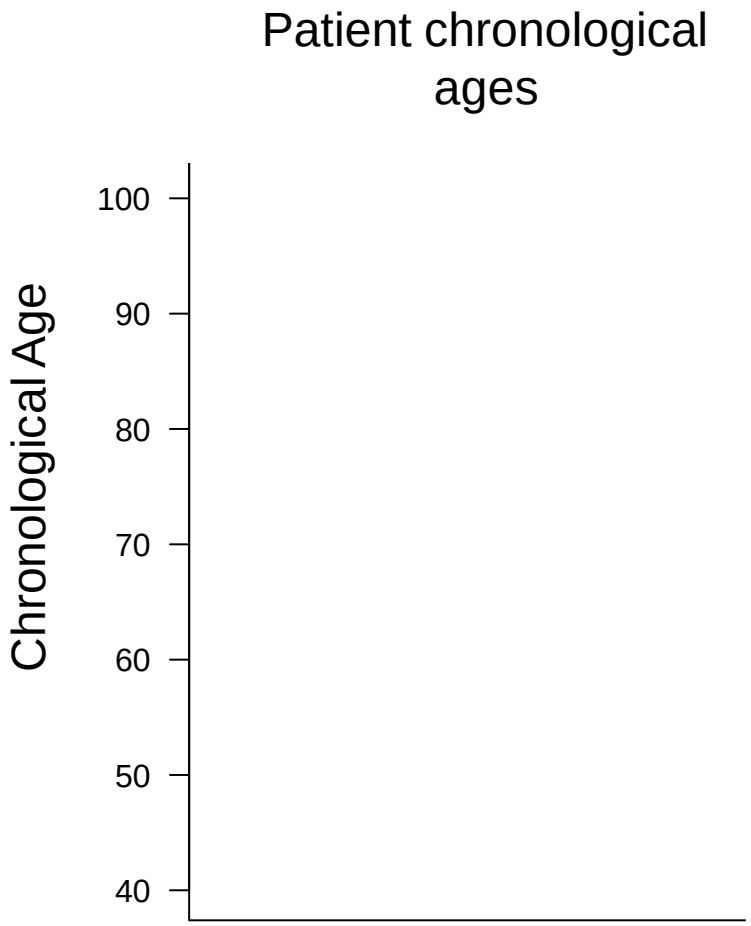
Part of aging is executing a **genetic program of development**, another is the accumulation of the **substances and experiences** that we are exposed to in our lives

Moqri, Mahdi, et al. "Biomarkers of aging for the identification and evaluation of longevity interventions." *Cell* 186.18 (2023): 3758-3775.

Can you guess someone’s **age** by looking at them?

Can we fit to **age** using parameters in a blood test?

Can we fit to **age** using parameters in a blood test?



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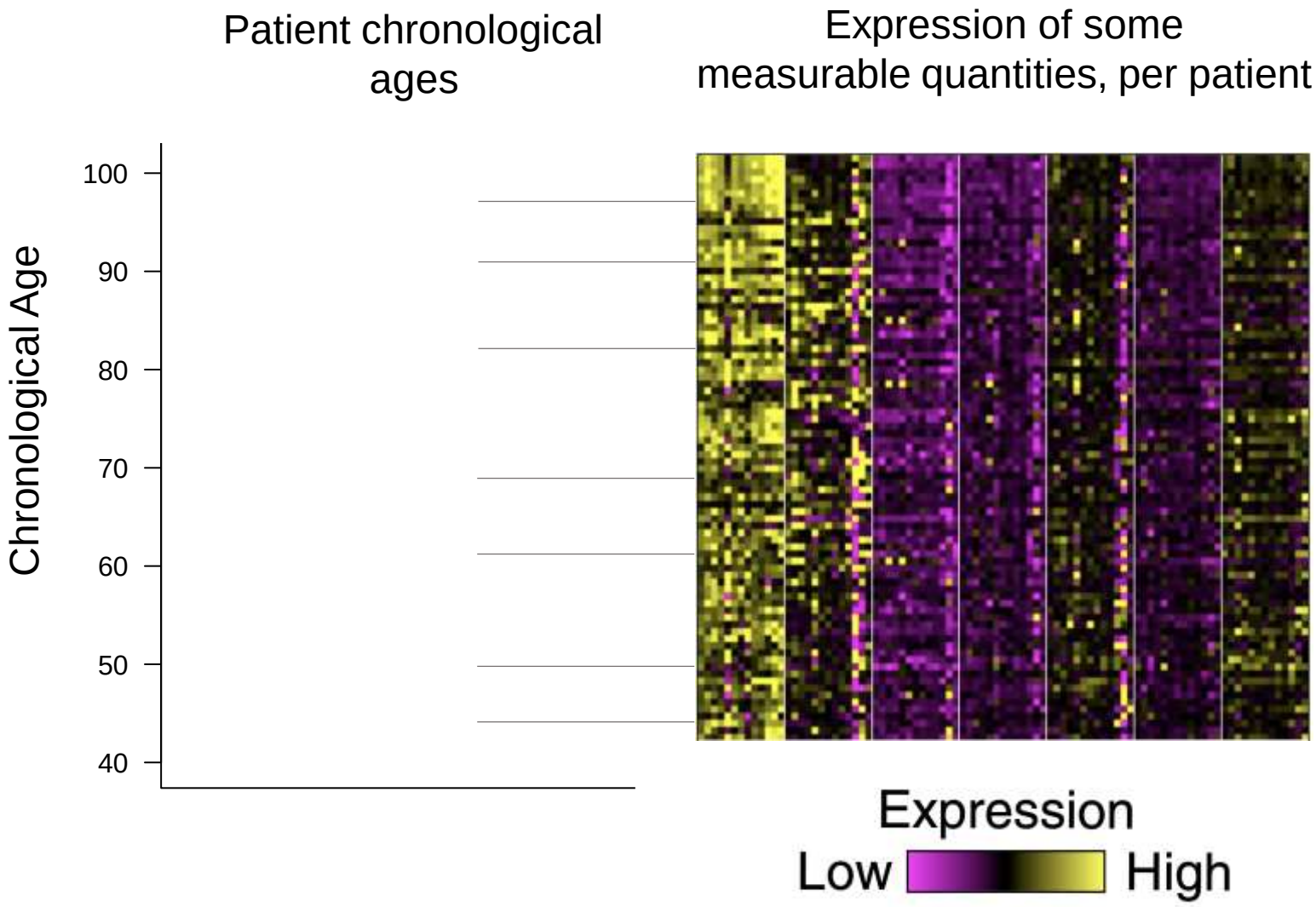

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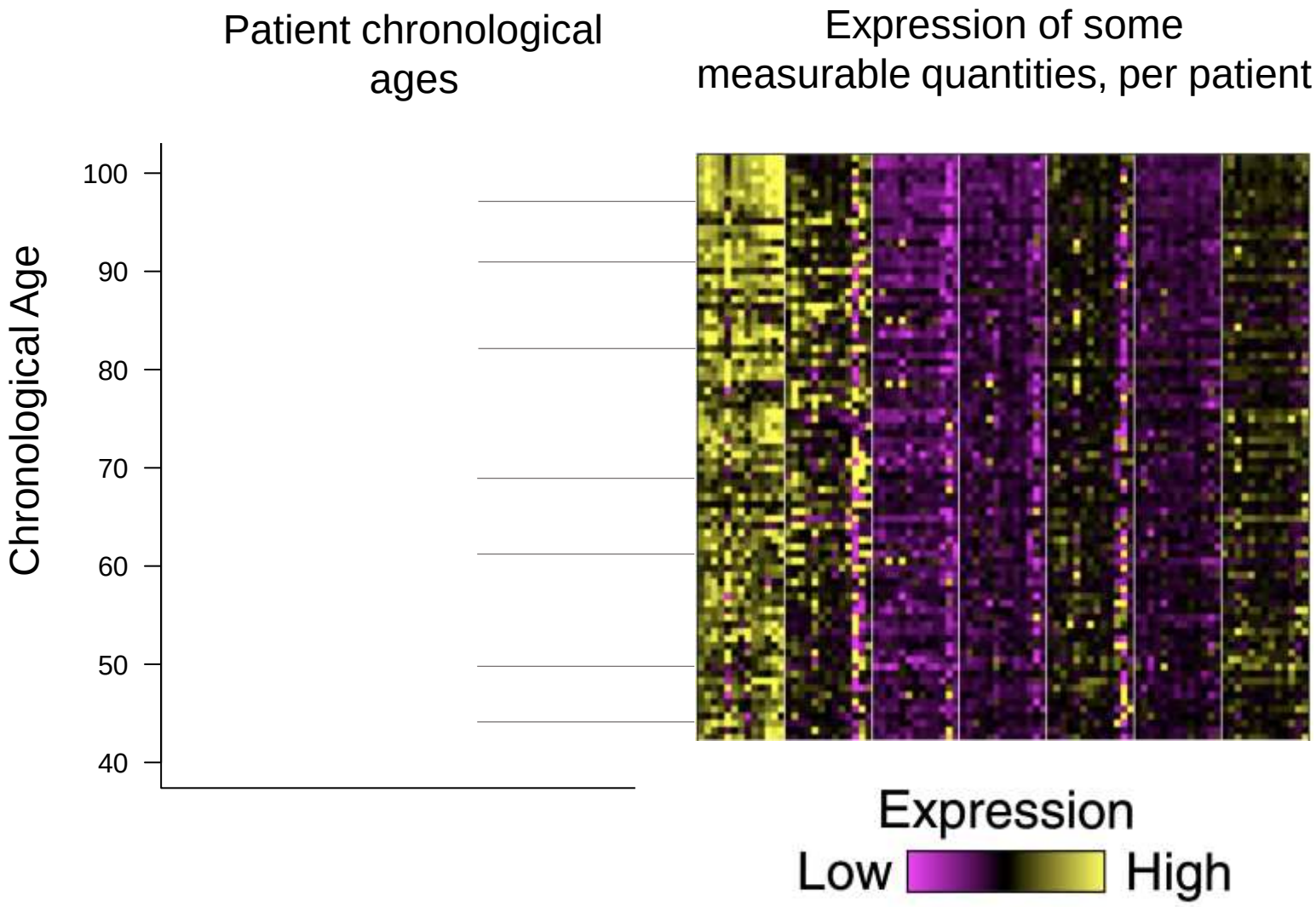
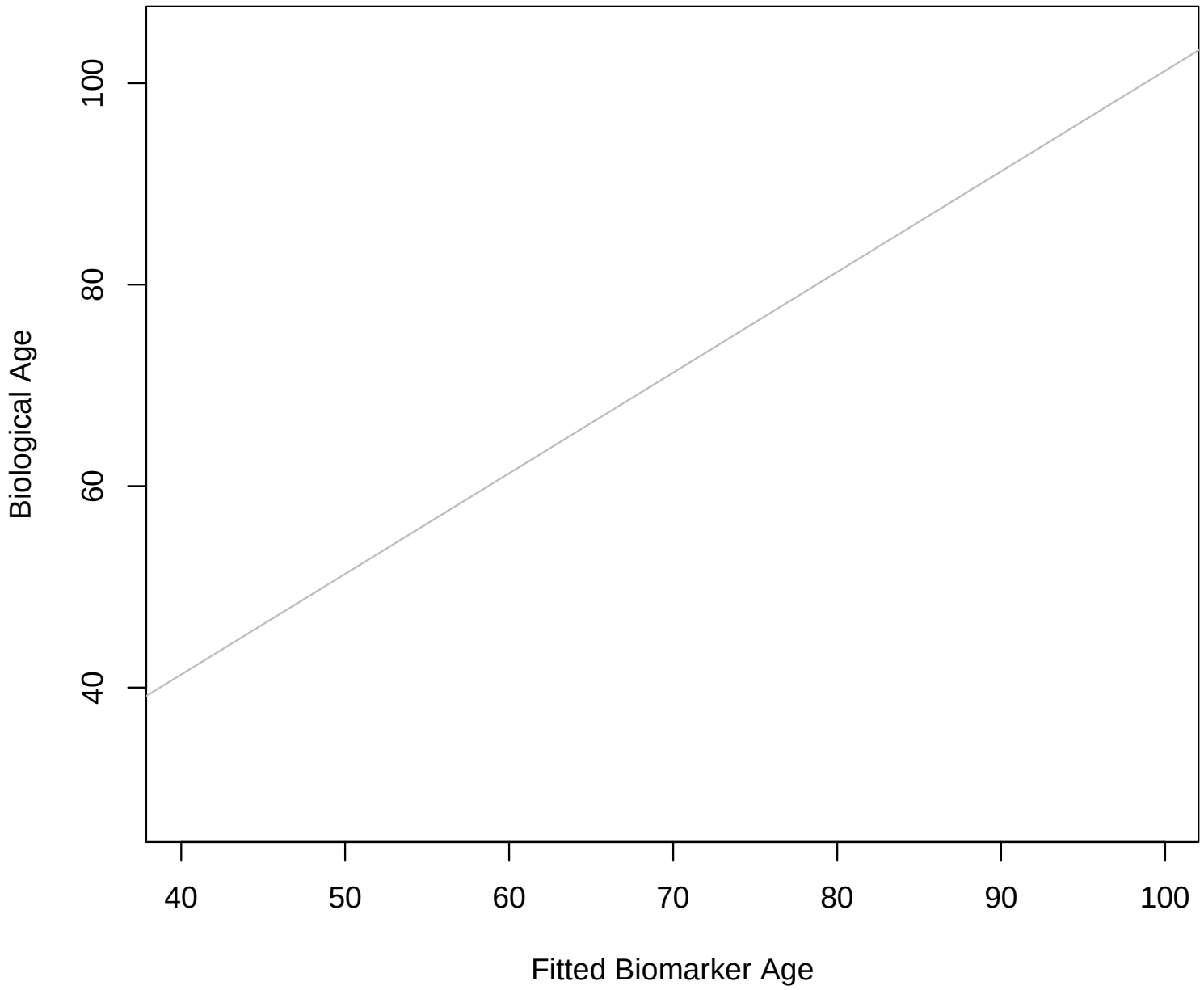


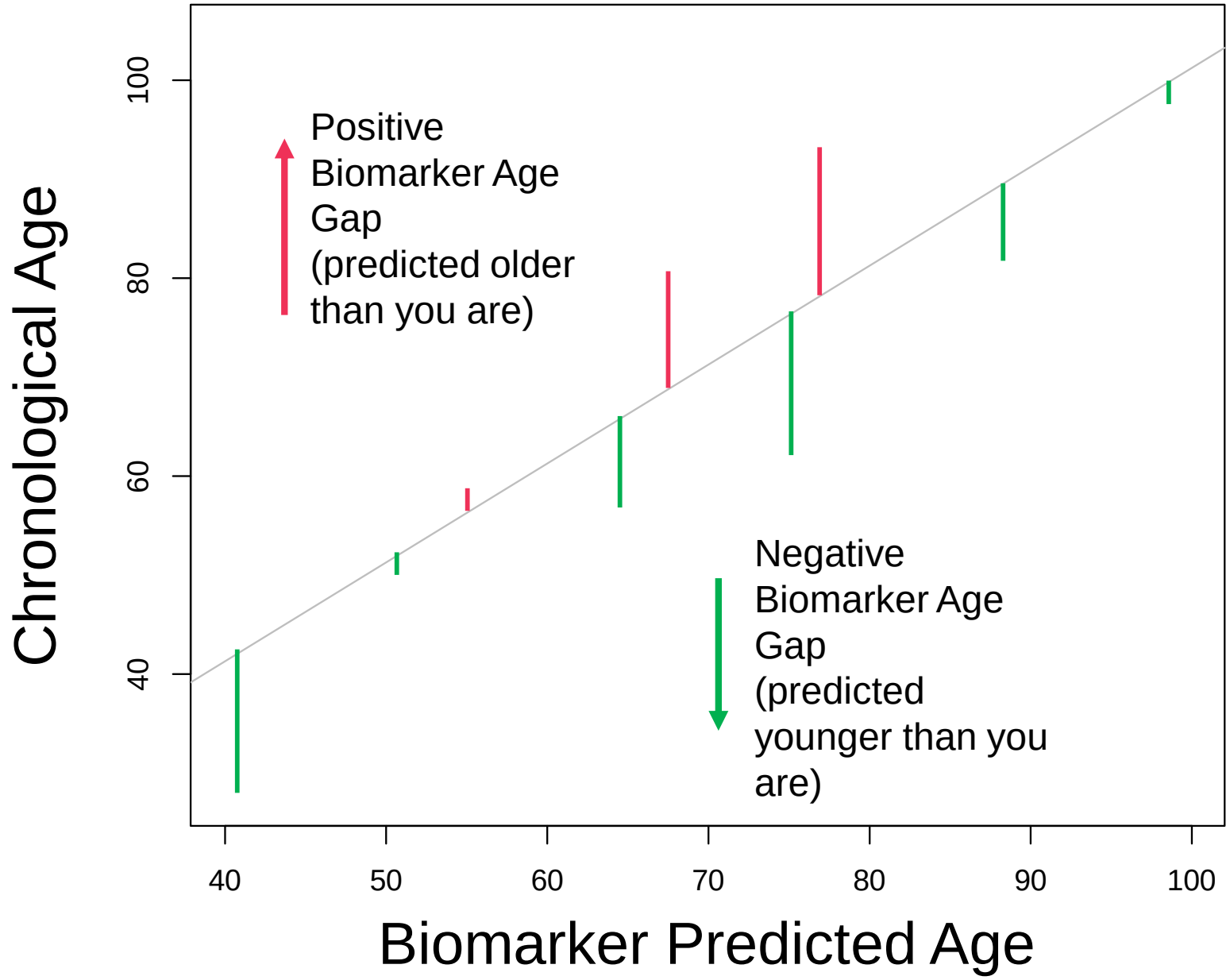
Creating a **biomarker** by fitting a **model** to chronological age

Plot chronological vs fitted **biomarker age**



In this way we create the **biomarker age gap**

Calculate the delta chronologic v. **biomarker age**



2023

nature medicine

Article

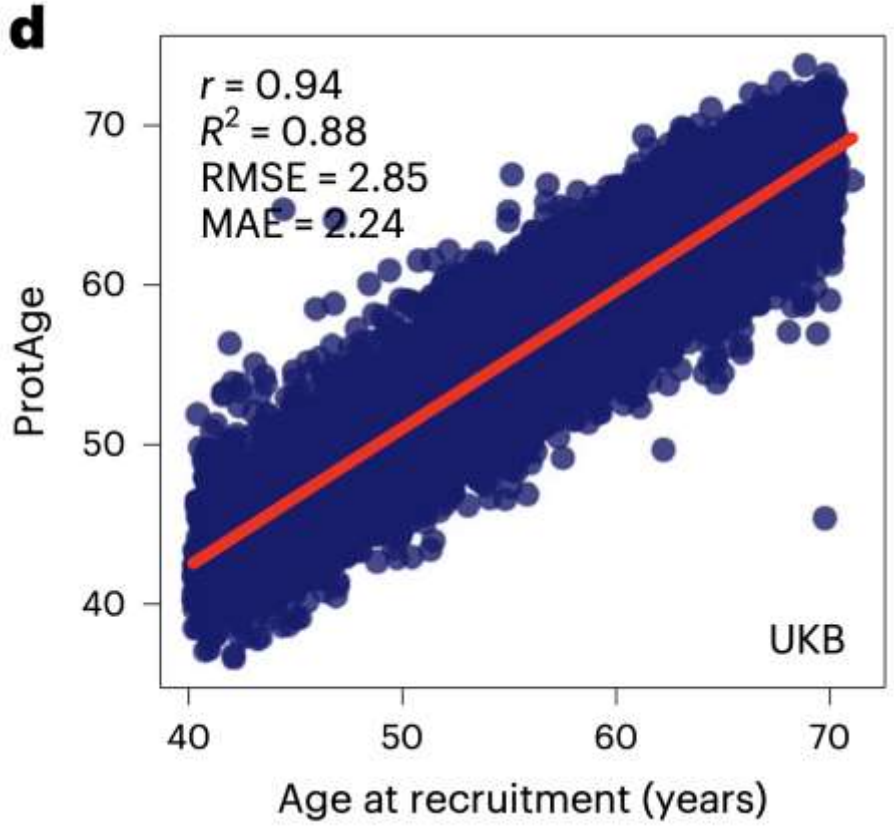
https://doi.org/10.1038/s41591-024-03164-7

Proteomic aging clock predicts mortality and risk of common age-related diseases in diverse populations

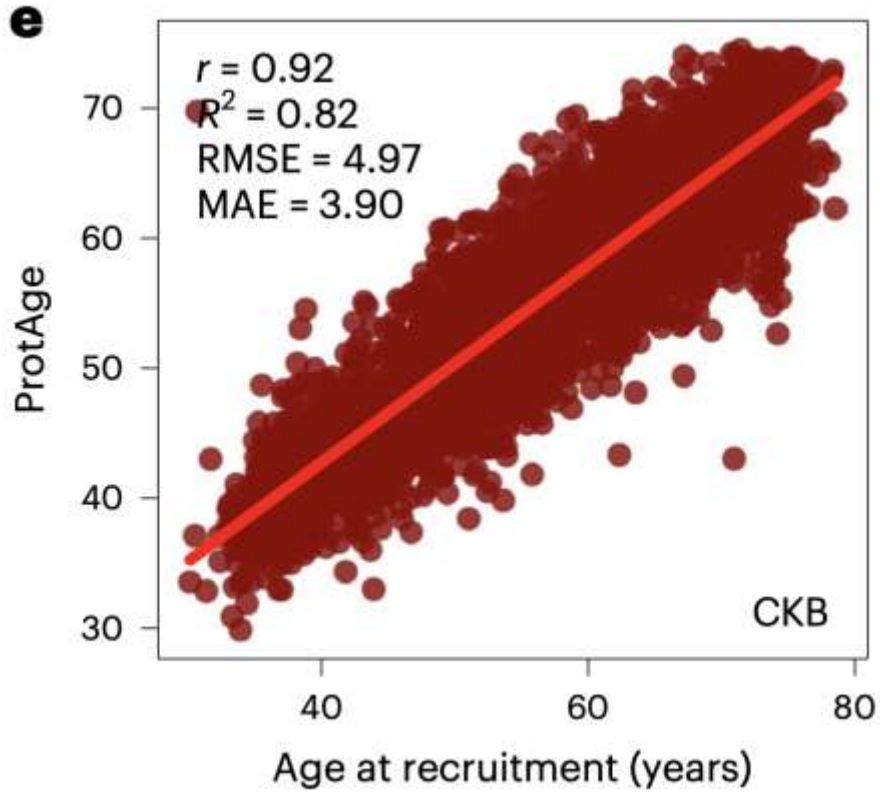
Biomarker = an ensemble of proteins in the blood in a machine learning model

Biomarker Age = “**ProtAge**”
Biomarker Age Gap = “**ProtAgeGap**”

Training the ProtAge Biomarker on the UK Biobank Database

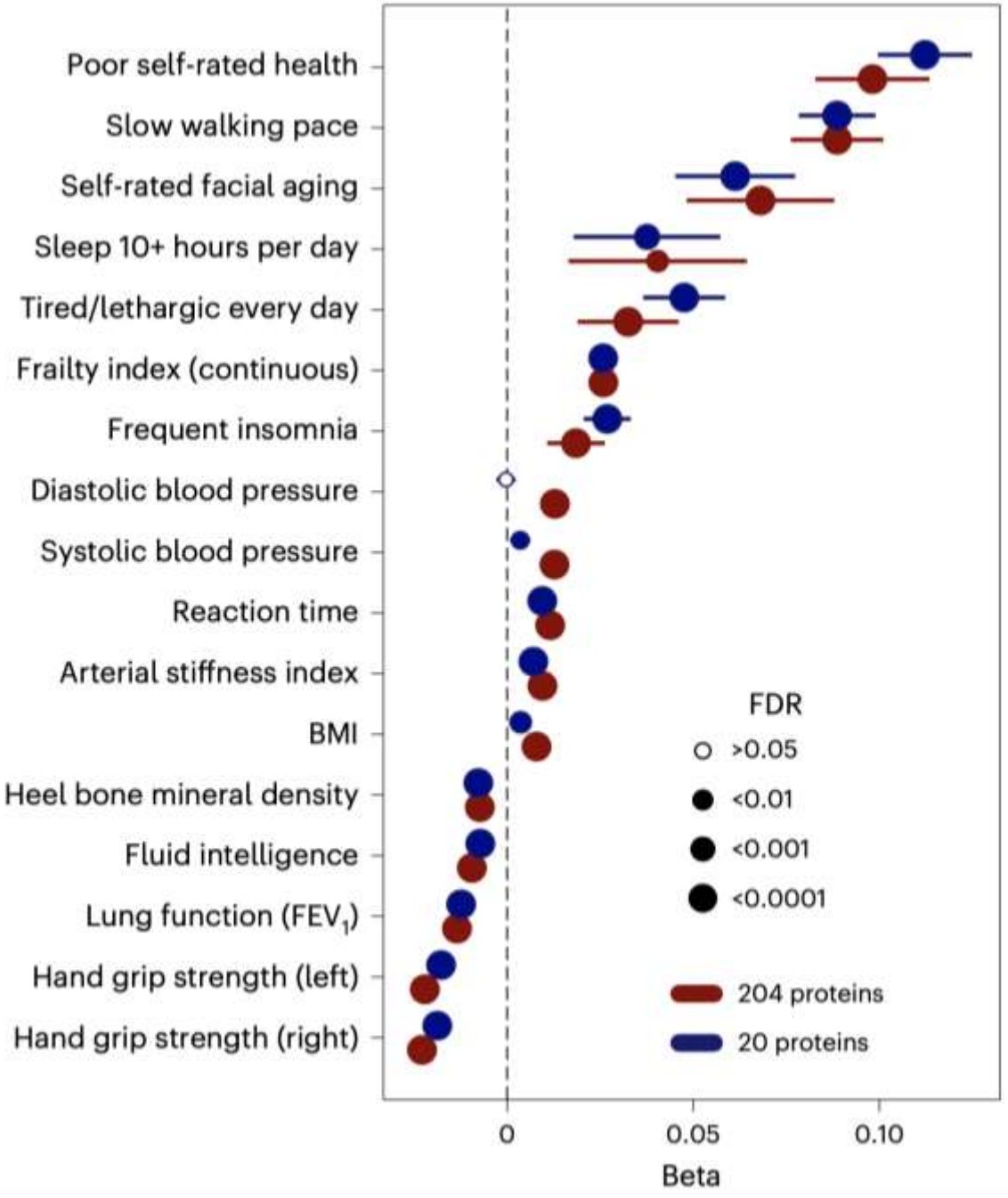


Evaluating the ProtAge Biomarker on the China Kadoorie Biobank Biobank Database



Argentieri, M. Austin, et al. "Proteomic aging clock predicts mortality and risk of common age-related diseases in diverse populations." *Nature medicine* 30.9 (2024): 2450-2460.

The ProtAge **biomarker** correlates with several other measurable biomarkers of health



Argentieri, M. Austin, et al. "Proteomic aging clock predicts mortality and risk of common age-related diseases in diverse populations." *Nature medicine* 30.9 (2024): 2450-2460.

Some of the things we can measure: *X*-ome

Moqri, Mahdi, et al. "Biomarkers of aging for the identification and evaluation of longevity interventions." *Cell* 186.18 (2023): 3758-3775.

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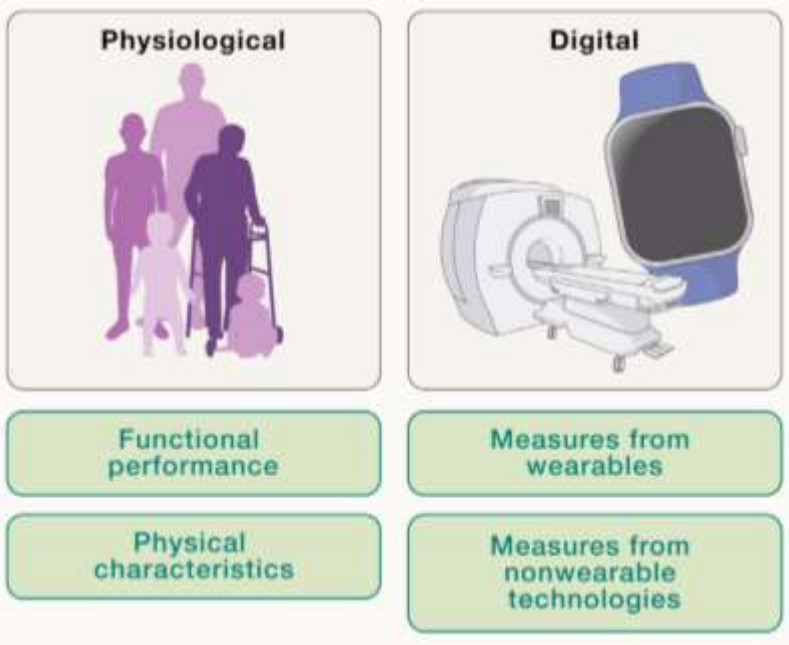

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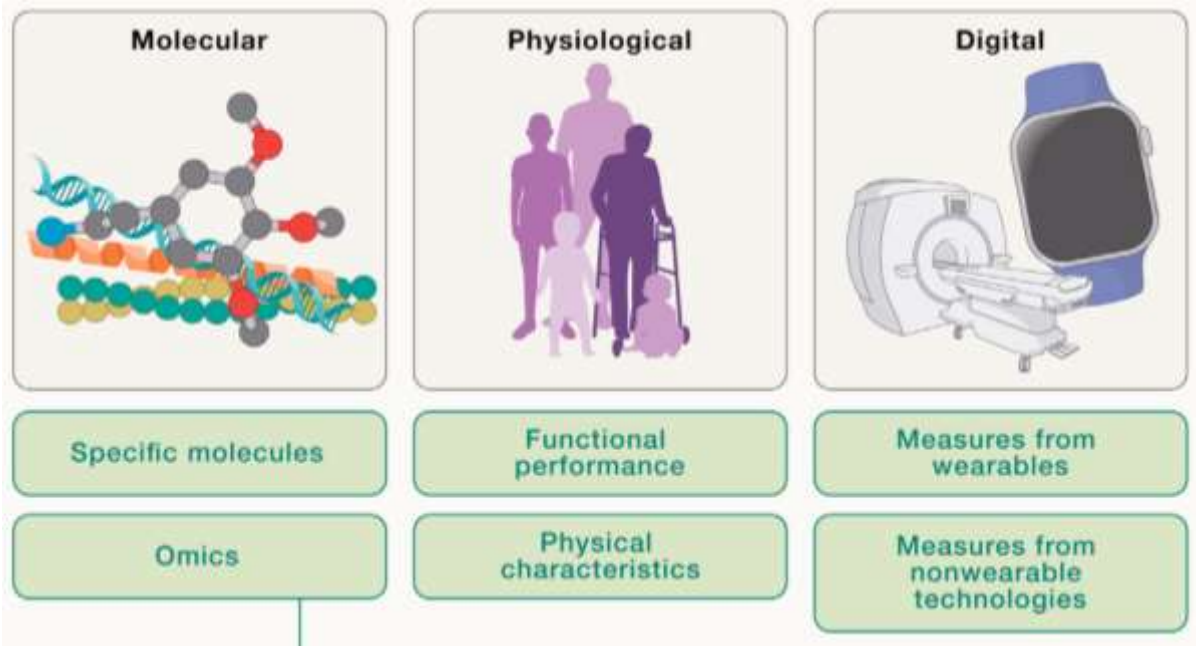

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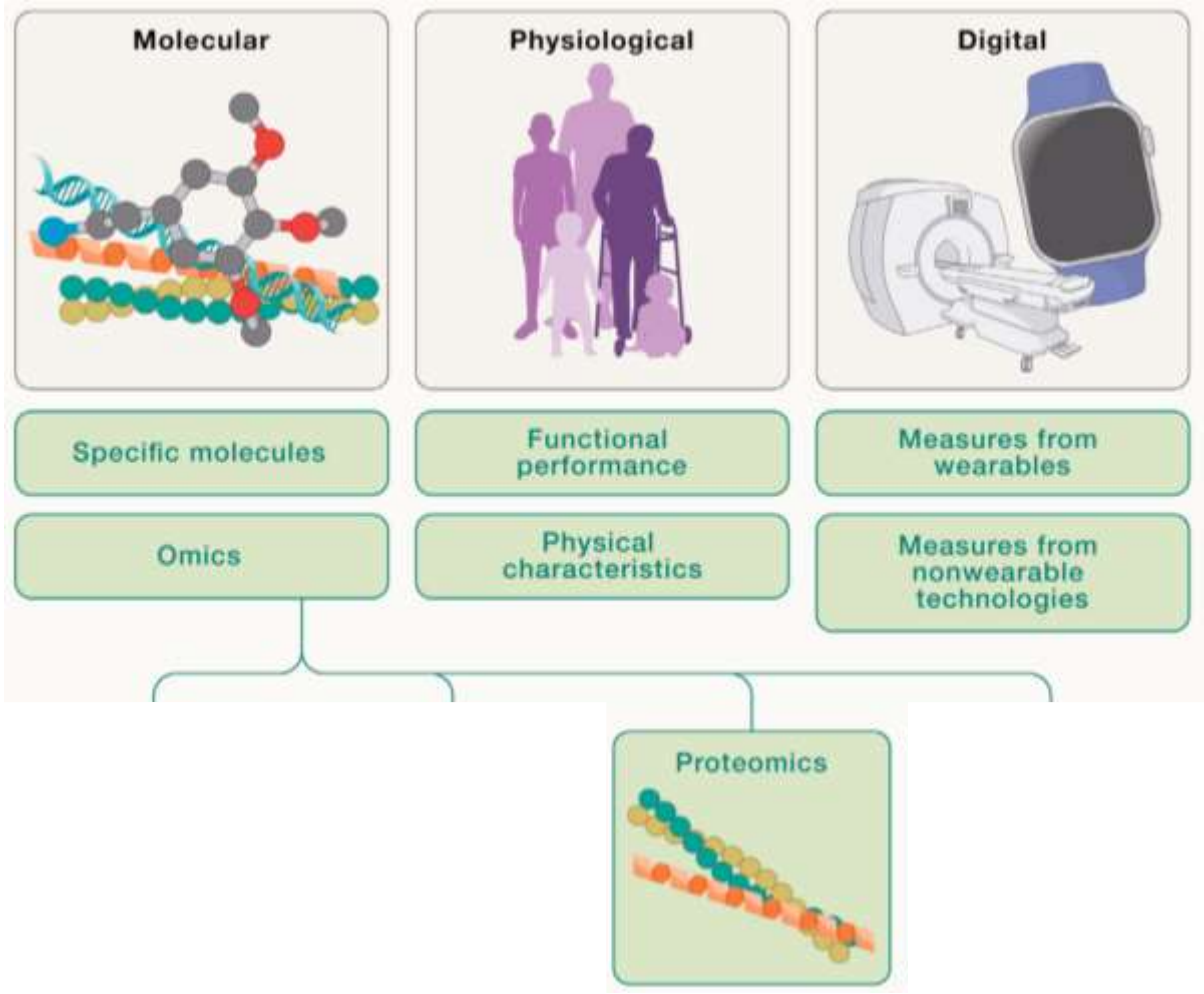

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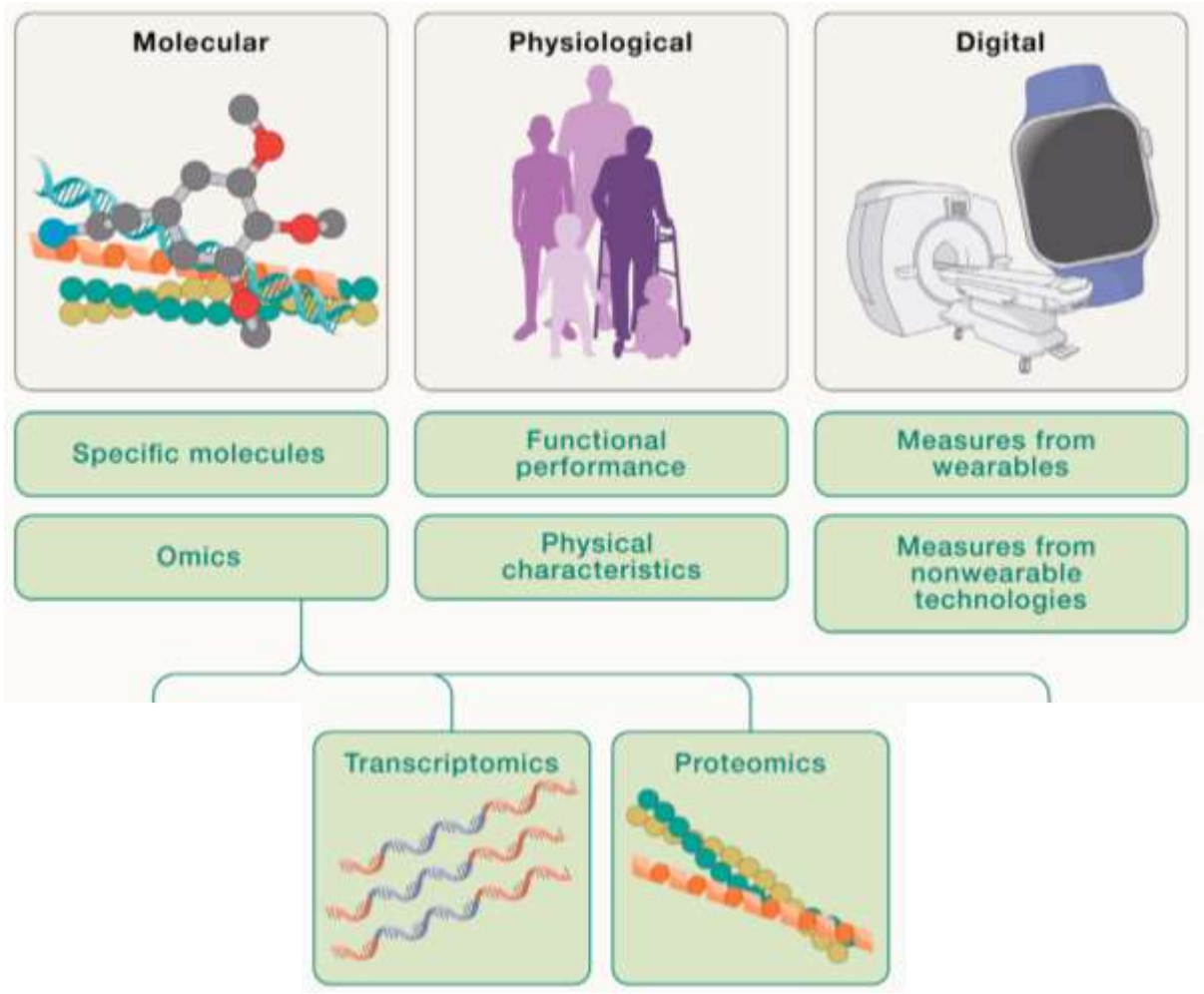

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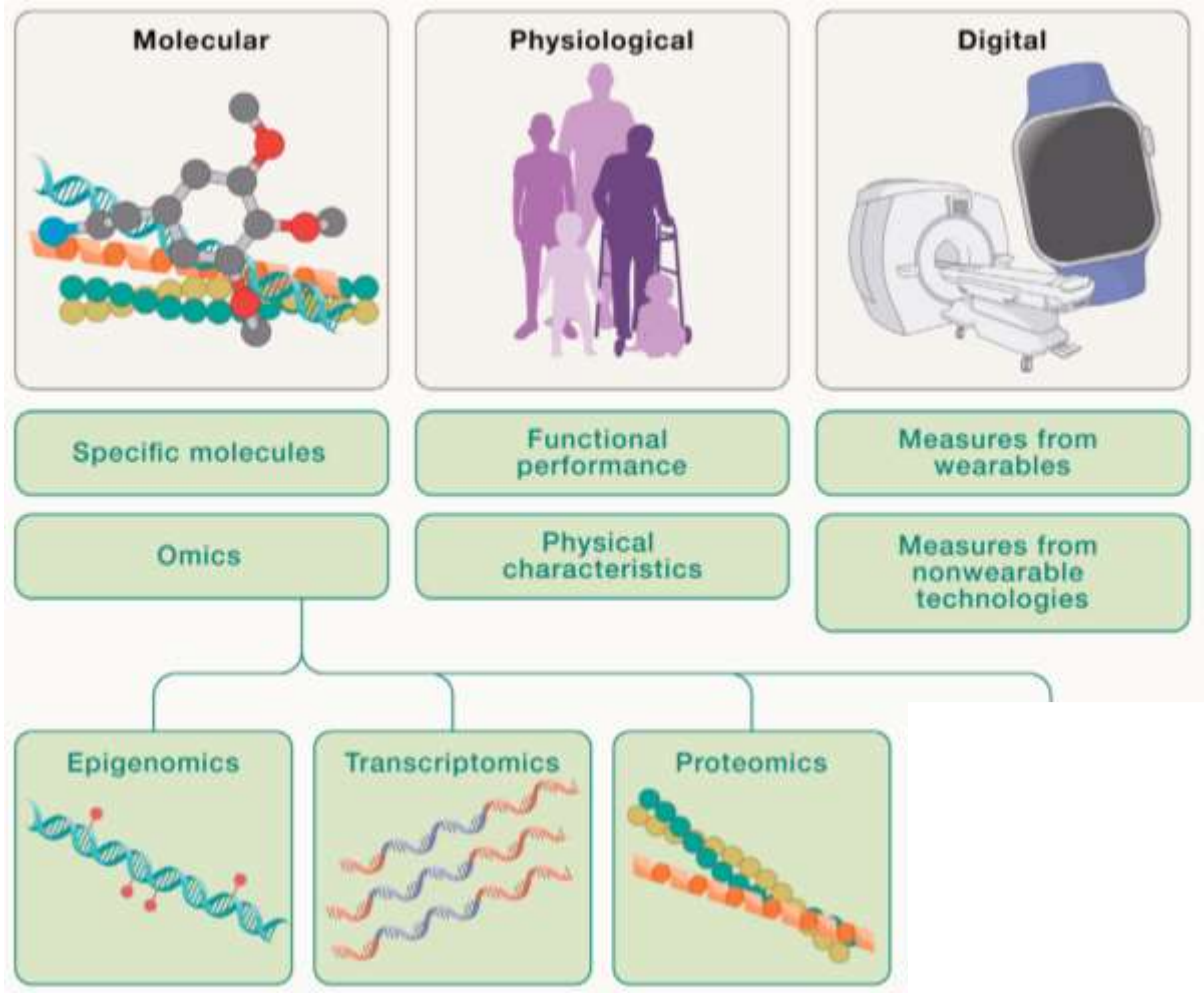

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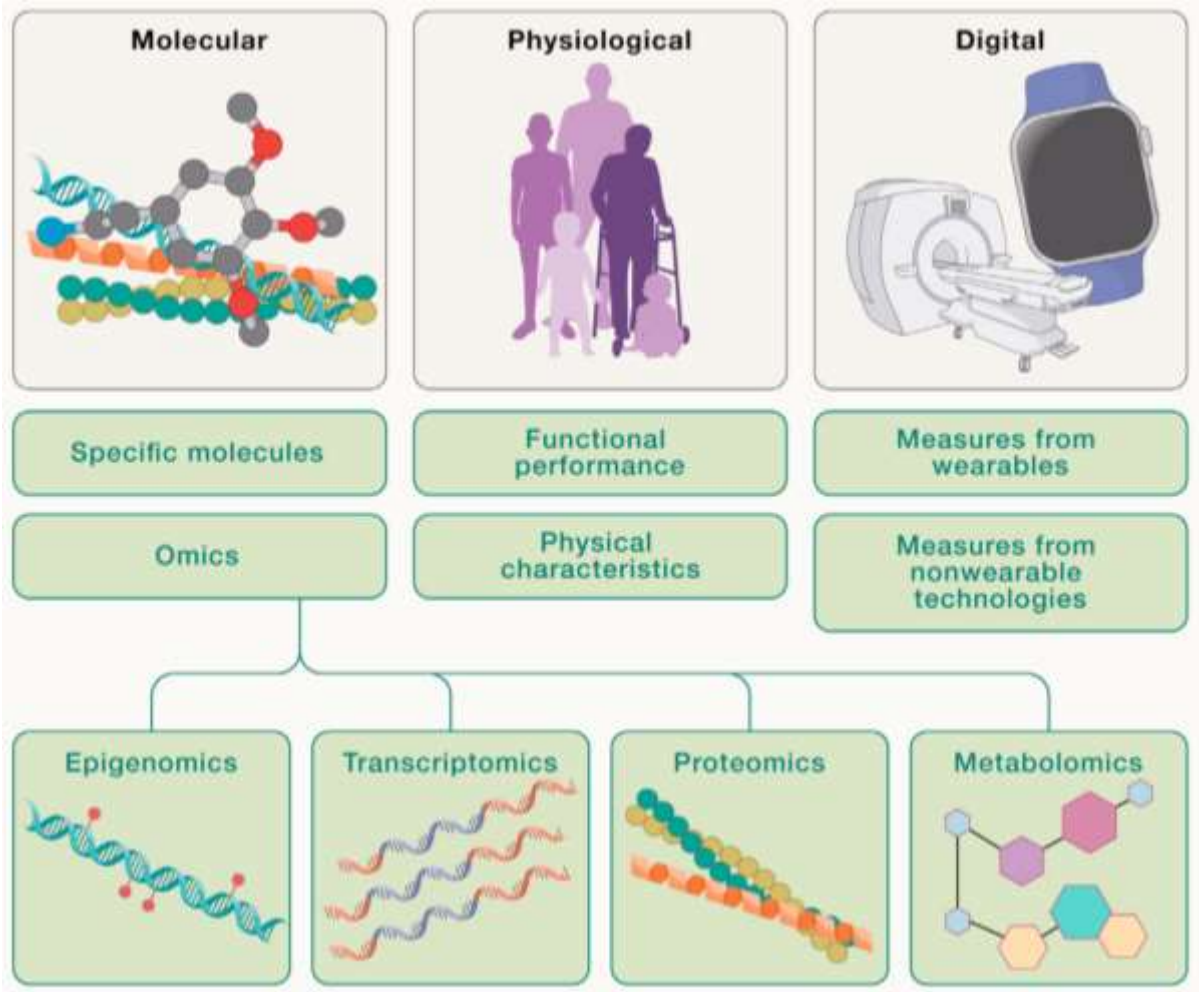

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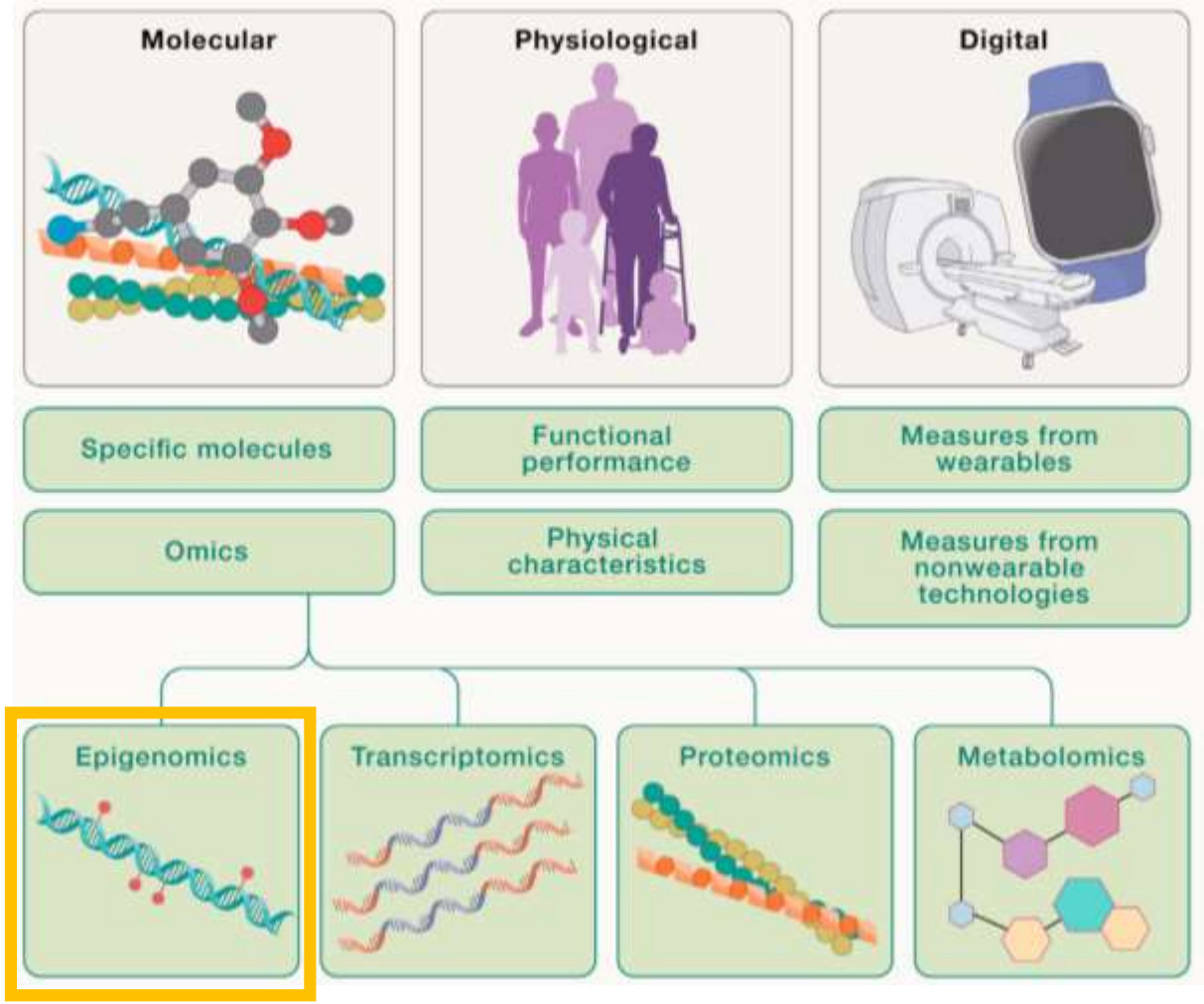

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2013

Horvath *Genome Biology* , **14**:R115
http://genomebiology.com//14/10/R115

RESEARCH Open Access

DNA methylation age of human tissues and cell types

Steve Horvath[1,2,3]

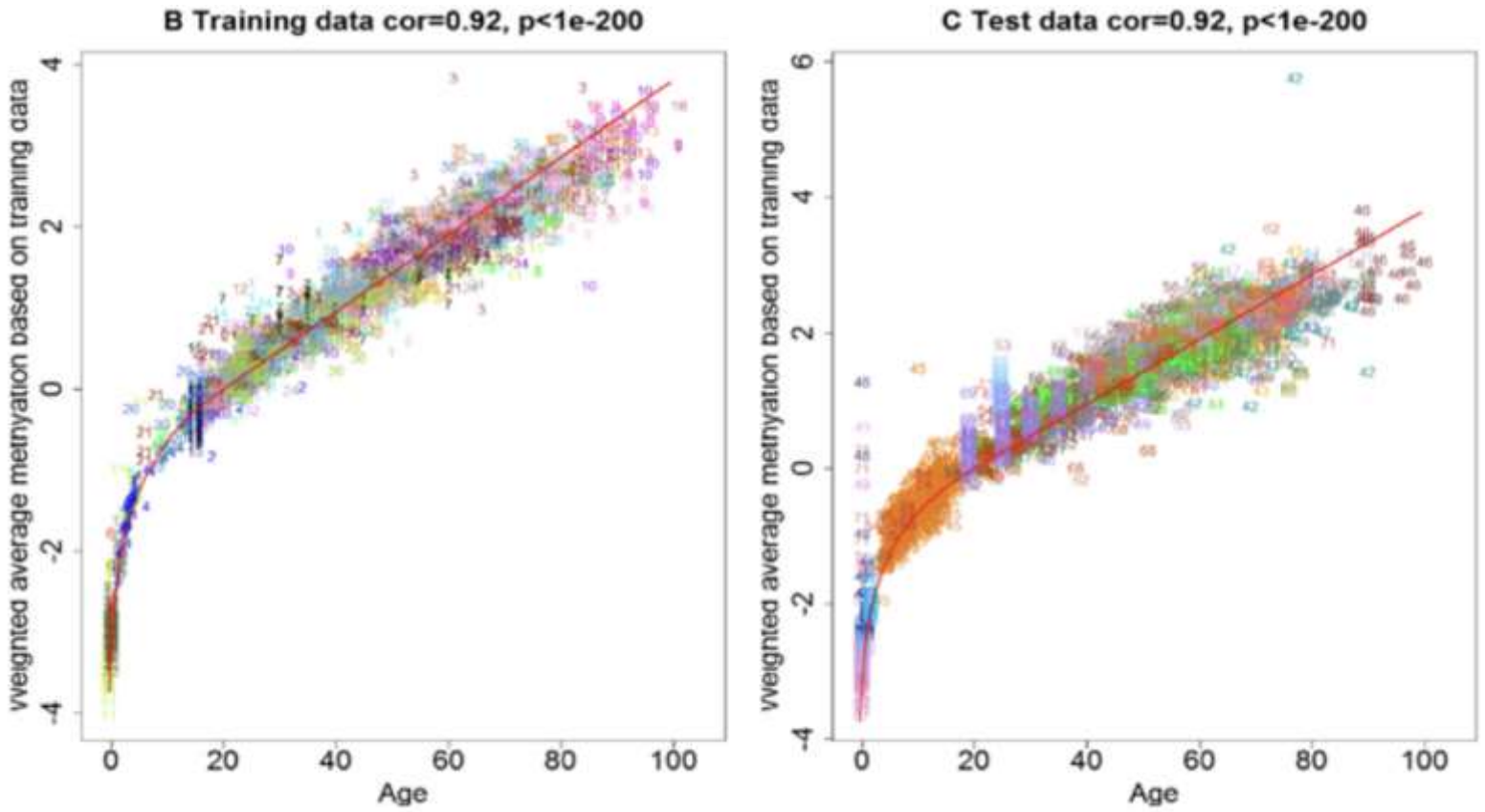
Biomarker = methylation data

Biomarker Age = "**Methylation Age**"

This is commercially available (an open source avail)

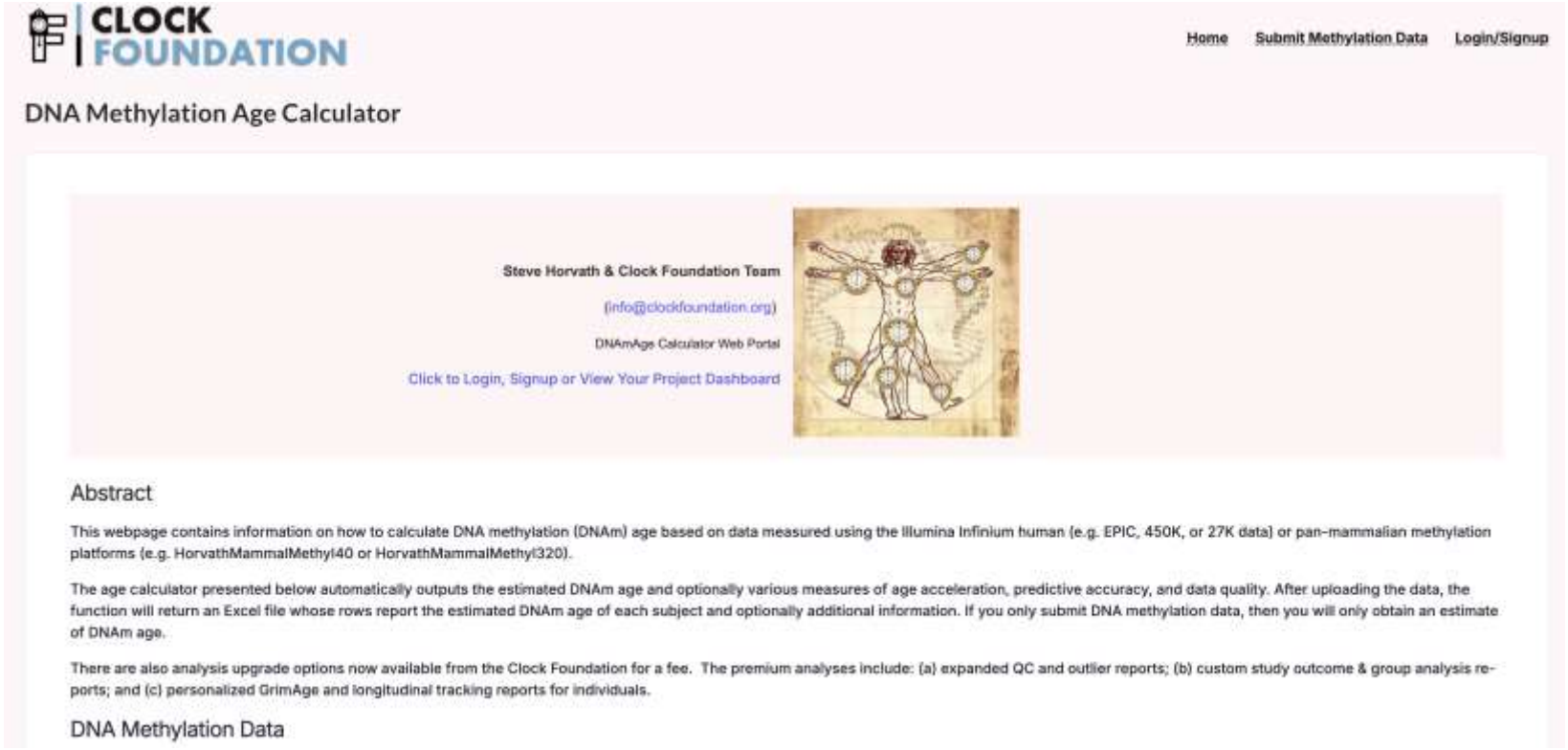
DNA **methylation** age of human tissues and cell types

The **Horvath** Clock



Horvath, Steve. "DNA methylation age of human tissues and cell types." *Genome biology* 14 (2013): 1-20.

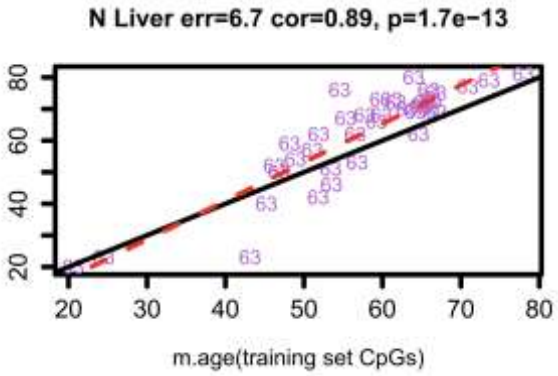
You can upload your or a patient's **methylome** to obtain a **methylation age**



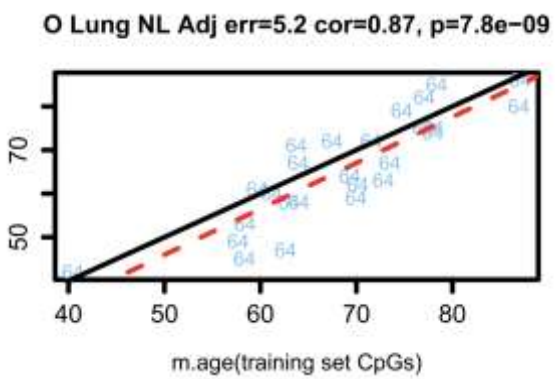
We can probe **methylation** age from tissue in each **specific organ**

True Human Age

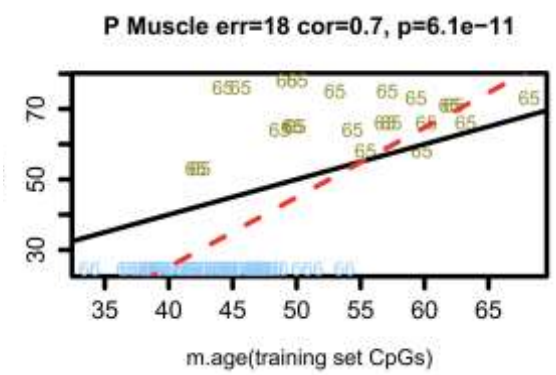
Liver



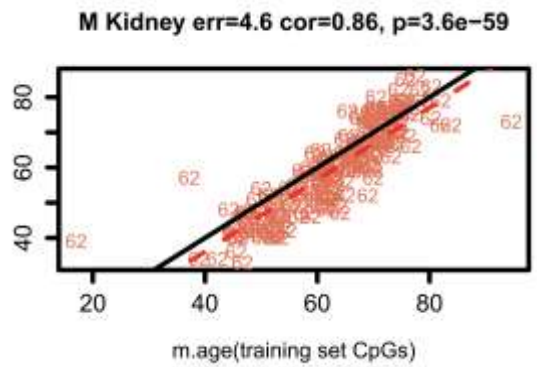
Lung



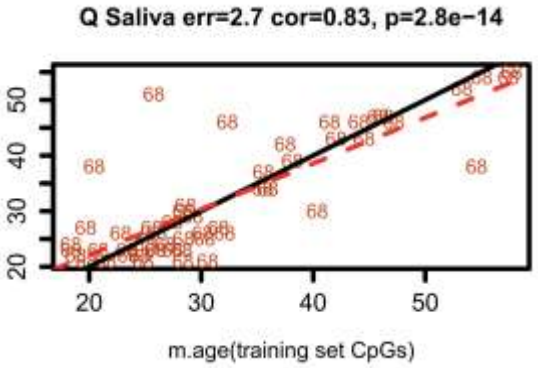
Muscle



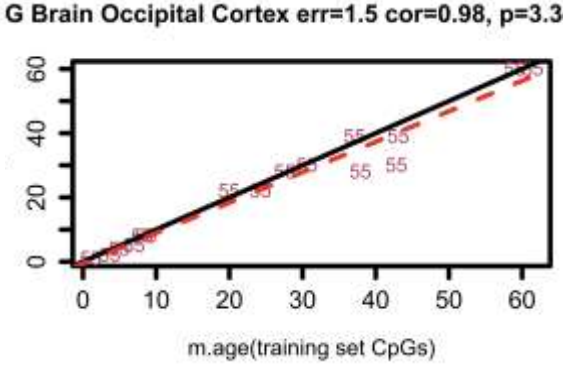
Kidney



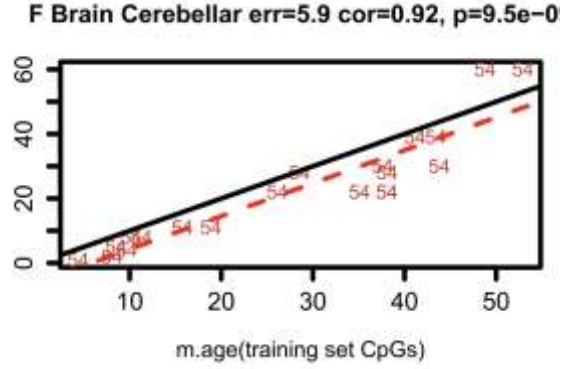
Saliva



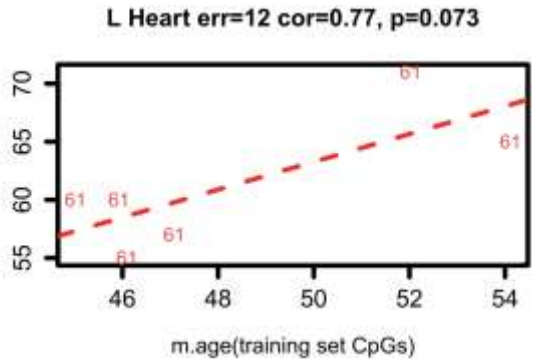
Brain (Occipital Cortex)



Brain (Cerrebelum)



Heart



Horvath, Steve. "DNA methylation age of human tissues and cell types." *Genome biology* 14 (2013): 1-20.

Methylation Age (Trained on CpG sites in the paper's training set)

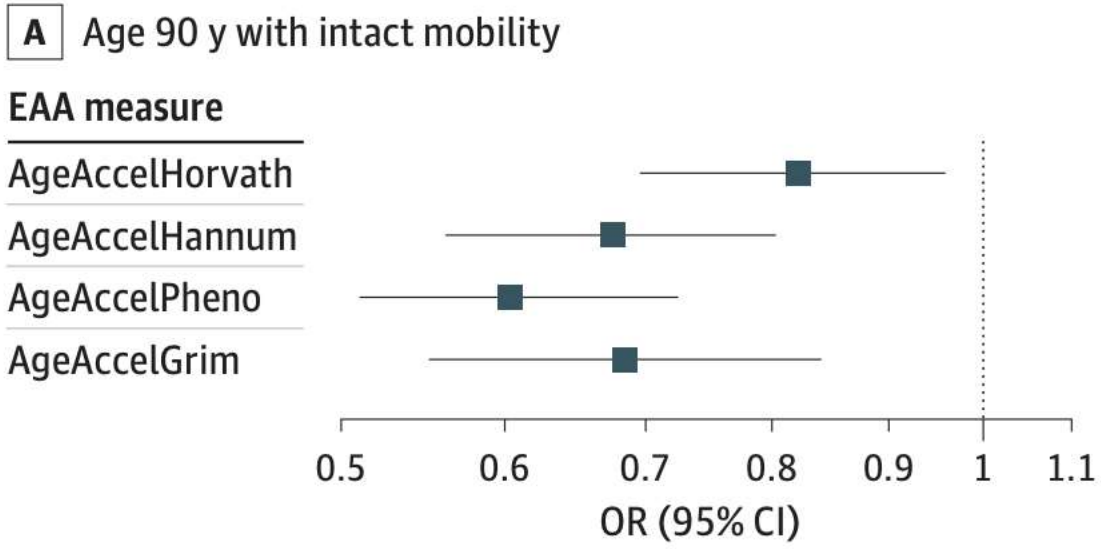
Epigenetic age correlates with longevity, intact mobility, and cognitive function

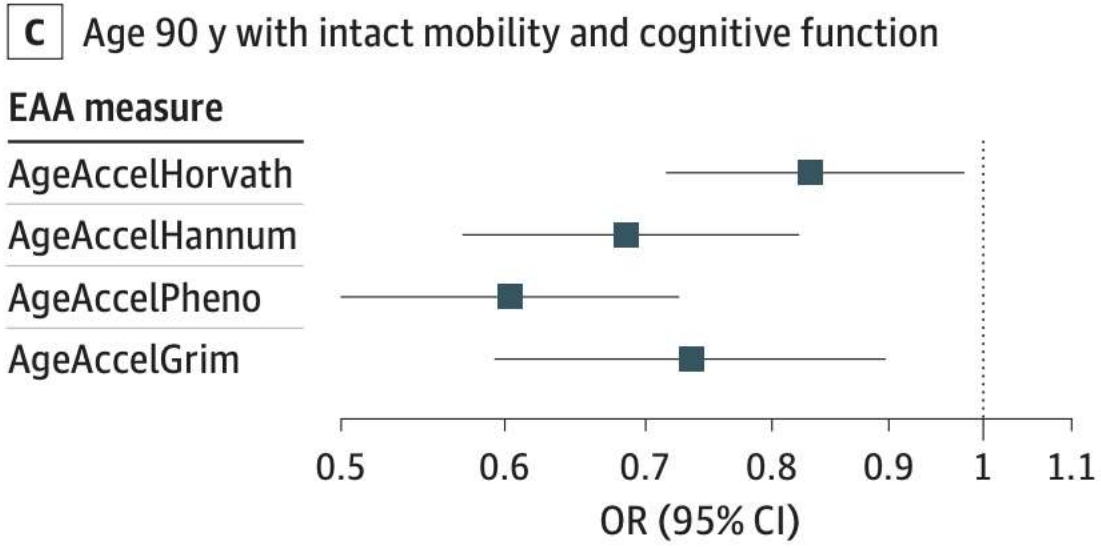
JAMA Network Open

Original Investigation | Public Health

Analysis of Epigenetic Age Acceleration and Healthy Longevity Among Older US Women

Purva Jain, PhD, MPH; Alexandra M. Binder, ScD, ScM; Brian Chen, PhD; Humberto Parada Jr, PhD, MPH; Linda C. Gallo, PhD; John Alcaraz, PhD; Steve Horvath, PhD, ScD; Parveen Bhatti, PhD; Eric A. Whitsel, MD, MPH; Kristina Jordahl, PhD; Andrea A. Baccarelli, MD, PhD; Lifang Hou, MD, PhD; James D. Stewart, PhD; Yun Li, PhD; Jamie N. Justice, PhD, MS; Andrea Z. LaCroix, PhD



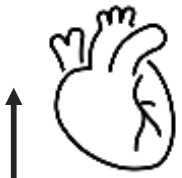


Does Jain, Purva, et al. "Analysis of epigenetic age acceleration and healthy longevity among older US women." *network open* 5.7 (2022): e2223285-e2223285.

Can we measure multidimensional **age**, and in so doing obtain insights that will allow us to slow the **march of time**

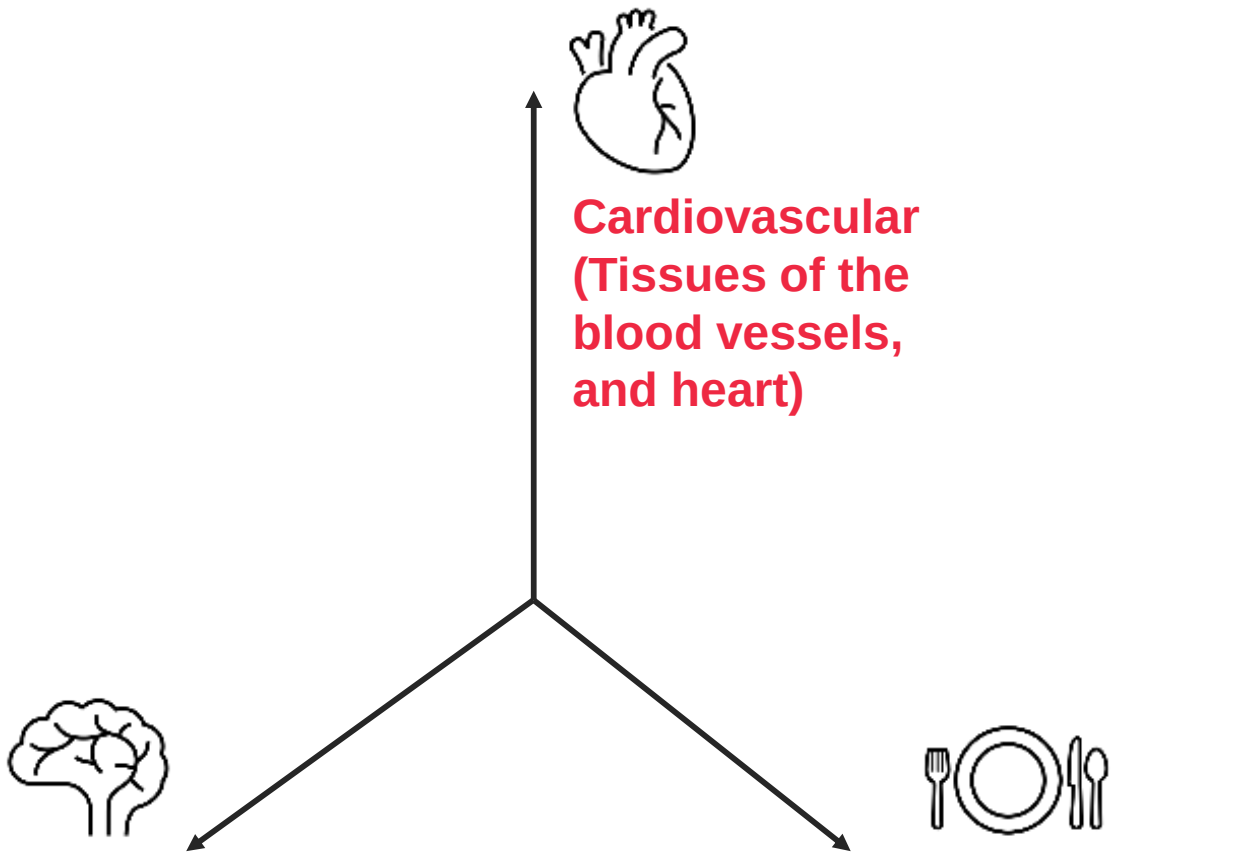
Are there **multiple dimensions** to **Age**?

Cardiovascular (Tissues of the blood vessels, and heart)



Cardiovascular (Tissues of the blood vessels, and heart)

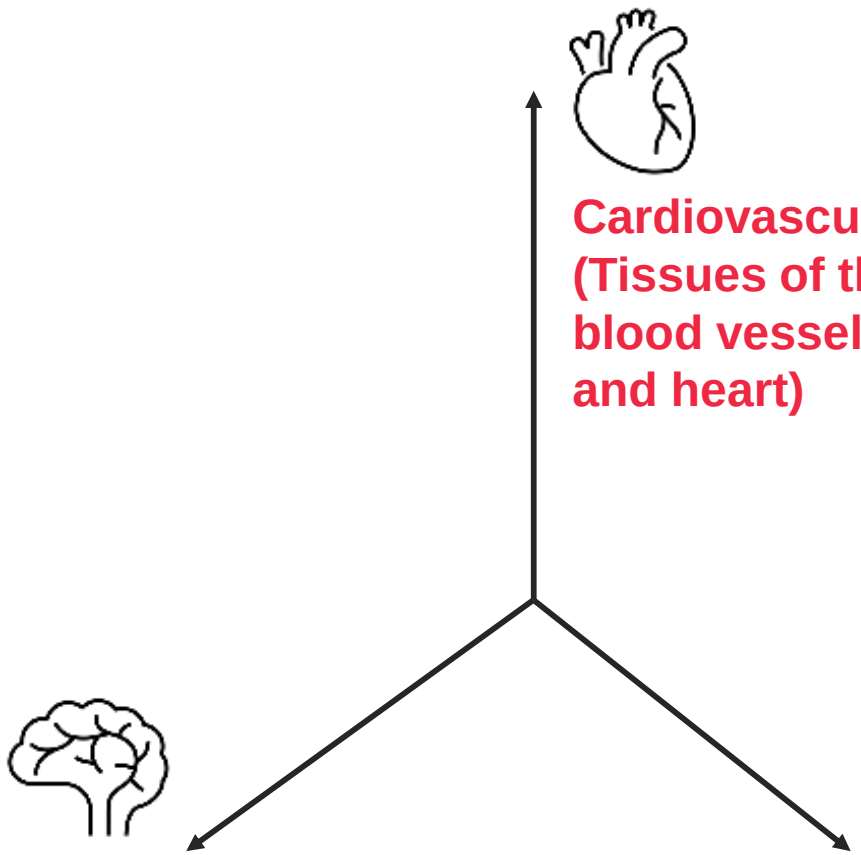
Metabolic (The ensemble of metabolic interactions in our body)



Cardiovascular (Tissues of the blood vessels, and heart)

Neurological (Tissues of the nervous system)

Metabolic (The ensemble of metabolic interactions in our body)

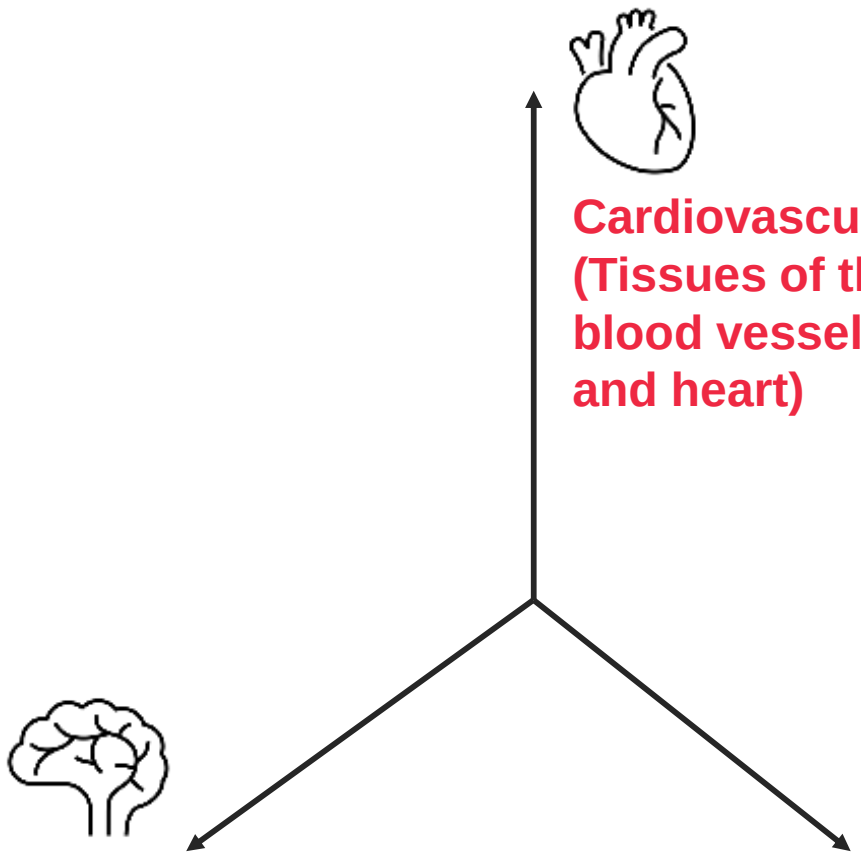


Cardiovascular (Tissues of the blood vessels, and heart)

Neurological (Tissues of the nervous system)

Metabolic (The ensemble of metabolic interactions in our body)

⇌ Genetics



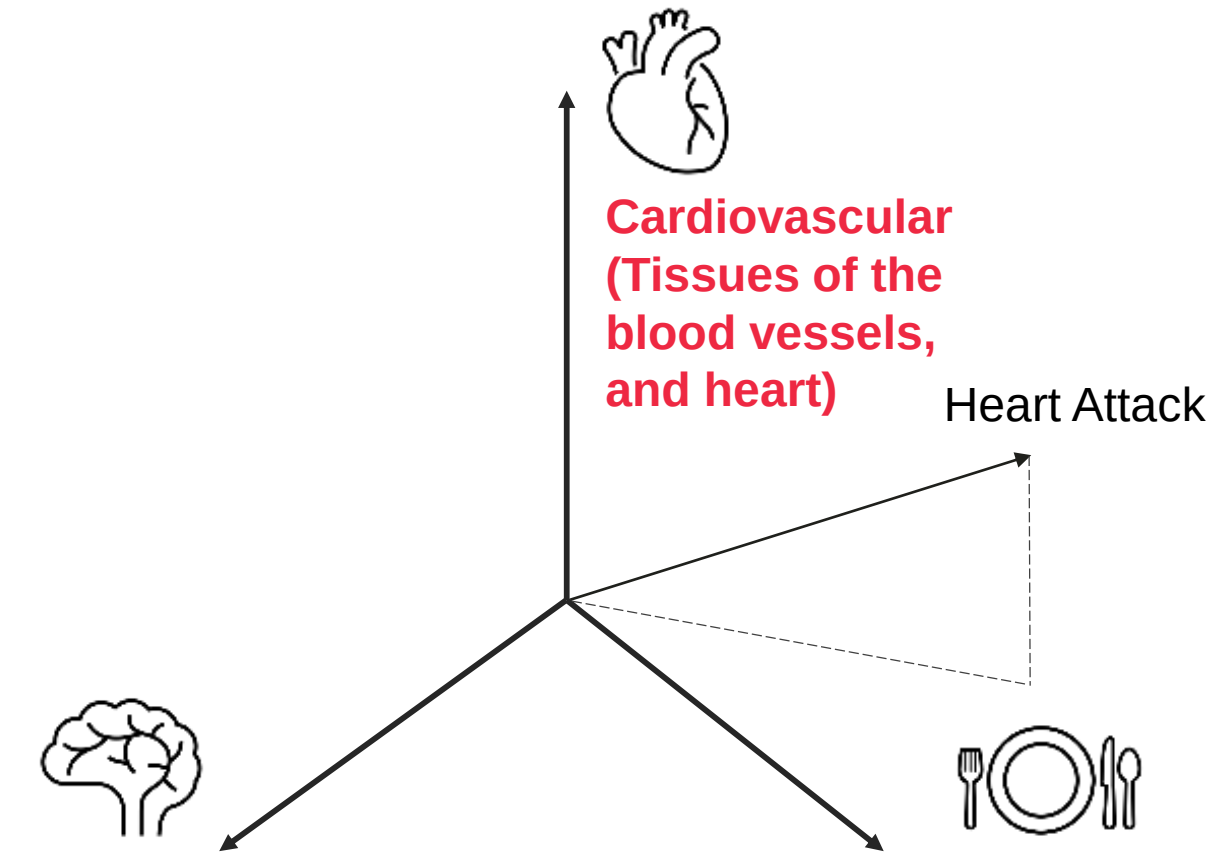
Cardiovascular
(Tissues of the blood vessels, and heart)

Neurological
(Tissues of the nervous system)

Metabolic
(The ensemble of metabolic interactions in our body)

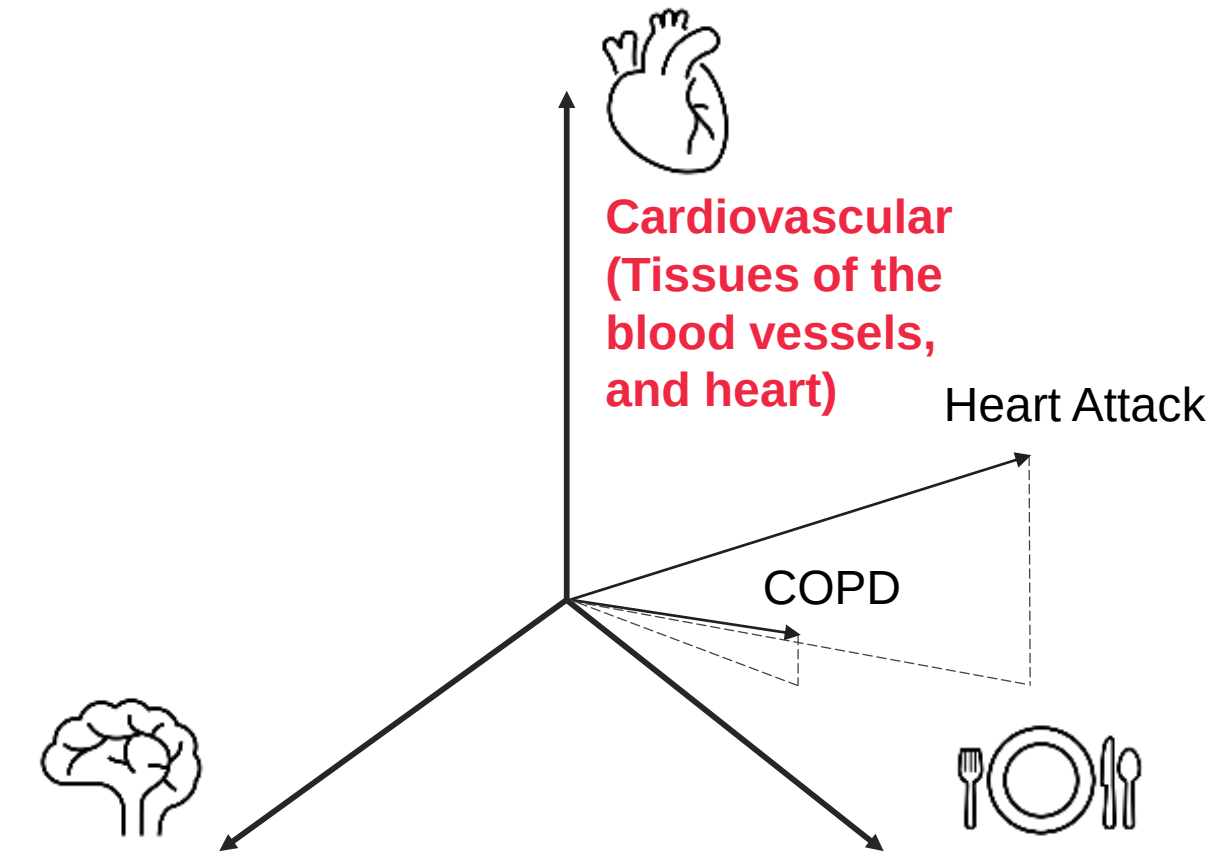
⇌ Genetics

⇌ Environment



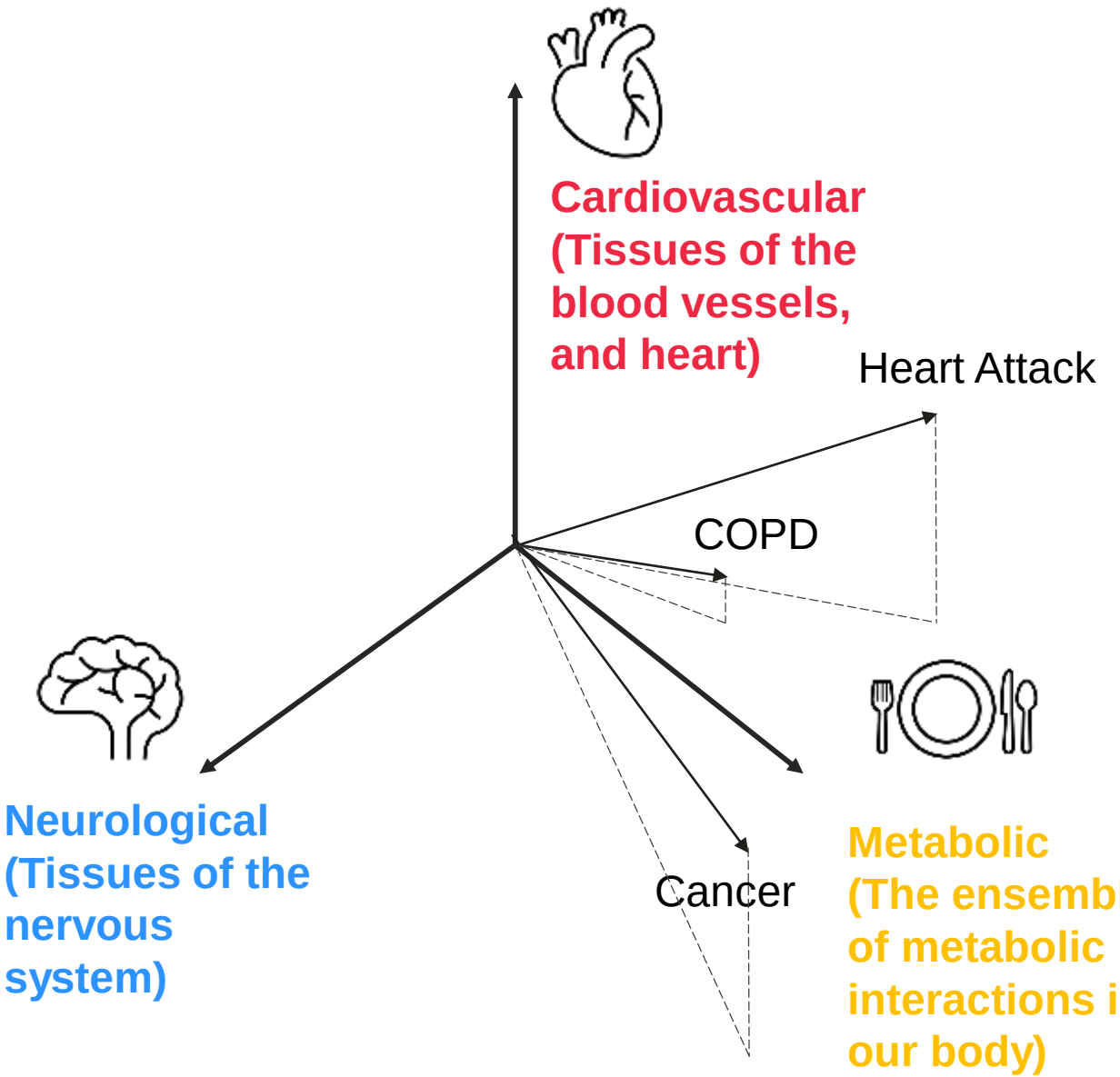
Genetics

Environment



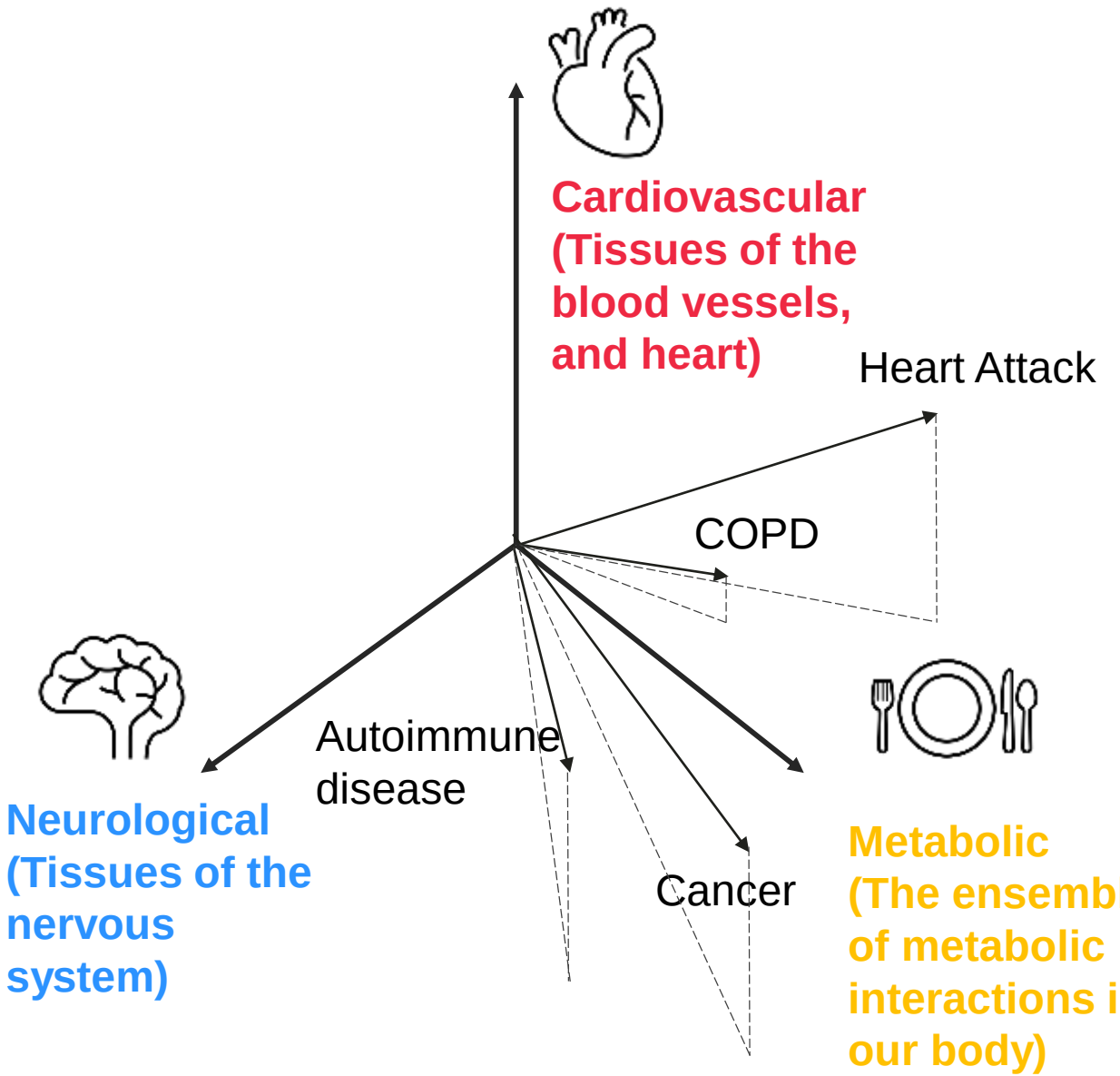
Genetics

Environment



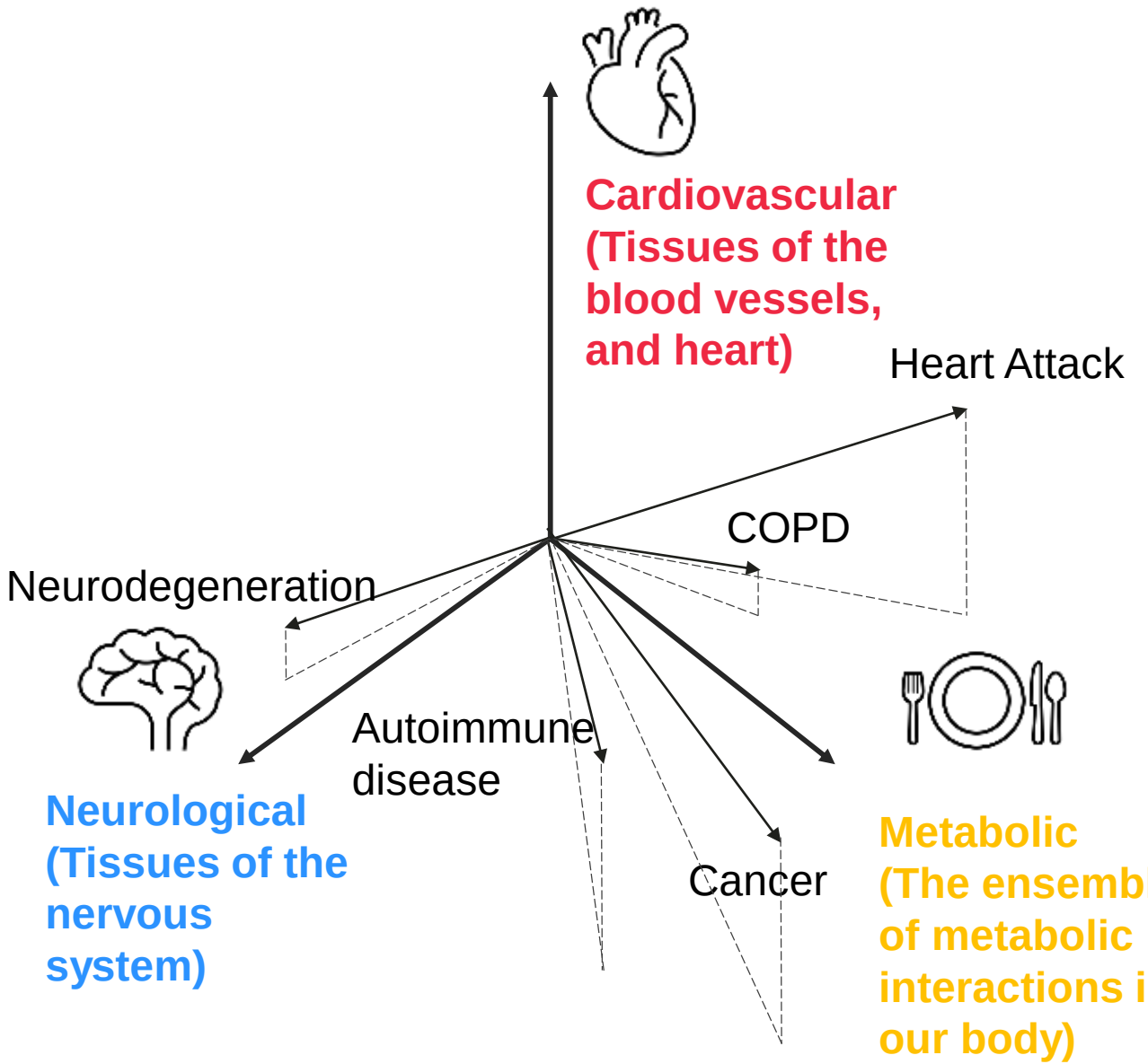
Genetics

Environment



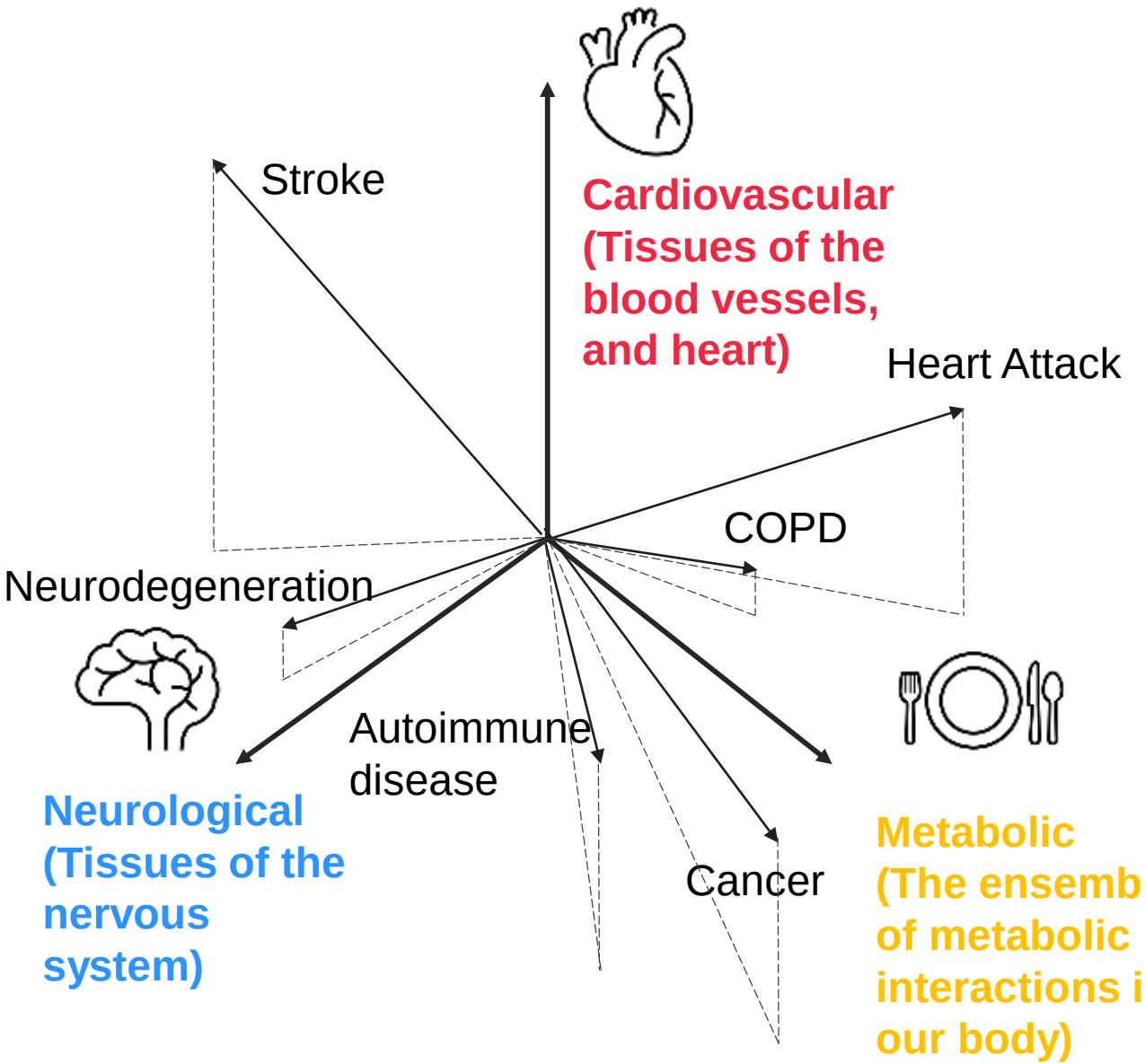
Genetics

Environment



Genetics

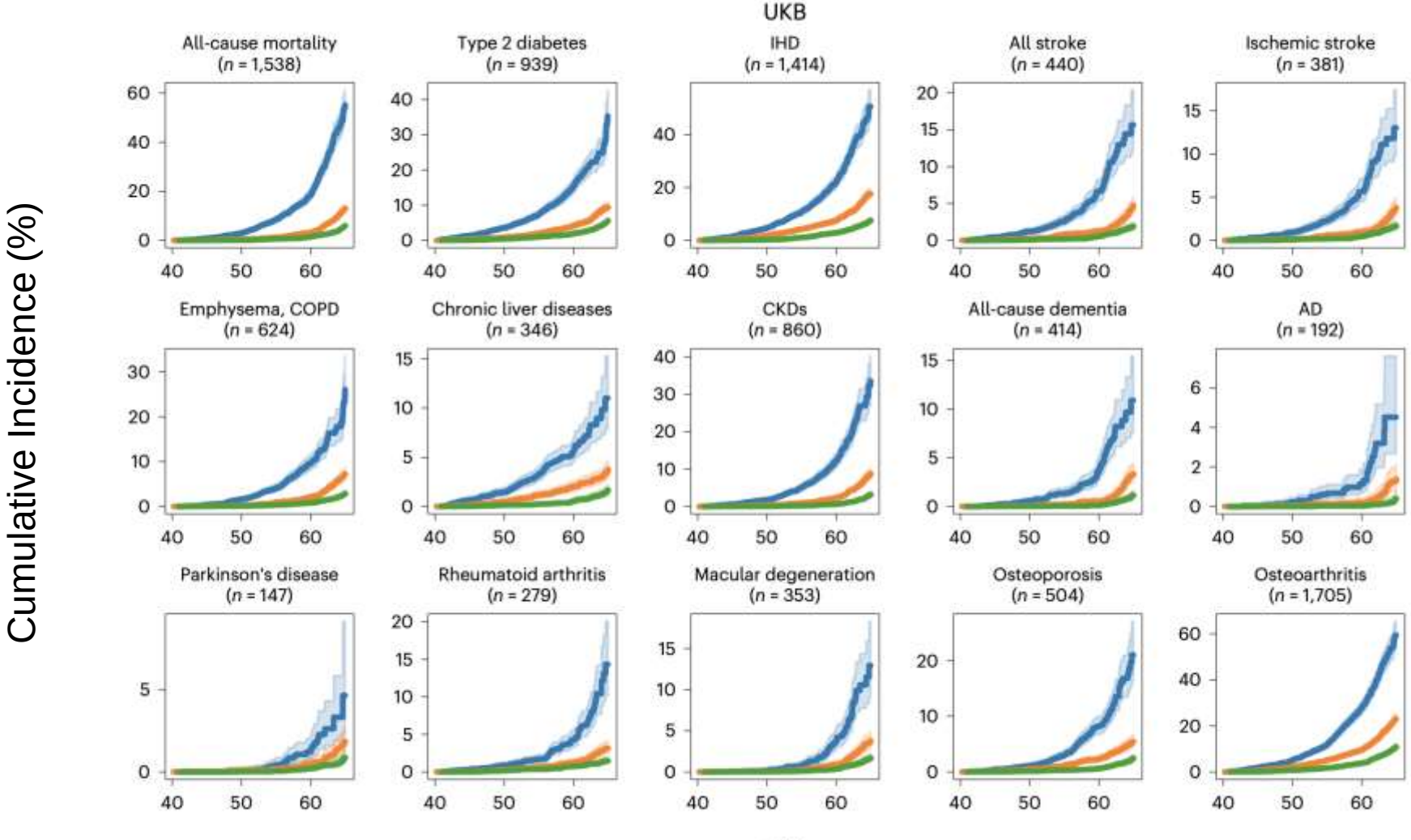
Environment



⇌ Genetics

⇌ Environment

Back to the Protein (ProtAge) Blood Biomarker



Protein Age Gap

ProtAgeGap

Top 10%

Median 10%

Bottom 10%

Argentieri, M. Austin, et al. "Proteomic aging clock predicts mortality and risk of common age-related diseases in diverse populations." *Nature medicine* 30.9 (2024): 2450-2460.

Journals of Gerontology: Biological Sciences
cite as: J Gerontol A Biol Sci Med Sci, 2019, Vol. 74, No. S1, S52–S60
doi:10.1093/gerona/glz220

THE GERONTOLOGICAL SOCIETY OF AMERICA®

OXFORD

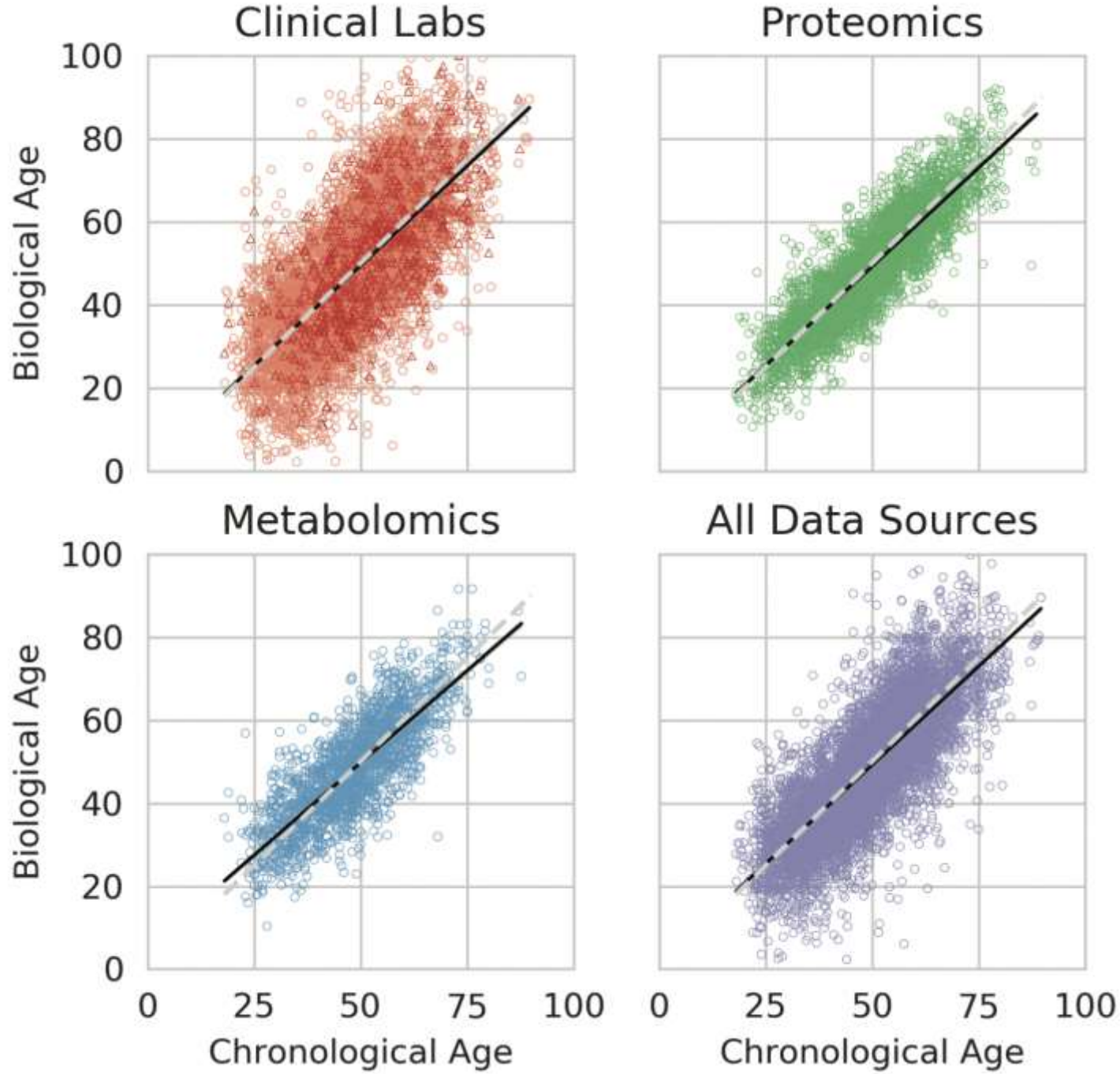
Healthy Longevity 2019: Supplement Article

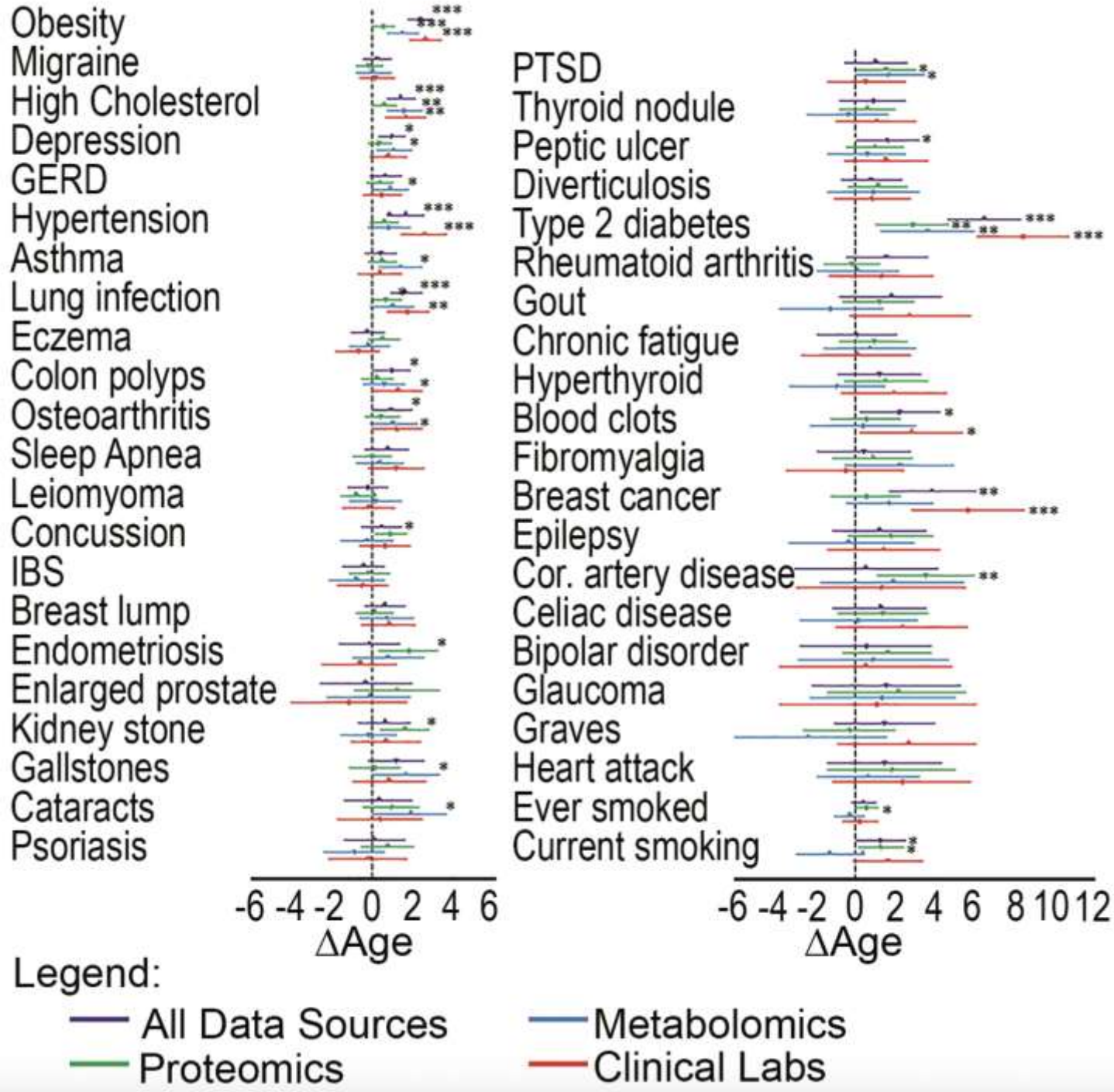
Multi-Omic Biological Age Estimation and Its Correlation With Wellness and Disease Phenotypes: A Longitudinal Study of 3,558 Individuals

John C. Earls, MSc,[1,2] Noa Rappaport, PhD,[1] Laura Heath, PhD,[1] Tomasz Wilmanski, PhD,[1] Andrew T. Magis, PhD,[1] Nicholas J. Schork, PhD,[3] Gilbert S. Omenn, MD, PhD,[4] Jennifer Lovejoy, PhD,[1] Leroy Hood, MD, PhD,[1,5,*] and Nathan D. Price, PhD,[1,2]

Biomarker = multimodal data including metabolites, proteins, and lab values

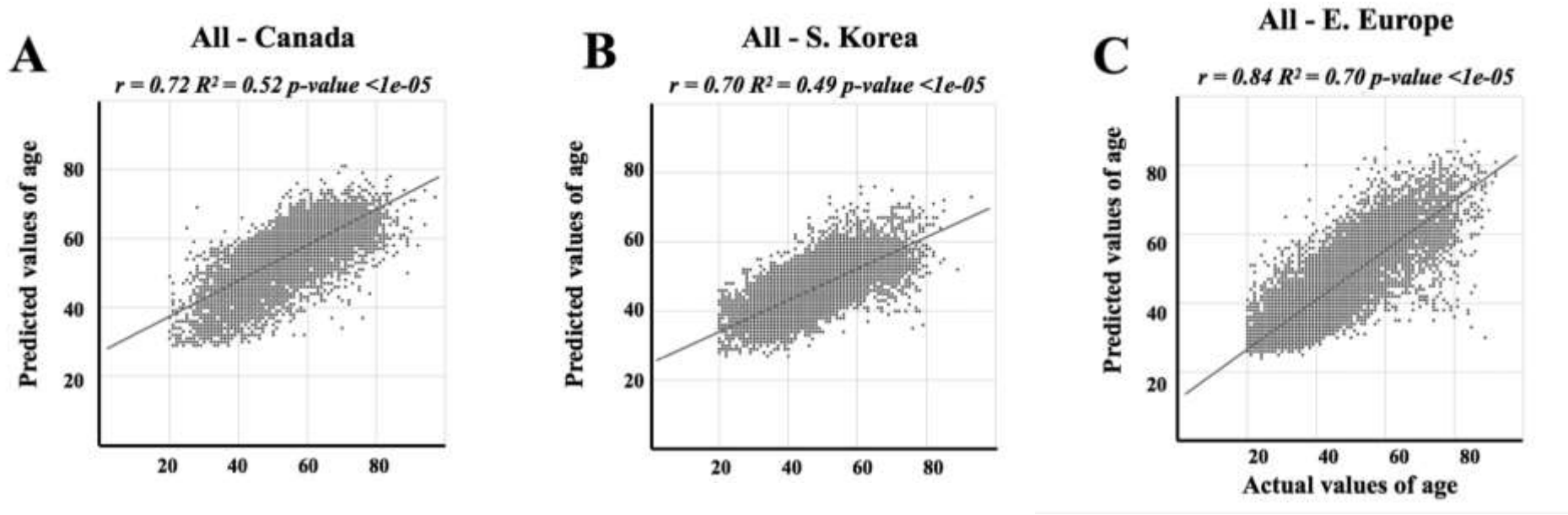
This is commercially available


Clinical Labs
Proteomics
Metabolomics
All Data Sources
Biological Age
Chronological Age
0
20
40
60
80
100
0
25
50
75
100


Obesity
Migraine
High Cholesterol
Depression
GERD
Hypertension
Asthma
Lung infection
Eczema
Colon polyps
Osteoarthritis
Sleep Apnea
Leiomyoma
Concussion
IBS
Breast lump
Endometriosis
Enlarged prostate
Kidney stone
Gallstones
Cataracts
Psoriasis
-6 -4 -2 0 2 4 6
ΔAge
PTSD
Thyroid nodule
Peptic ulcer
Diverticulosis
Type 2 diabetes
Rheumatoid arthritis
Gout
Chronic fatigue
Hyperthyroid
Blood clots
Fibromyalgia
Breast cancer
Epilepsy
Cor. artery disease
Celiac disease
Bipolar disorder
Glaucoma
Graves
Heart attack
Ever smoked
Current smoking
-6 -4 -2 0 2 4 6 8 10 12
ΔAge
Legend:
All Data Sources
Proteomics
Metabolomics
Clinical Labs

Do **biomarkers** generally hold across ethnic, cultural, and geographic differences?

Biomarkers generally work across ethnic, geographic, and cultural backgrounds, but may require **fine tuning**



Mamoshina, Polina, et al. "Population specific biomarkers of human aging: a big data study using South Korean, Canadian, and Eastern European patient populations." *The Journals of Gerontology: Series A* 73.11 (2018): 1482-1490.

5:39 5G

Post

Chamath Palihapitiya ALL IN
@chamath

Souscrire

This is my HRV and VO2Max over the past three months of using Whoop.

I travelled more, exercised less, slept less, ate more poorly and drank more often than normal. But I still spent time with my wife and kids consistently and kept my poker game on Thursdays which is my way for me to spend time with my friends.

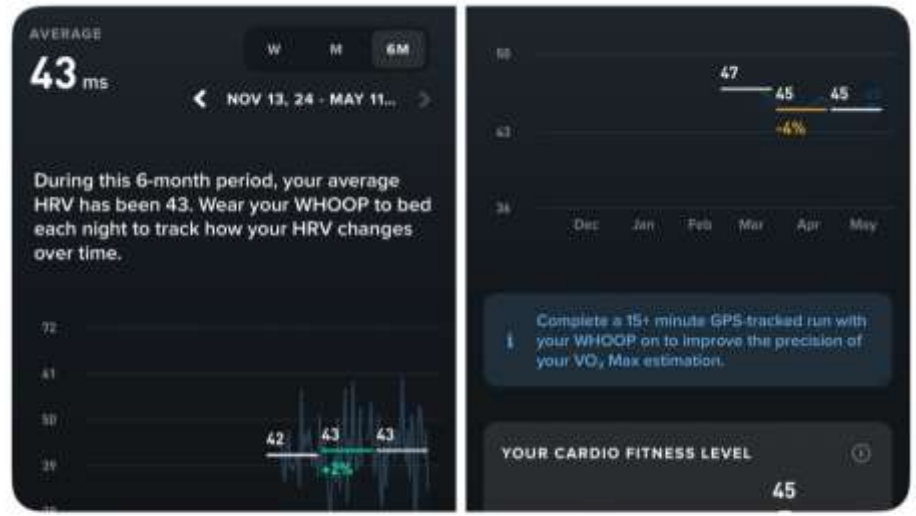
All of this said, I think this is what it looks like if you have to make trade offs and live a normal life.

I don't want to change what I accomplished these past three months.

Now what?

I'm asking this more philosophically in the context of what I'm supposed to be getting out of all of this measurement?

Postez votre réponse



12:49 p.m. · 5/11/25 · **299k** vues

Kevin Bass PhD MS @kevinnb... · 4 h

Bodyfat, LDL, blood pressure, how active you are is much better validated HRV. If HRV is declining, that's probably not good, but it's questionable. Just focus on staying fit. There is a reason Whoop isn't something doctors prescribe. It's because they have much better metrics Voir plus

6 6.7k

Bryan Johnson @bryan_johnson · 3 h

I'd focus in on a few power laws so that you can keep the lifestyle you want and also feel excellent, clear headed and have a stable mood.

The #1 thing I'd focus on is resting heart rate before bed. Try to get it as low as possible.

Eat earlier and lighter;
try to lessen Voir plus

17 22 523 52.6k

ericosiu @ericosiu · 4 h

Don’t know if I’d trust the vo2 max measurement from a wearable right now

7 2.3k

Chandan Ganwani @chandan... · 4 h

Throw it in the trash can and start working out.
Two words

Progressive Overload

677

Daniel Quigley @ddquigs · 4 h

Way too much measuring.

152

Will Ahmed @willahmed · 3 h

Hi Chamath whoop founder here. thanks for being on whoop. have you gotten the MG or 5.0 yet? I think you will like the Healthspan feature which shows you how metrics like RHR and VO2 max are trending relative to men your age. Explained here. x.com/willahmed/stat...

Will Ahmed @willahmed · 3 j

Our latest software innovations unlock entirely new dimensions of health.

Healthspan with WHOOP Age: a dynamic view of your biological age and pace of aging, based on your behaviors and physiology.

May 8 2025

Whoop

Healthspan: An all-new way to extend your prime for years to come

May 08, 2025

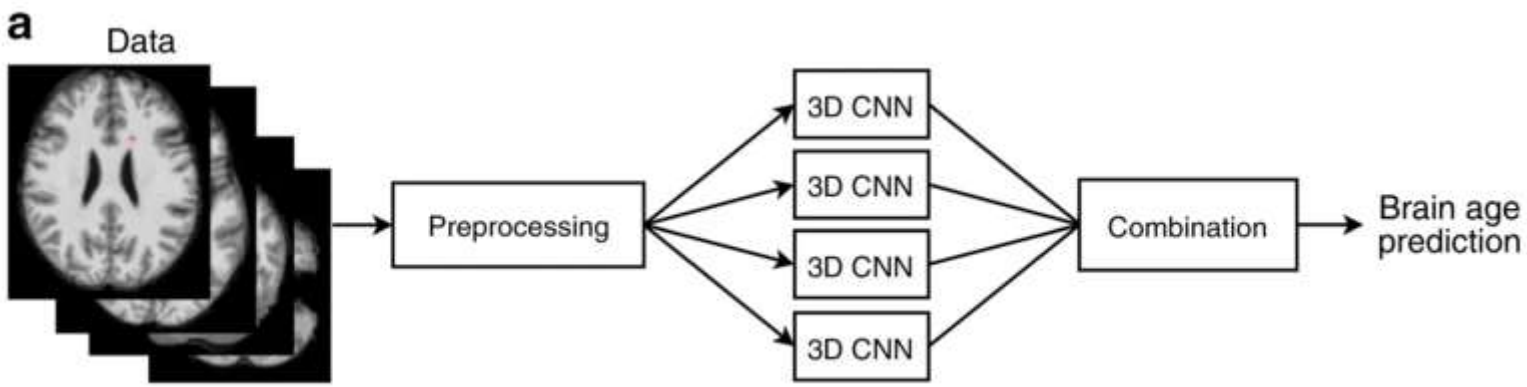
How will **AI** and **LLMs**
measure and act as
biomarkers, and how will
they allow us to **understand**
and even **extend** longevity

ARTICLE

https://doi.org/10.1038/s41467-019-13163-9 OPEN

Brain age prediction using deep learning uncovers associated sequence variants

B.A. Jonsson [1,2], G. Bjornsdottir [1], T.E. Thorgeirsson [1], L.M. Ellingsen [2], G. Bragi Walters [1,2], D.F. Gudbjartsson [1,2], H. Stefansson [1], K. Stefansson [1,2*] & M.O. Ulfarsson [1,2*]

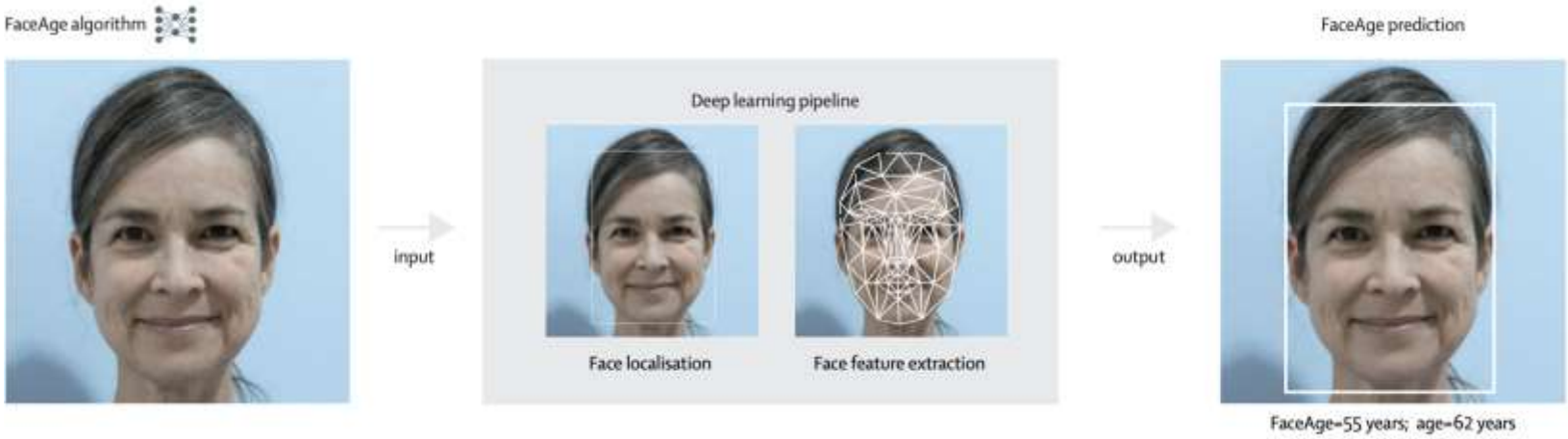


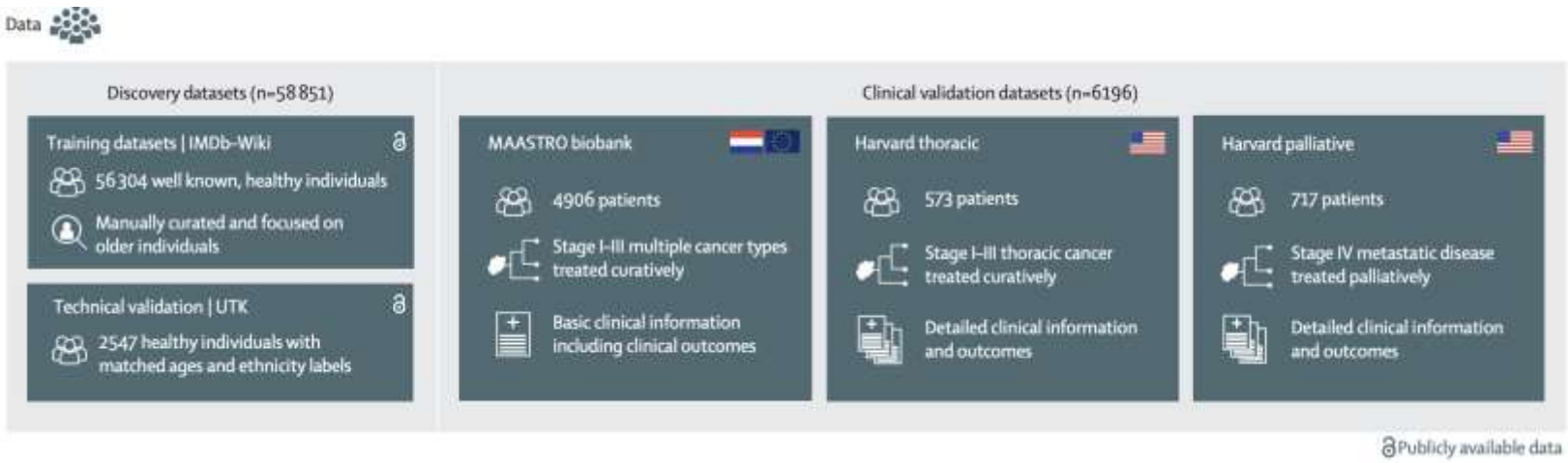
FaceAge, a deep learning system to estimate biological age from face photographs to improve prognostication: a model development and validation study

May 8 2025

Dennis Bontempi, Osbert Zalay*, Danielle S Bitterman, Nicolai Birkbak, Derek Shyr, Fridolin Haugg, Jack M Qian, Hannah Roberts, Subha Perni, Vasco Prudente, Suraj Pai, Andre Dekker, Benjamin Haibe-Kains, Christian Guthier, Tracy Balboni, Laura Warren, Monica Krishan, Benjamin H Kann, Charles Swanton, Dirk De Ruysscher, Raymond H Mak†, Hugo J W L Aerts†*

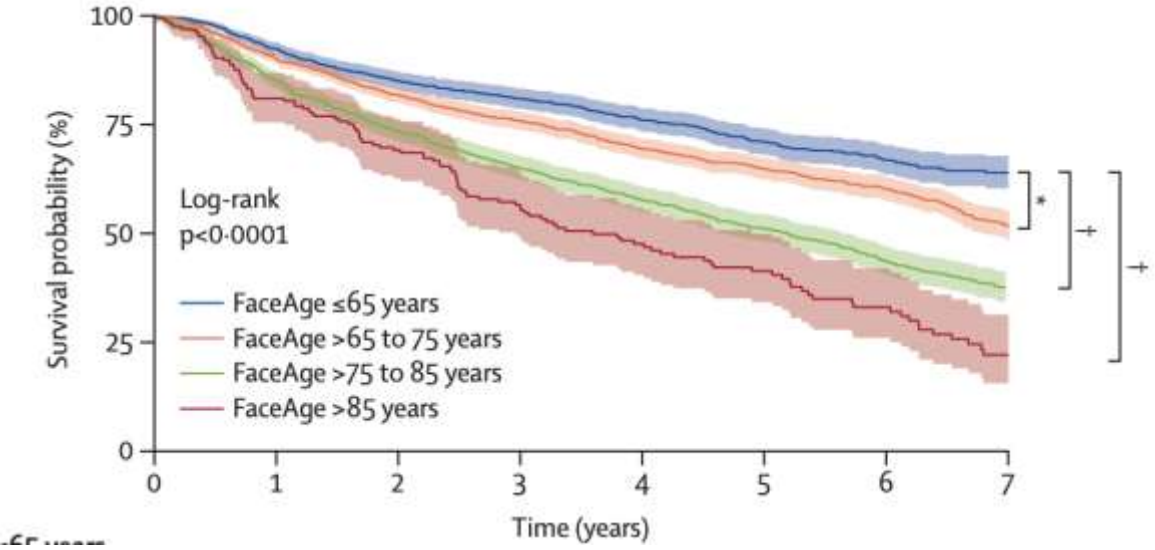
Lancet Digit Health 2025

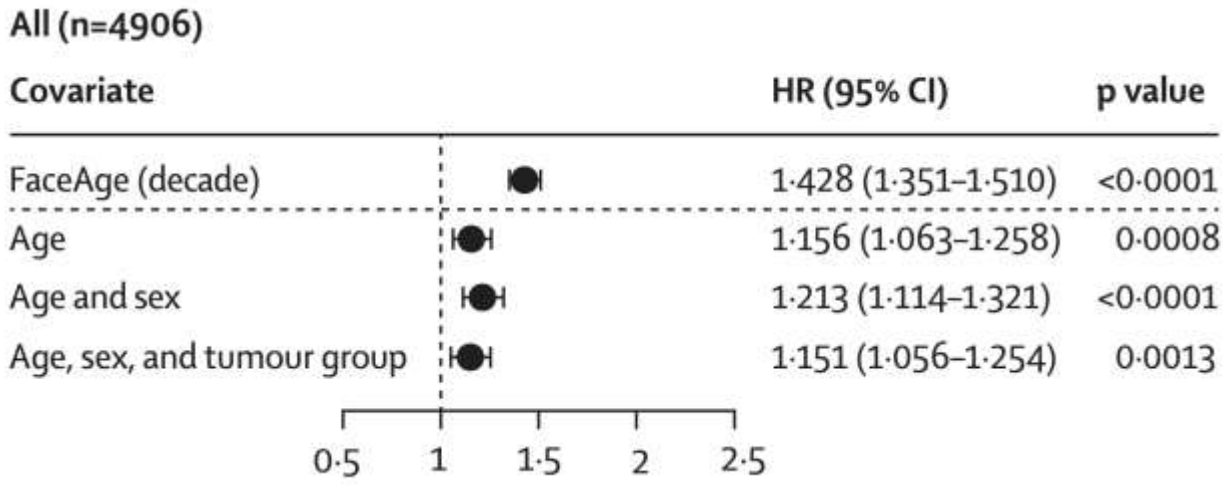




Bontempi, Dennis, et al. "FaceAge, a deep learning system to estimate biological age from face photographs to improve prognostication: a model development and validation study." *The Lancet Digital Health* (2025).

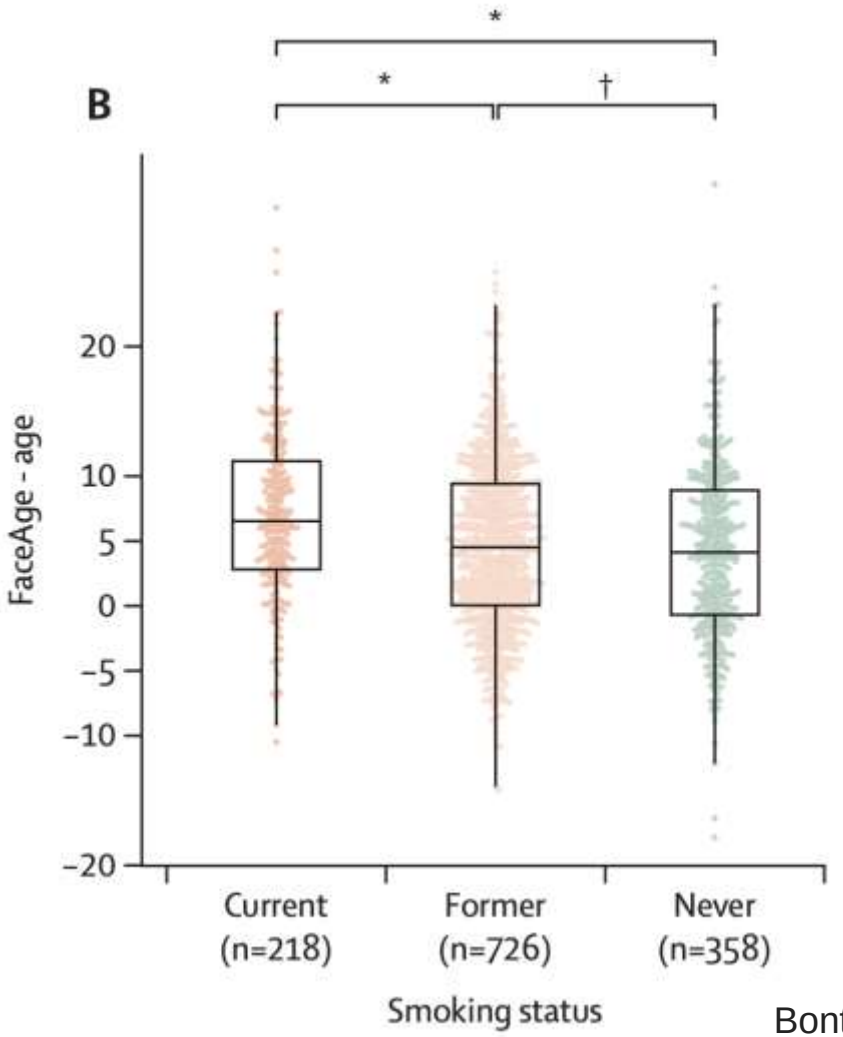
FaceAge determined by AI significantly predicts and stratifies overall survival in patients with cancer





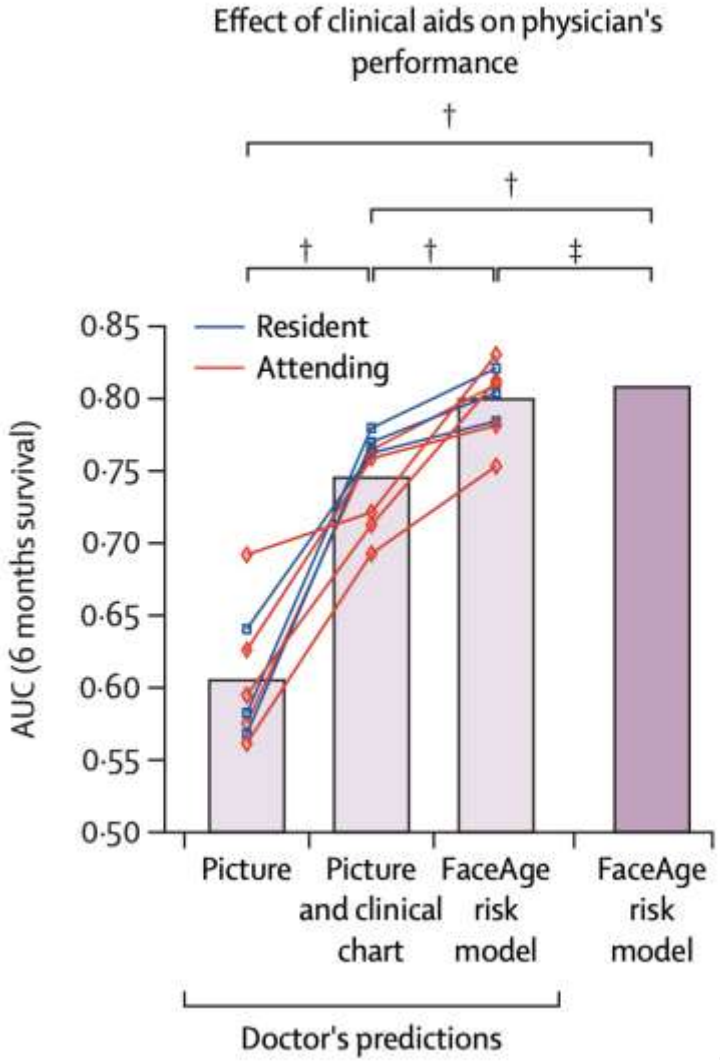
Bontempi, Dennis, et al. "FaceAge, a deep learning system to estimate biological age from face photographs to improve prognostication: a model development and validation study." *The Lancet Digital Health* (2025).

FaceAge determined by AI significantly distinguishes patients who smoke from non-smokers



Bontempi, Dennis, et al. "FaceAge, a deep learning system to estimate biological age from face photographs to improve prognostication: a model development and validation study." *The Lancet Digital Health* (2025).

FaceAge AI strongly predicts survival at 6 months, does so better than doctors, and can be used by doctors to improve their own predictions



Bontempi, Dennis, et al. "FaceAge, a deep learning system to estimate biological age from face photographs to improve prognostication: a model development and validation study." *The Lancet Digital Health* (2025).

Let’s reflect upon our journey through chronological time and chronological age

Santorio Santorio

1613

Santorio Santorio

1613

2025

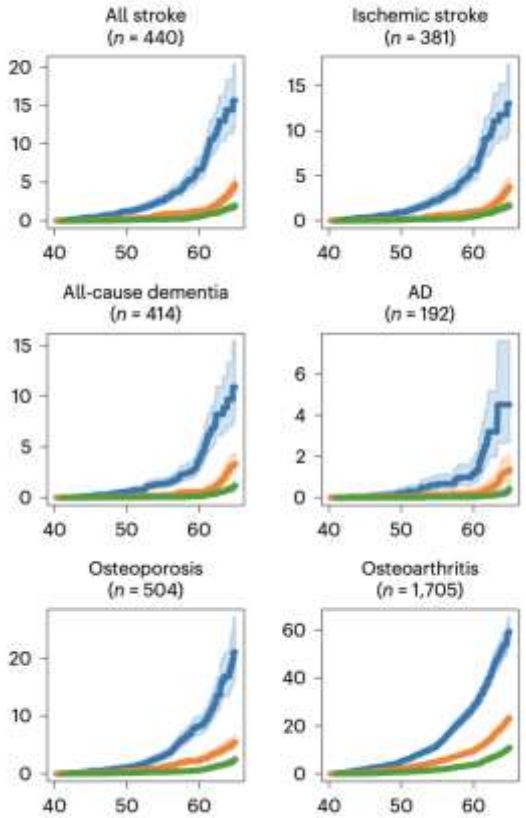
Next steps

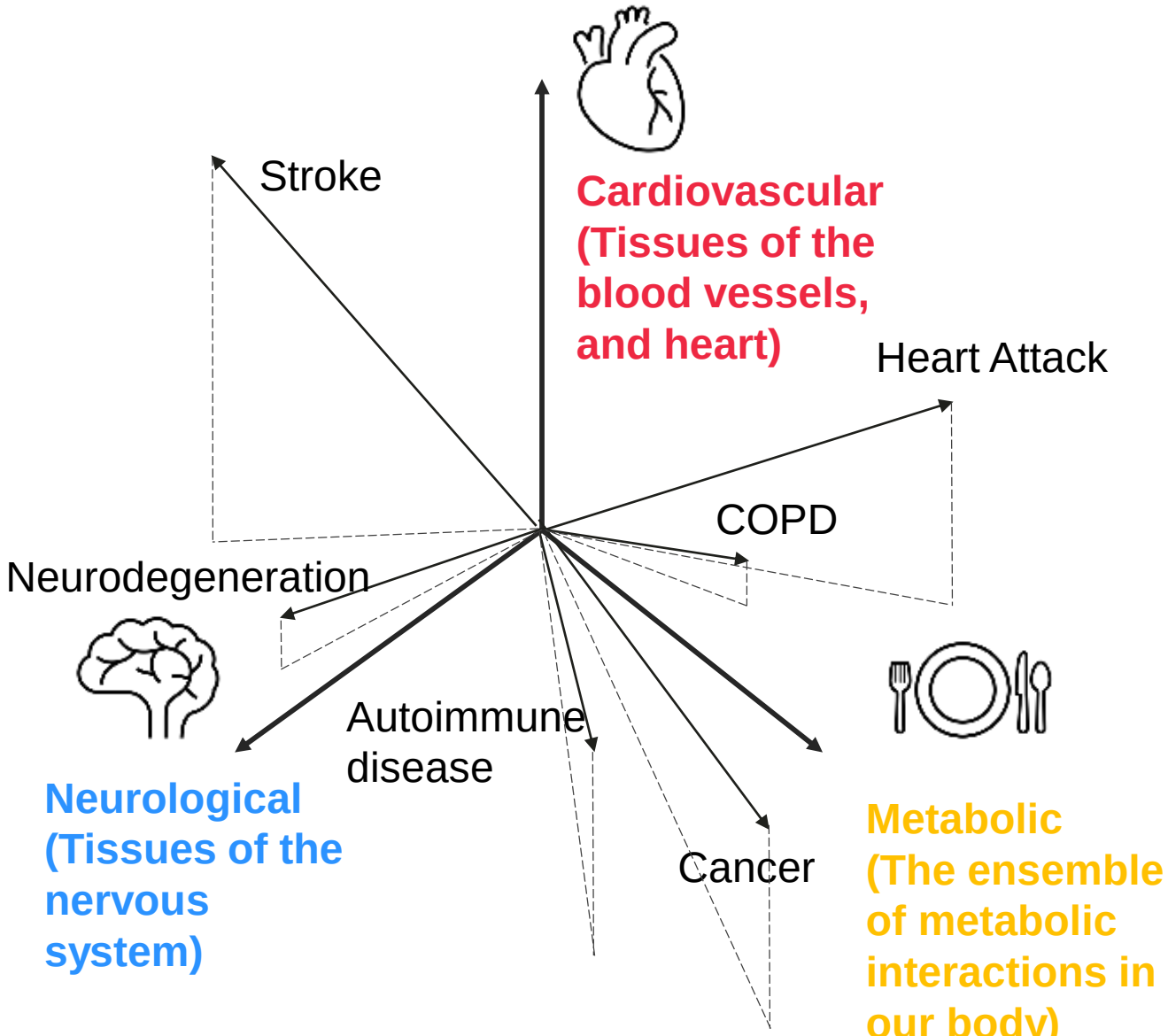
Just because something **correlates** with age, doesn't mean that it **causes** age

But if there is real biology at play, biomarkers may give hints for new therapeutic targets against aging

How much can we **personalize** recommendations using this biomarker data?

How much can we **personalize** recommendations using this biomarker data?





What do we actually do with all of this **data:**
Clinical trial end points

2 years of calorie restriction and cardiometabolic risk (CALERIE): exploratory outcomes of a multicentre, phase 2, randomised controlled trial

*William E Kraus, Manjushri Bhapkar, Kim M Huffman, Carl F Pieper, Sai Krupa Das, Leanne M Redman, Dennis T Villareal, James Rochon, Susan B Roberts, Eric Ravussin, John O Holloszy, Luigi Fontana, on behalf of the CALERIE Investigators**

Lancet Diabetes Endocrinol
2019; 7: 673–83

Can we demonstrate that measuring these biomarkers actually improves **healthspan**?

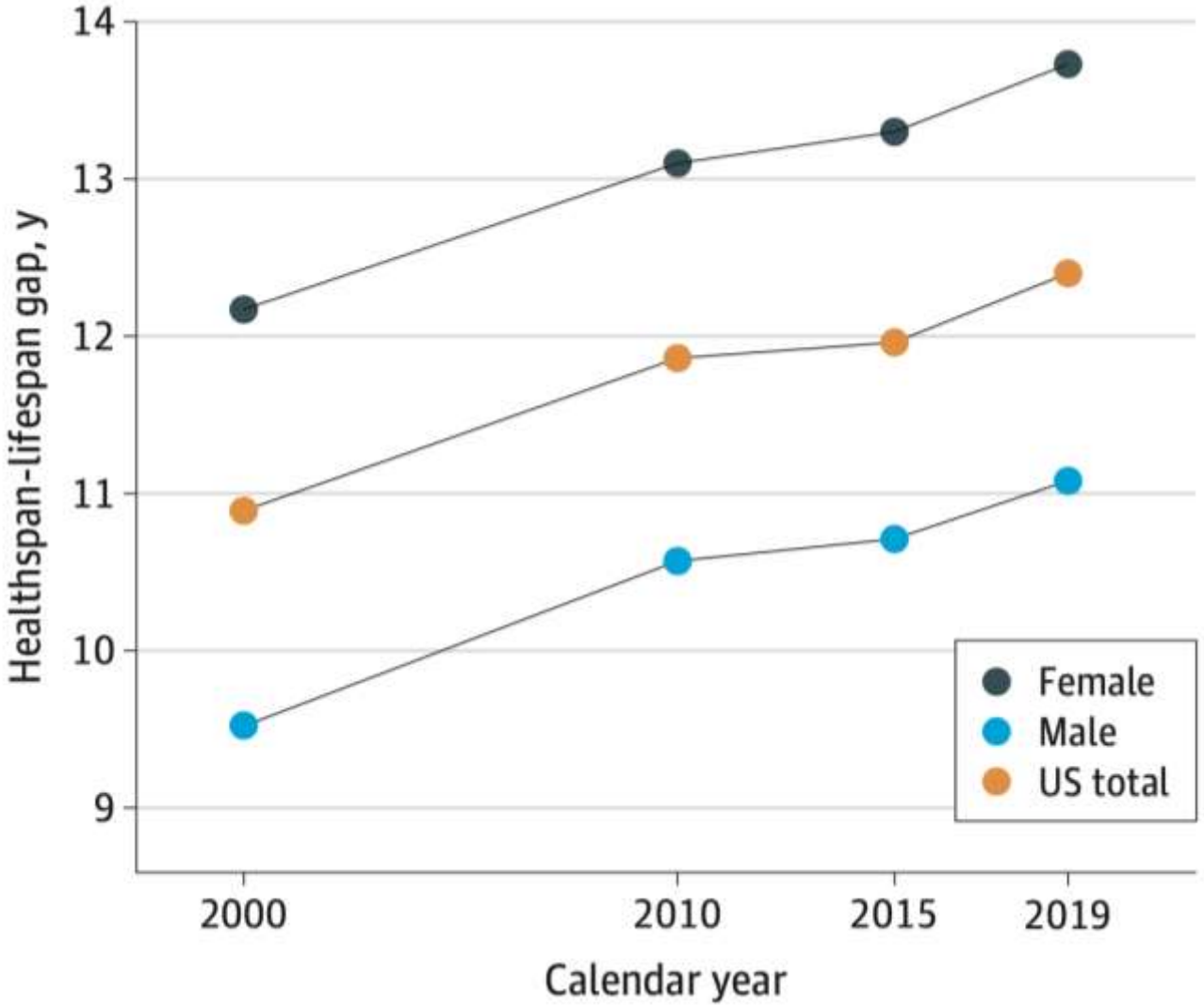
Now what?

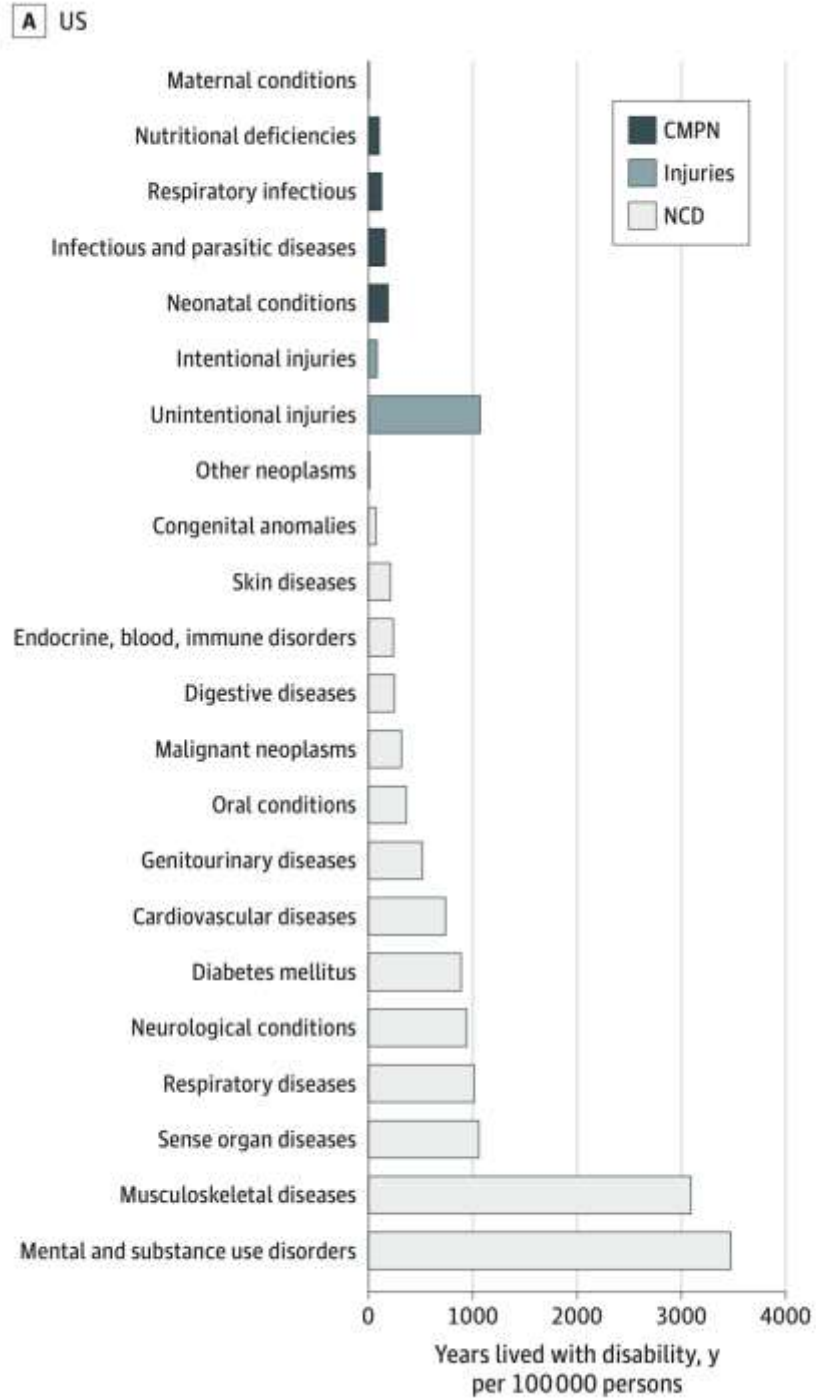
I'm asking this more philosophically in the context of what I'm supposed to be getting out of all of this measurement?

Maybe it is a **vibe**?

Where we came from:
One of the great challenges of our time is that human **lifespan** has stopped increasing, and **healthspan** has contracted

Will we be able to improve **healthspan**?



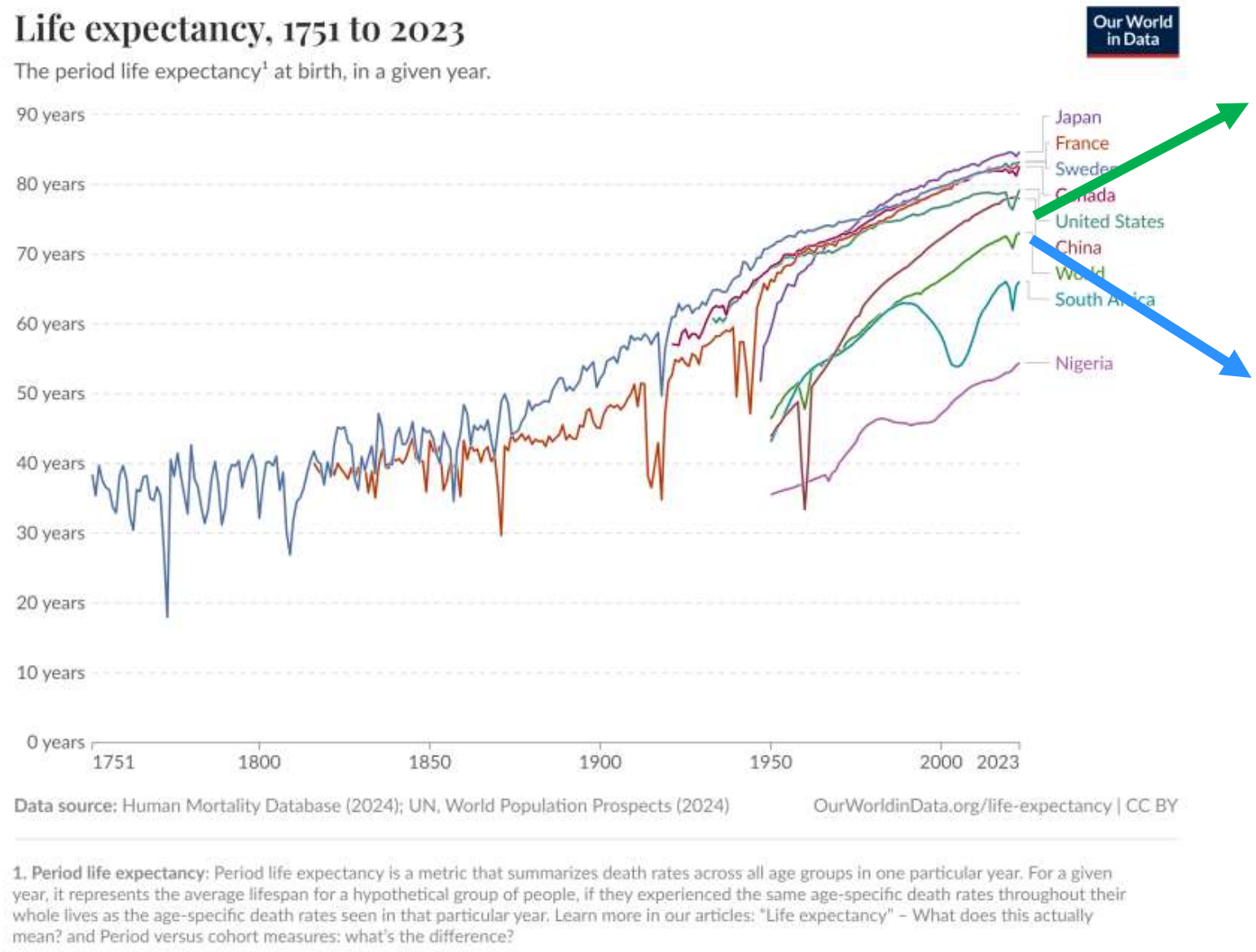

A US
Maternal conditions
Nutritional deficiencies
Respiratory infectious
Infectious and parasitic diseases
Neonatal conditions
Intentional injuries
Unintentional injuries
Other neoplasms
Congenital anomalies
Skin diseases
Endocrine, blood, immune disorders
Digestive diseases
Malignant neoplasms
Oral conditions
Genitourinary diseases
Cardiovascular diseases
Diabetes mellitus
Neurological conditions
Respiratory diseases
Sense organ diseases
Musculoskeletal diseases
Mental and substance use disorders
CMPN
Injuries
NCD
0
1000
2000
3000
4000
Years lived with disability, y
per 100 000 persons

What will life expectancy in the next 50 years look like

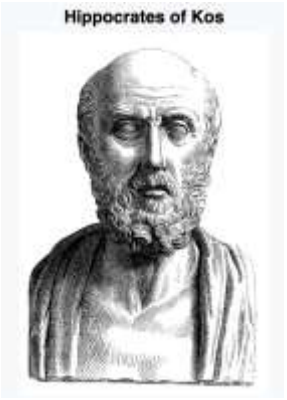
1600,
~33 years

400 BC,
~25 years

400 BC — 1600



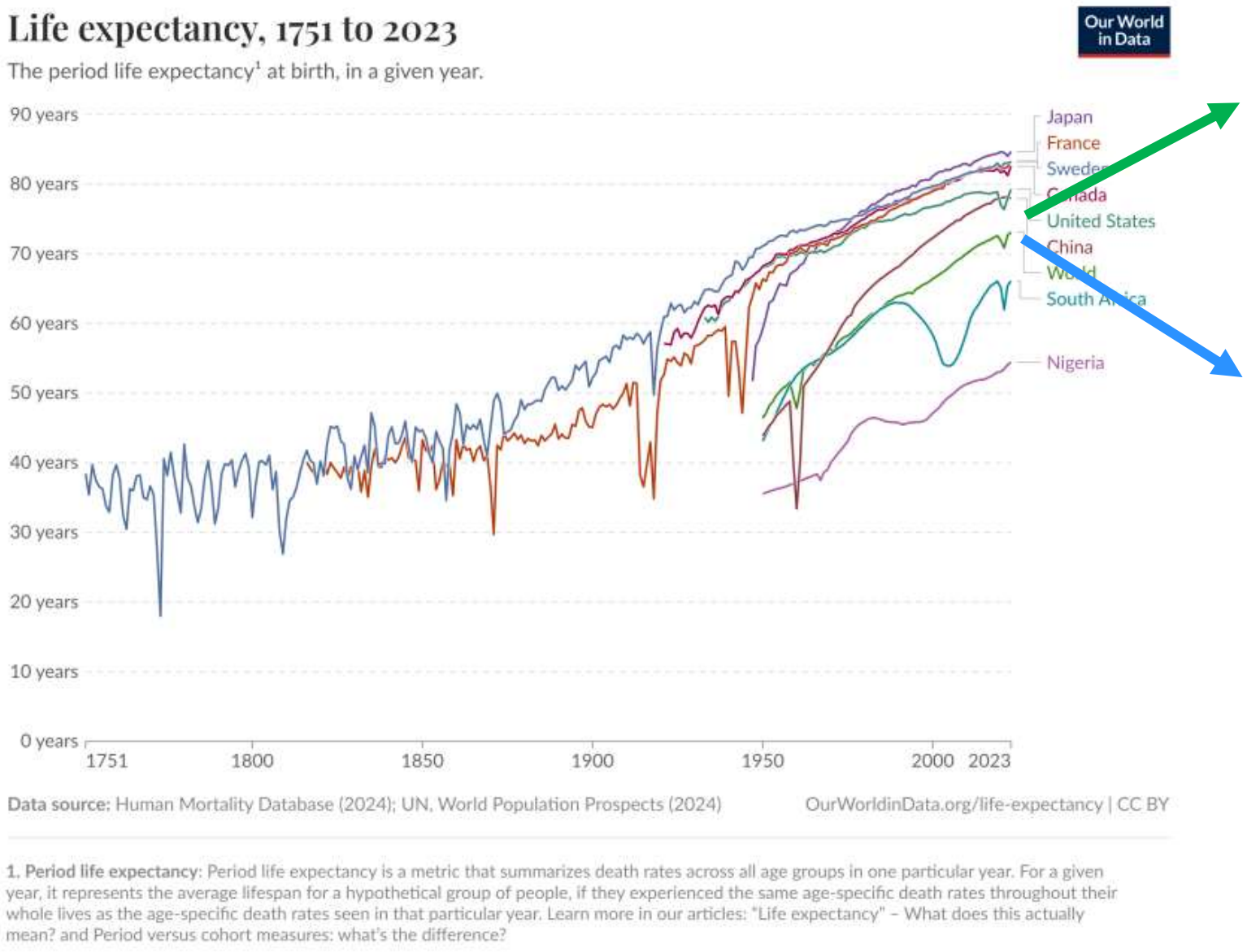
How do we overcome health and lifespan **stagnation**



400 BC,
~25 years

1600,
~33 years

400 BC — 1600



Biomarkers will allow us not only to measure the progress in our own health journey

But also our progress in the critical human endeavor of increasing **health and life span**

You have years ahead of you, and I want those years to be filled with ***health*** *and* ***happiness***

Thank you

TODO:

Bring it back to Grip Strenght, blood pressure, cholesterol, the basics
Add any evaluation of Whoop healthspan
Add another wearable?
Delete second age biomarker paper
Show that organ specific data matters
Show that there are RCTs where they use these biomarkes as endpoints, so that they actually matter

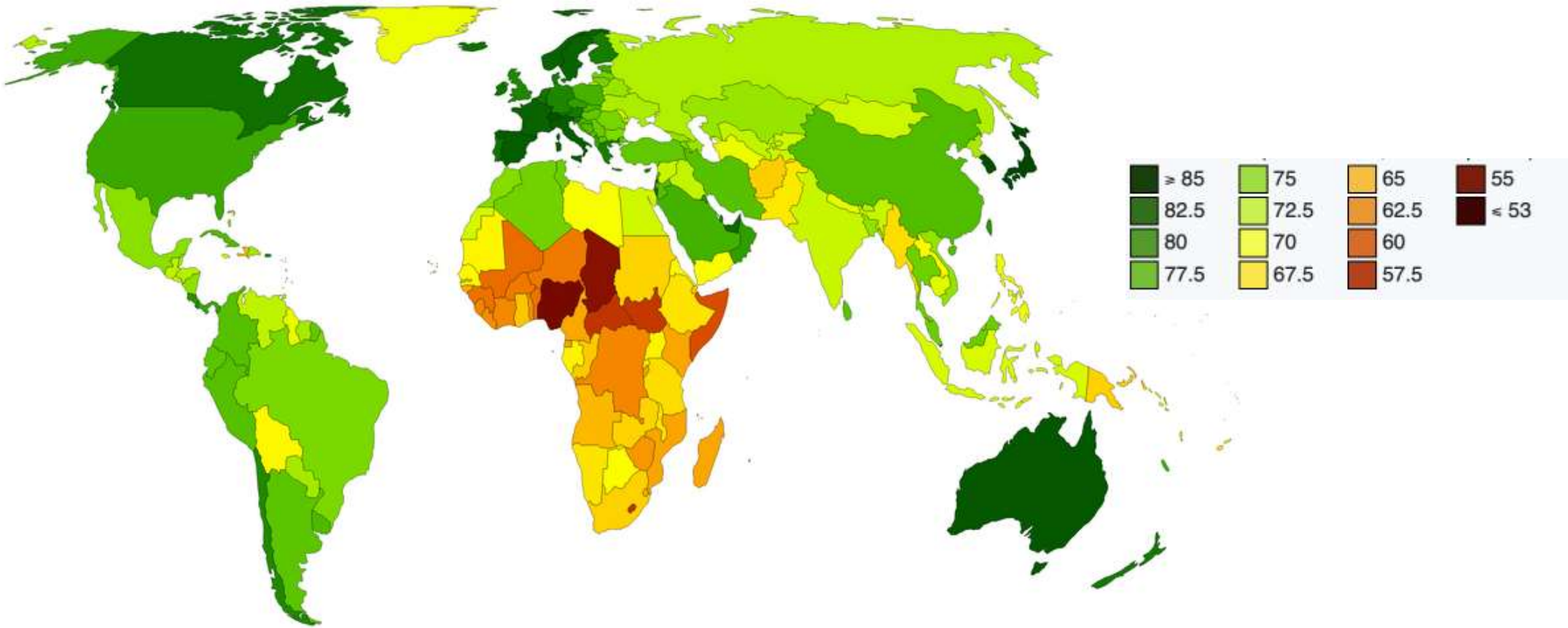
AI
Bring it back to lifespan and age rates over time

EXTRA SLIDES NOT USED

EXTRA SLIDES NOT USED

EXTRA SLIDES NOT USED

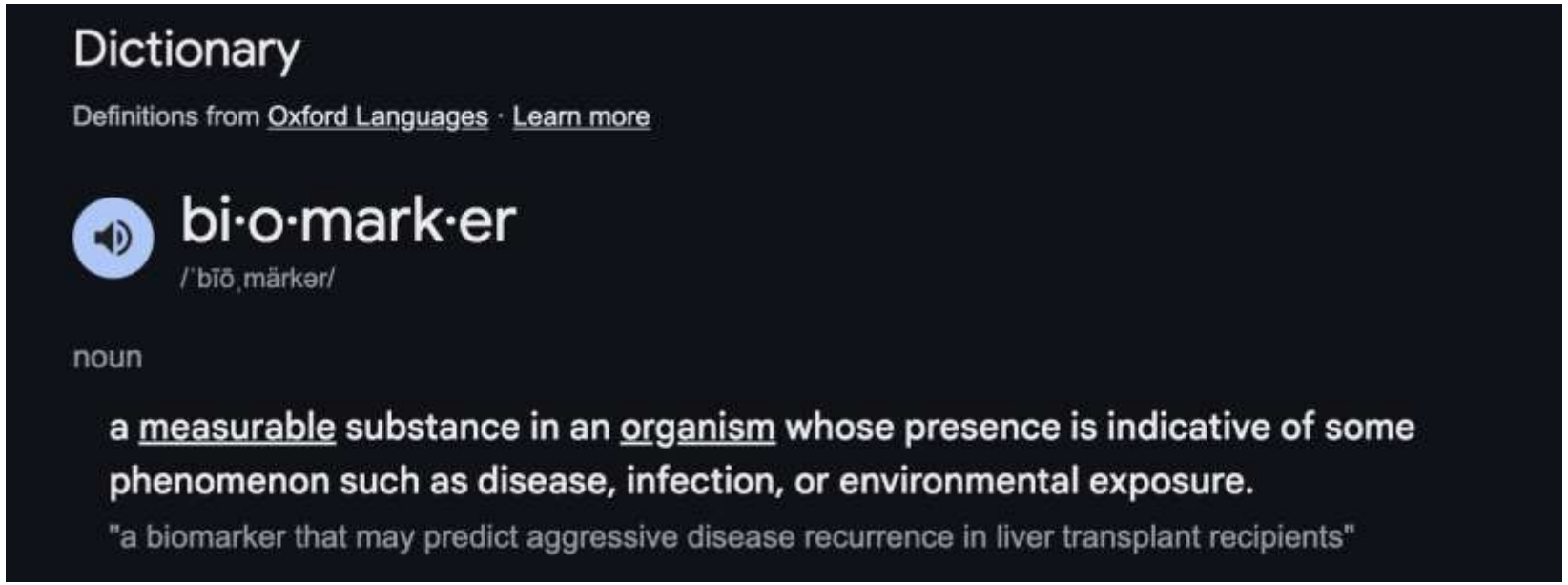
Life expectancy, 2023



Wikipedia

But what is a life worth living

What is a life of **thriving**


Dictionary
Definitions from Oxford Languages · Learn more
bi·o·mark·er
/ˈbīōˌmärkər/
noun
a measurable substance in an organism whose presence is indicative of some phenomenon such as disease, infection, or environmental exposure.
"a biomarker that may predict aggressive disease recurrence in liver transplant recipients"

bi·o·mark·er
/ˈbīōˌmärkər/

1935 Caloric restriction in rats is seen to increase lifespan

safety[15] for application to biomarkers of aging. Among the listed categories of biomarkers, predictive and response biomarkers are currently the most relevant in the context of aging research, although it should be noted that no aging biomarkers of any category have been approved by U.S. regulators for clinical applications.

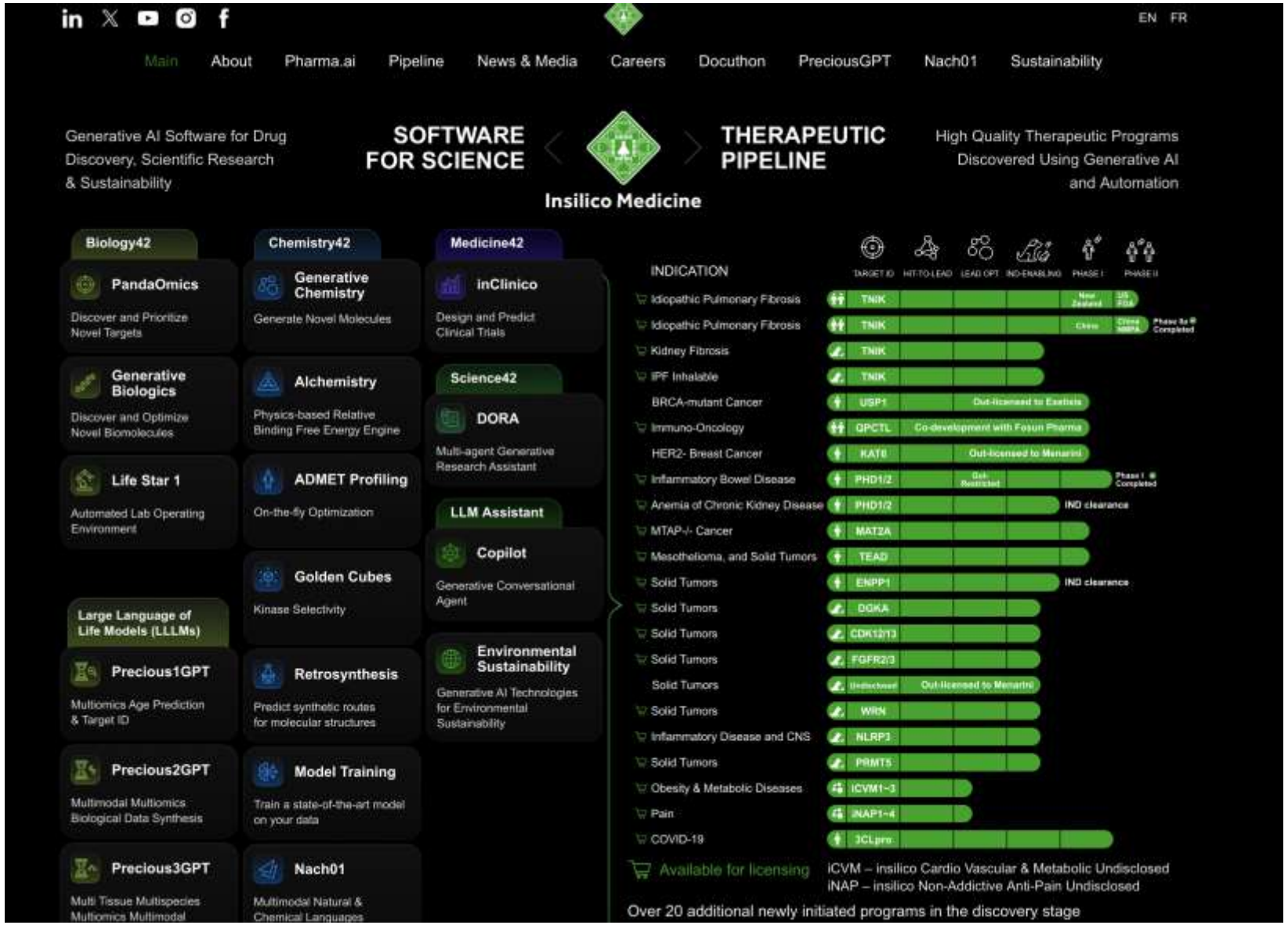
Predictive biomarkers

Epigenetic Clock

Jim Kirkland Aging

American Federation for Aging

Buck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Main About Pharma.ai Pipeline News & Media Careers Docuthon PreciousGPT Nach01 Sustainability
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SOFTWARE FOR SCIENCE
Insilico Medicine
THERAPEUTIC PIPELINE
High Quality Therapeutic Programs Discovered Using Generative AI and Automation
Biology42
PandaOmics
Discover and Prioritize Novel Targets
Generative Biologics
Discover and Optimize Novel Biomolecules
Life Star 1
Automated Lab Operating Environment
Chemistry42
Generative Chemistry
Generate Novel Molecules
Alchemistry
Physics-based Relative Binding Free Energy Engine
ADMET Profiling
On-the-fly Optimization
Golden Cubes
Kinase Selectivity
Medicine42
inClinico
Design and Predict Clinical Trials
Science42
DORA
Multi-agent Generative Research Assistant
LLM Assistant
Copilot
Generative Conversational Agent
Environmental Sustainability
Generative AI Technologies for Environmental Sustainability
Large Language of Life Models (LLLMs)
Precious1GPT
Multiomics Age Prediction & Target ID
Precious2GPT
Multimodal Multiomics Biological Data Synthesis
Precious3GPT
Multi Tissue Multispecies Multiomics Multimodal
Retrosynthesis
Predict synthetic routes for molecular structures
Model Training
Train a state-of-the-art model on your data
Nach01
Multimodal Natural & Chemical Languages
INDICATION
TARGET ID
HIT-TO-LEAD
LEAD OPT
IND-ENABLING
PHASE I
PHASE II
Idiopathic Pulmonary Fibrosis
TNIK
Idiopathic Pulmonary Fibrosis
TNIK
Kidney Fibrosis
TNIK
IPF Inhalable
TNIK
BRCA-mutant Cancer
USP1
Out-licensed to Exelixis
Immuno-Oncology
GPCTL
Co-development with Fosun Pharma
HER2- Breast Cancer
KAT6
Out-licensed to Menarini
Inflammatory Bowel Disease
PHD1/2
Anemia of Chronic Kidney Disease
PHD1/2
IND clearance
MTAP-/- Cancer
MAT2A
Mesothelioma, and Solid Tumors
TEAD
Solid Tumors
ENPP1
IND clearance
Solid Tumors
DGKA
Solid Tumors
CDK12/13
Solid Tumors
FGFR2/3
Solid Tumors
Out-licensed to Menarini
Solid Tumors
WRN
Inflammatory Disease and CNS
NLRP3
Solid Tumors
PRMT5
Obesity & Metabolic Diseases
iCVM1~3
Pain
iNAP1~4
COVID-19
3CLpro
Available for licensing
iCVM – insilico Cardio Vascular & Metabolic Undisclosed
iNAP – insilico Non-Addictive Anti-Pain Undisclosed
Over 20 additional newly initiated programs in the discovery stage

https://einsteinmed.edu/faculty/484/nir-barzilai

Response biomarkers

Prognostic

Table 2. A select list of human predictive biomarkers of aging associated with various age-related conditions and their commercial applications

Biomarker of aging	Biomarker type	Age-related conditions	Commercial application[a]
DNAmAge (Horvath,[13] Hannum[21])	Epigenetic clocks, based on a set of DNA methylation measures associated with chronological age	Associated with multiple aging diseases and time-to-death, based on meta-analyses[22,23]	Licensed for estimating chronological age
GlycanAge[24]	A panel of molecular measures based on glycans attached to Immunoglobulin G (IgG) antibodies associated with chronological age	Associated with multiple diseases[25]	Commercially used to track responses to lifestyle changes
PhenoAge[26] and GrimAge[27]	Epigenetic clocks, based on a set of DNA methylation measures associated with "clinical phenotypic age measures" (a panel of age-associated molecular and physiological biomarkers, measured in blood)	Higher association with multiple aging-related diseases and time-to-death, compared to previous DNAm biomarkers, and associated with healthspan;[26,27] associated with multiple age-related clinical phenotypes (walking speed, frailty, and cognitive functions)[28]	Licensed for optimizing life insurance
DunedinPoAm and DunedinPACE[29]	Epigenetic clocks, based on a set of DNA methylation measures associated with "pace of aging measures" (a panel of age-associated molecular and physiological biomarker measurements of different organ systems)	Associated with the incidence of multiple chronic diseases, including dementia, disability, and mortality[29,30]	Licensed for tracking the rate of aging
Multi-omic biological age estimation based on KDM (Klemera-Doubal method)[31]	KDM applied to over 900 principal component transformed biomarkers (metabolites, proteins, genomics, and clinical measures)	Positively and negatively modulated by "healthy" and "unhealthy" behaviors/health conditions (e.g., type 2 diabetes), respectively[31]	Licensed for tracking biological age
Aging.AI, Deep Transcriptomic and Proteomic Clocks	AI-based blood clocks, based on hematological parameters and transcriptomic and proteomic data	Associated with all-cause mortality[32] and muscle wasting[33]	Commercially available for use in clinical trials

[a]See Table S1 for commercial application details.

Table 3. A list of recently completed or ongoing registered clinical trials or *post hoc* analyses using epigenetic biomarkers of aging with a focus on longevity

Type[a]	Study	Intervention	Title	Design, N, age range, (m/f)	Primary outcome measure	Biomarker	Biomarker outcome measure	Result
Lifestyle	CALERIE	Caloric restriction for 2 years	Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy	RCT, 218, 21–50	Change in core body temperature and metabolic rate at 24 months compared to baseline	DunedinPACE, GrimAge, PhenoAge (blood chemistry), Horvath and Hannum clocks	*Post hoc* analysis	Significant reduction of DunedinPACE and PhenoAge (blood chemistry), no significant effects for other biomarkers of aging[34,35]
	DAMA	Plant-food-rich diet, exercise	Diet Exercise and Mammography Trial	RCT, 219, 50–69 (f)	Change in mammographic breast density	GrimAge	*Post hoc* analysis	Dietary intervention: 0.66 years ↓ (GrimAge)[36]
	MDL	Diet, exercise, stress management, phytonutrient and probiotic supplements	Methylation Diet and Lifestyle Study	RCT, 44, 50–72 (m)	Health-related quality of life	Horvath clock	Exploratory	3.2 years ↓[37]
	TirolGESUND	Intermittent fasting or smoking cessation	TirolGESUND: General Exercise, Smoking Undone, and Nutrition Diet	BCS, 156, 30–60 (f)	Epigenetic biomarkers of aging and disease risk	WID-REA, -RIA, pcgtAge, and WID-SOLA	Primary	Not yet reported
Pharma-cological	Dasatinib/ Quercetin	Dasatinib and quercetin	Safety and Effectiveness of Quercetin & Dasatinib on Epigenetic Aging	BCS, 25*, >40	Epigenetic clock	DNAm (exact biomarker not defined)	Primary	Not yet reported
	RAPA	Rapamycin	Topical-RAPA Use in Inflammation Reversal and Re-setting the Epigenetic Clock	RCT, 50*, 65–95	Epigenetic clock	Horvath clock	Primary	Not yet reported
	SGLT2i	Dapagliflozin	SGLT2 Inhibition in Older Obese Adults With Pre-diabetes	RCT, 20*, >60	Advanced glycation end products in urine	DNAm (exact biomarker not defined)	Secondary	Not yet reported
	TRIIM-X	Growth hormone for 1 year	Thymus Regeneration, Immunorestoration, and Insulin Mitigation Extension	RCT, 85*, 40–80	Epigenetic clock, thymus regeneration	GrimAge	Primary	Not yet reported

Table 3. ***Continued***

Type[a]	Study	Intervention	Title	Design, N, age range, (m/f)	Primary outcome measure	Biomarker	Biomarker outcome measure	Result
Plasmapheresis	PLASMA	Young plasma	The Plasma for Alzheimer SymptoM Amelioration (PLASMA) Study	BCS, 18, 60–95	Adverse effects as a measure of safety and tolerability	GrimAge, Horvath, Hannum, and Skin and Blood[38] clocks, PhenoAge, DNAmTL[39]	*Post hoc* analysis	0.86 years ↓ (GrimAge), no change in other clocks[40]
	Plasma-pheresis	Young plasma	Effects of Plasmapheresis on Aging Biomarkers	O, 41*, 40–60	Epigenetic clock	DNAm (exact biomarker not defined)	Primary	Not yet reported
	RESET-YOUTH	Young plasma	Reversing Epigenetic and Other Markers of Senescence by Transfusing Young Plasma To Older Human Subjects	BCS, 2120*, >40 (m)	Epigenetic clock	DNAm (exact biomarker not defined)	Primary	Not yet reported
Supplement	AC11	AC-11 supplement for 2 months	AC-11 Supplement and Biological Aging	BCS, 32*, >55	Epigenetic clock, telomere length	DNAm (exact biomarker not defined)	Primary	Not yet reported
	D-SUNNY	Vitamin D for 4 months	Vitamin D Supplementation in Overweight/Obese African American Adults and Youth	RCT, 74, 13–45	Cardiovascular phenotypes, dose-response	Horvath and Hannum age deviation	*Post hoc* analysis	1.85 years ↓ (Horvath age deviation) compared to placebo[41]
	NMN	Nicotinamide mononucleotide	To Evaluate the Efficacy and Safety of NMN as an Anti-ageing Supplement in Middle Aged and Older Adults	RCT, 90, 40–65	Cellular NAD^+ levels, walking test, health questionnaire	Aging.AI 3.0 calculator (https://www.aging.ai)	Exploratory	Maintenance of blood biological age compared to placebo[42]
	Rejuvant	Alpha-ketoglutarate	Rejuvant™ Safety and Biomarker Study	RCT, 100, 45–75	c-reactive protein levels	DNAm (exact biomarker not defined)	Exploratory	Not yet reported

[a]Table is ordered by intervention type (lifestyle, pharmacological, plasmapheresis, and supplement) and alphabetically. Most clinical studies to date have used epigenetic clocks such as the Horvath Clock. N, number of participants; m, male participants only; f, female participants only; RCT, randomized controlled trial; BCS, baseline-controlled study; O, observational; *, estimated.

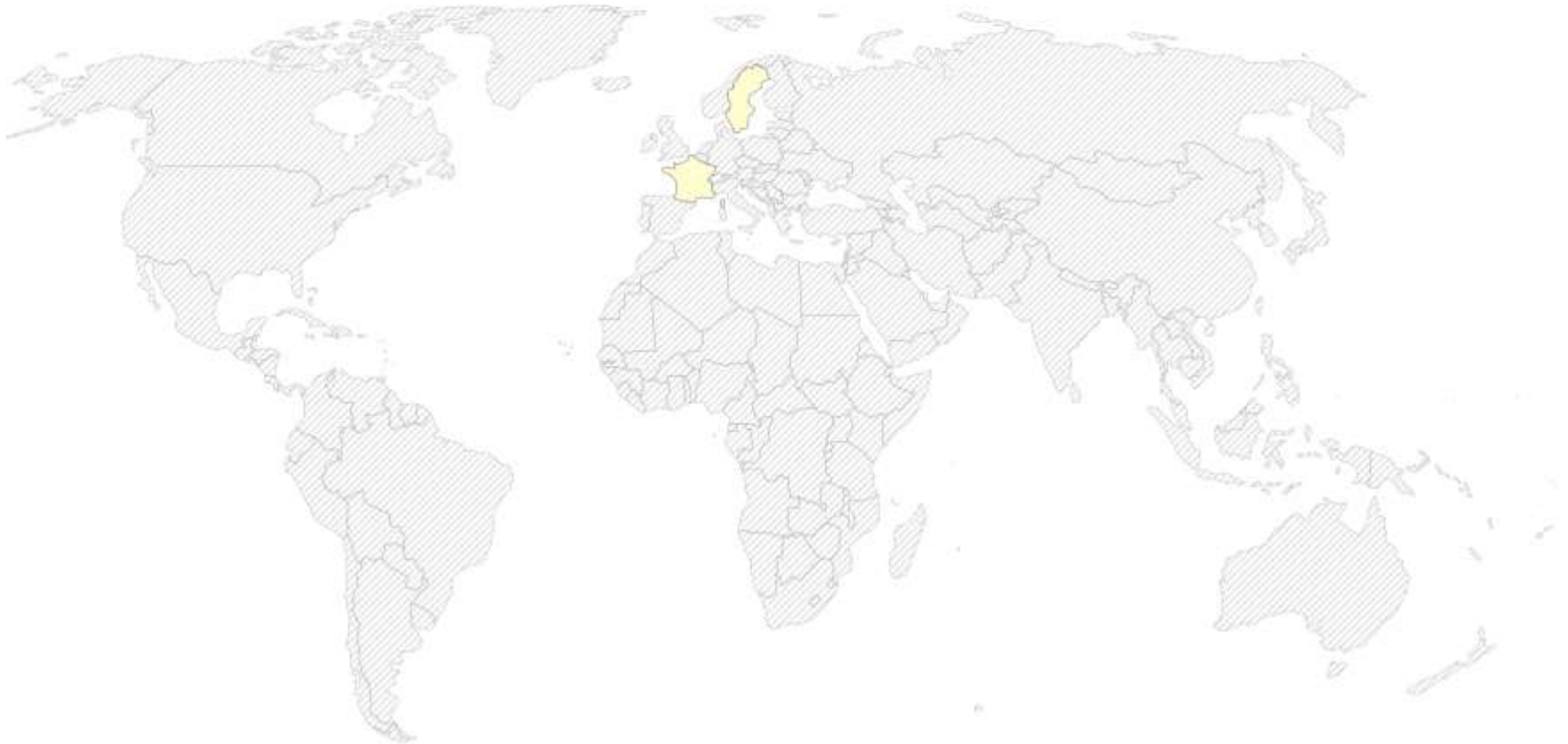
Life expectancy, 1831

The period life expectancy at birth, in a given year.

Our World in Data

Table | Map | Chart

World



No data | 40 years | 45 years | 1831 | 55 years | 60 years | 65 years | 70 years | 75 years | 80 years | 85 years

Pause time-lapse | 1751 | 2023

Data source: Human Mortality Database (2024); UN, World Population Prospects (2024) – Learn more about this data

OurWorldinData.org/life-expectancy | CC BY

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How far have we come

How far have we come

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Written by: Bryan Johnson | Published on: January 10, 2025

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Schedule your blood draw at LabCorp at a location close to you.

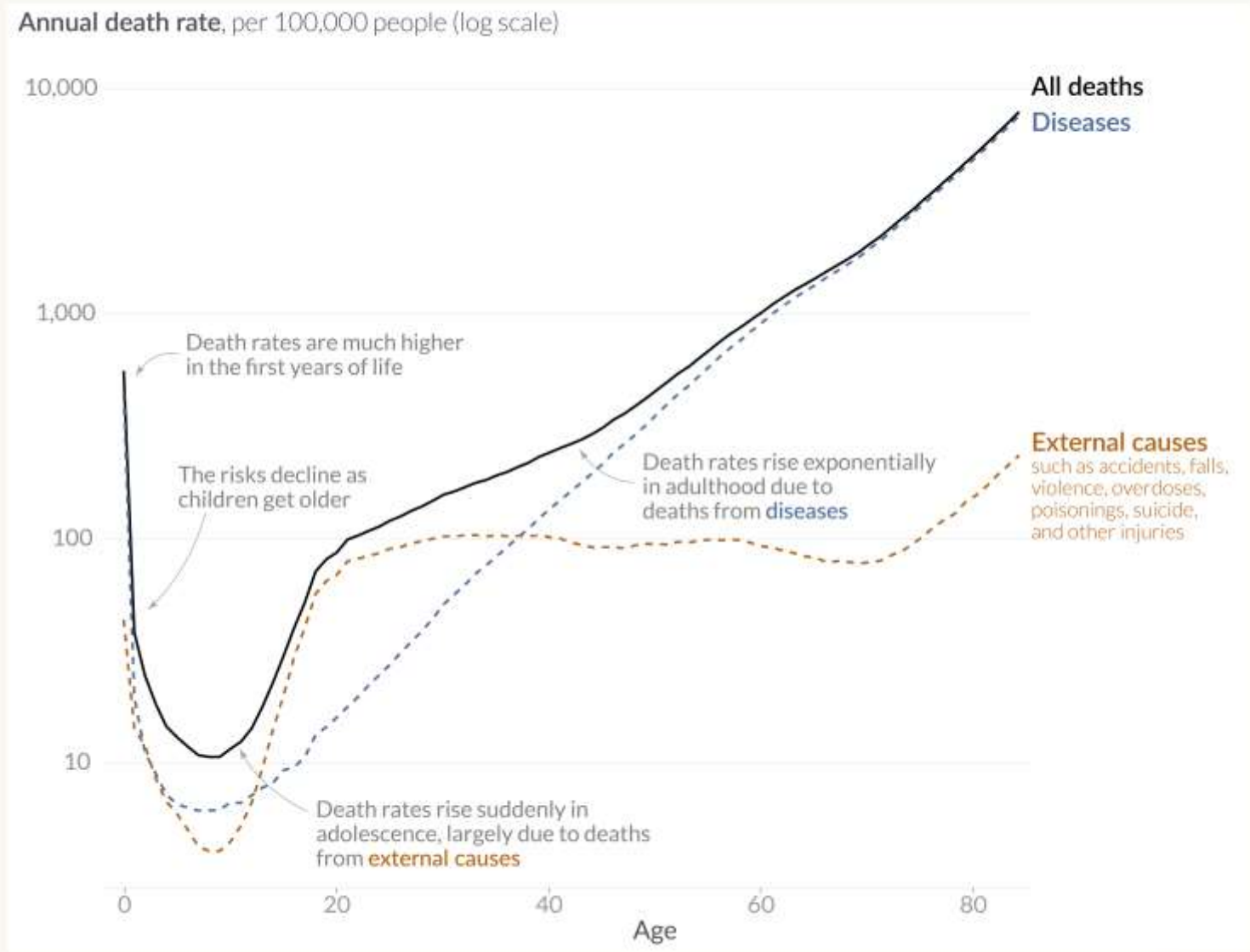
Step 3:

Get your full-body MRI, choosing from the basic to advance. You'll buy that on Ezra's website and schedule through them.

Death rates across ages

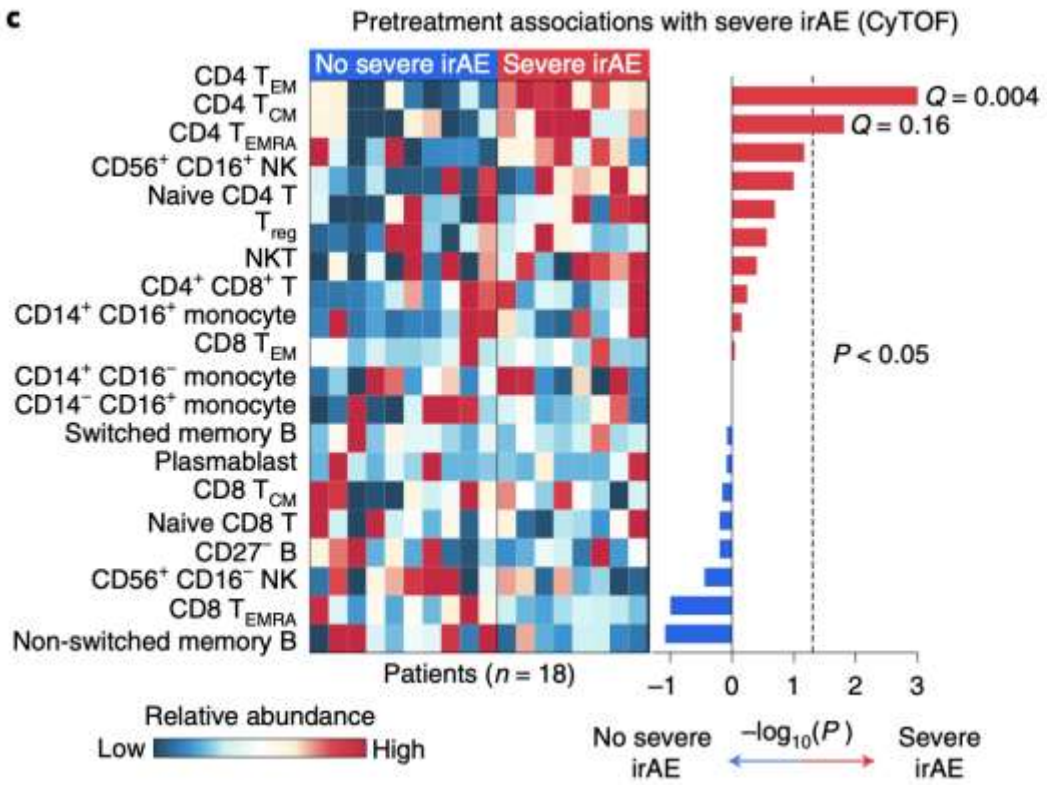
National data from the United States between 2018 and 2021.

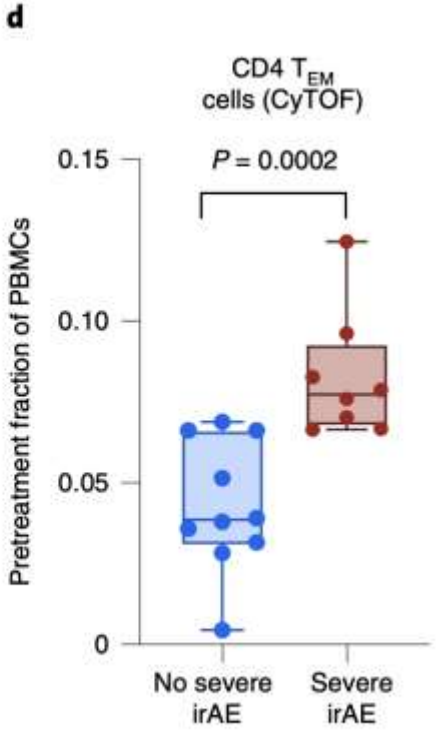
Our World in Data

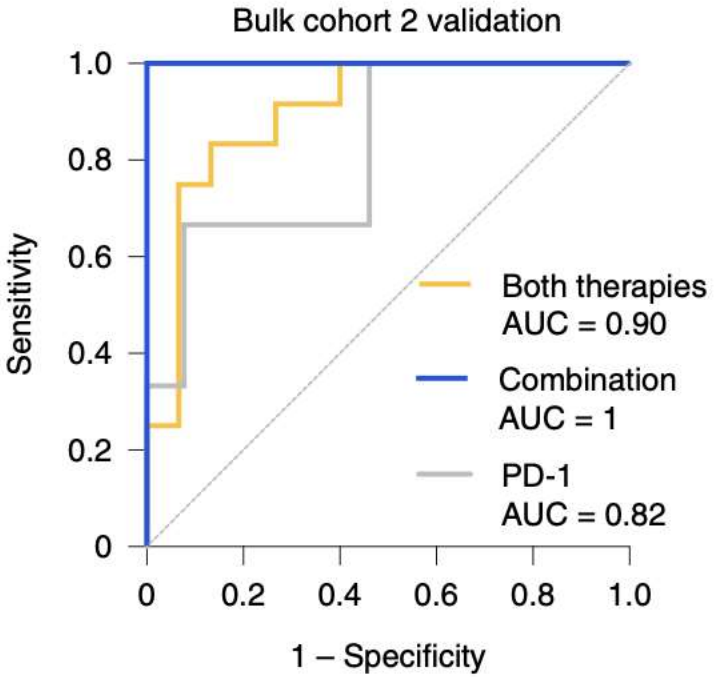


Note: Period death rates using ICD-10 categories. 'Diseases' includes all categories except 'external causes' and 'signs, symptoms and abnormal findings'.

Source: United States Centers for Disease Control and Prevention via CDC Wonder database



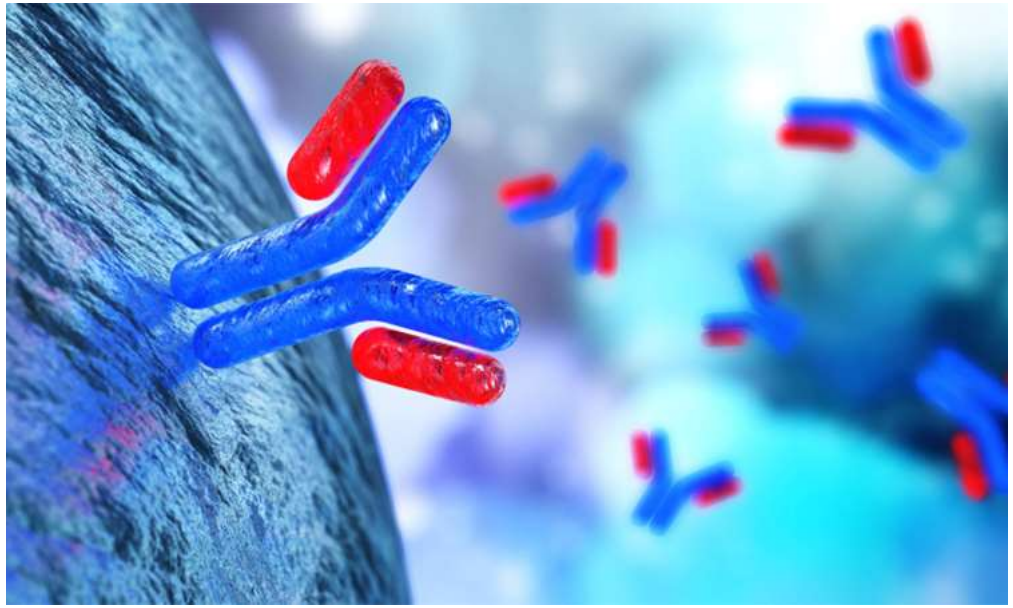




Lozano, Chaudhuri, Nene, Newman et al. **Nature Medicine** 2022

How far have we come

Biomarkers have been a part of western medicine for over 170 years



Serum Free Light Chains (antibodies) were first used as markers for myeloma (a blood cancer) in 1847

Image https://www.drugtargetreview.com/news/104433/a-new-study-has-highlighted-how-an-antibody-strengthens-bonds-between-cells/

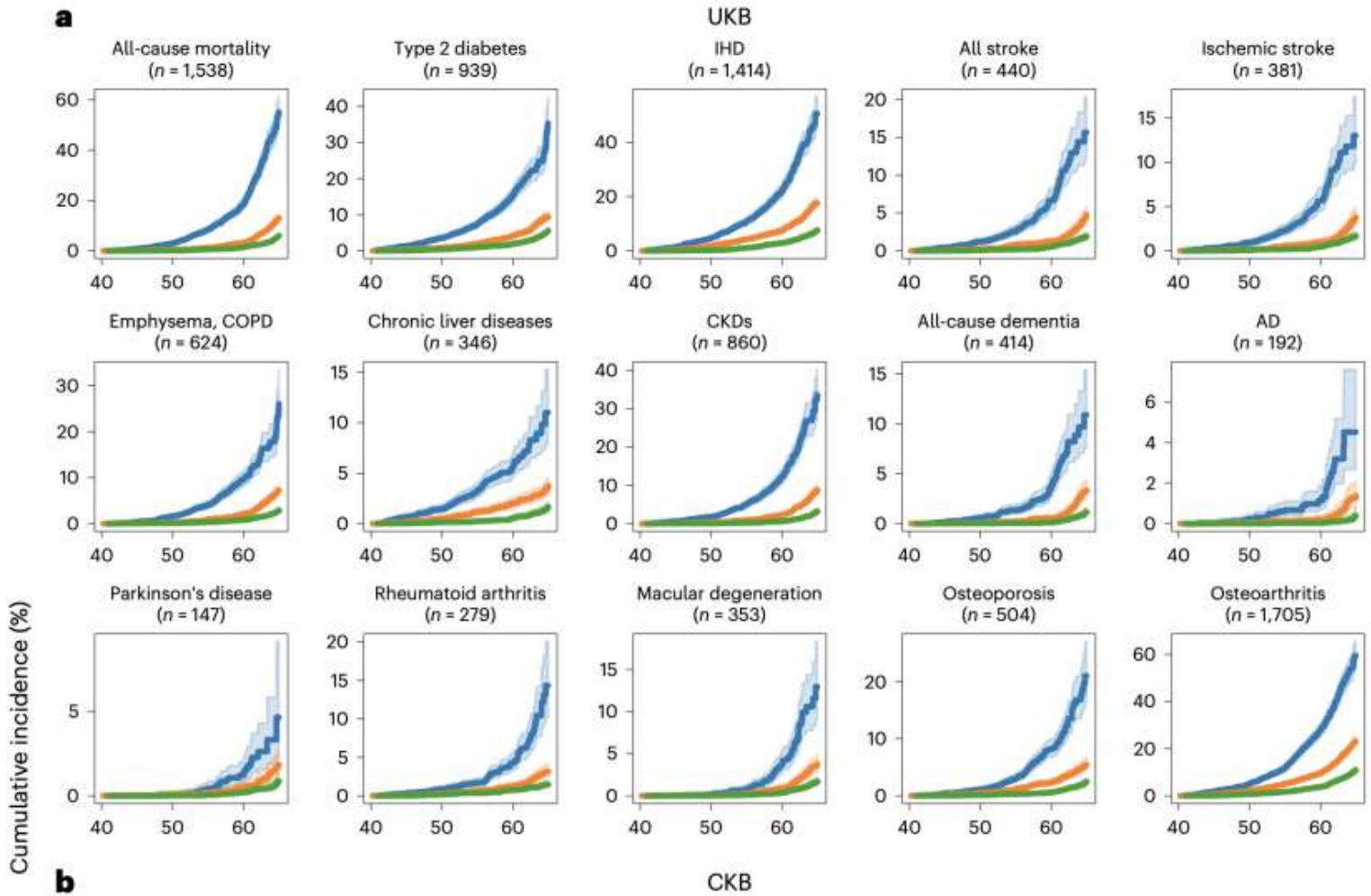
If **Age** is perhaps the most important predictor of disease, can we say that they share a **causal relationship**?

If **Age** causes disease, can we then treat it?

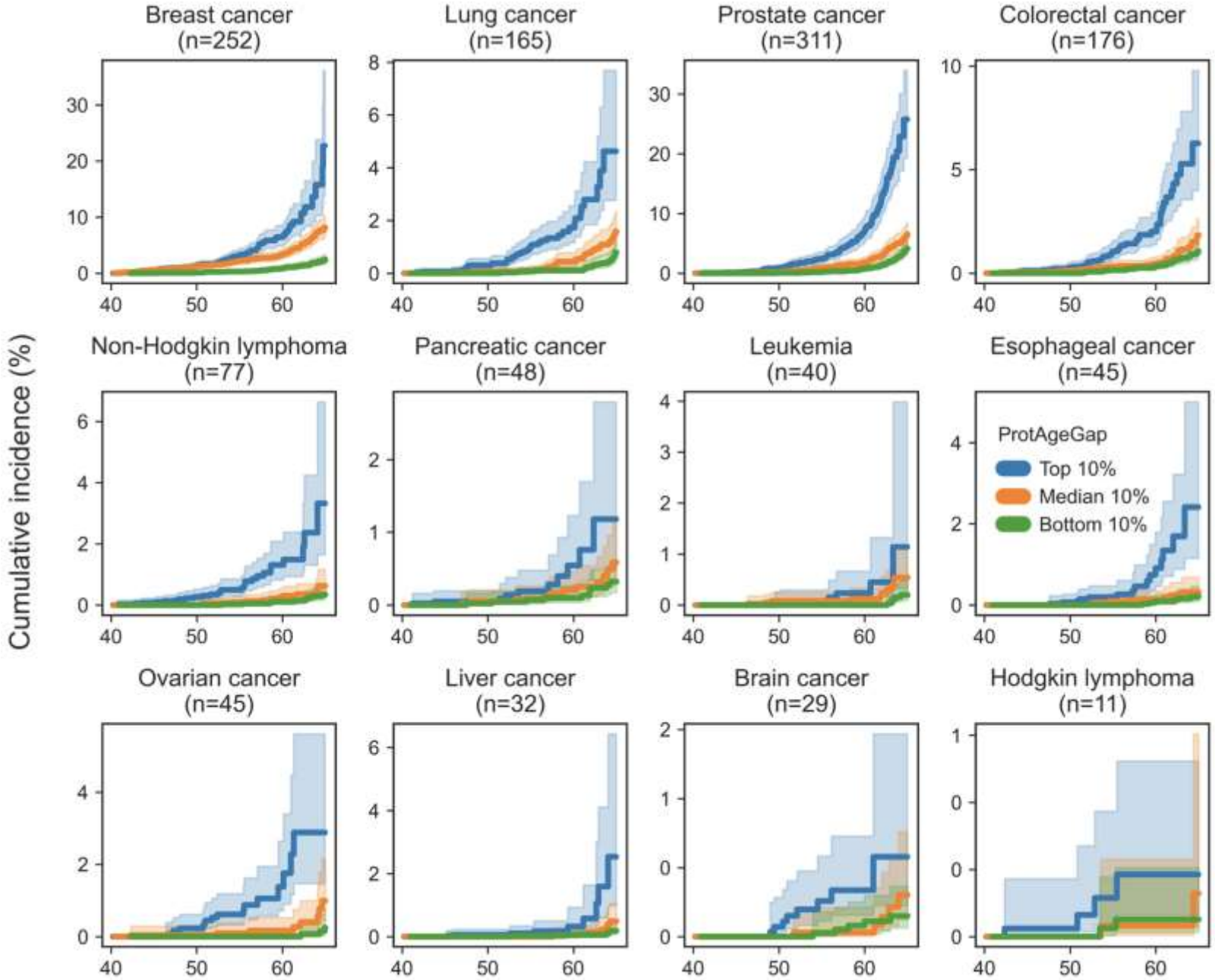
There is no **Age**, there is only health.

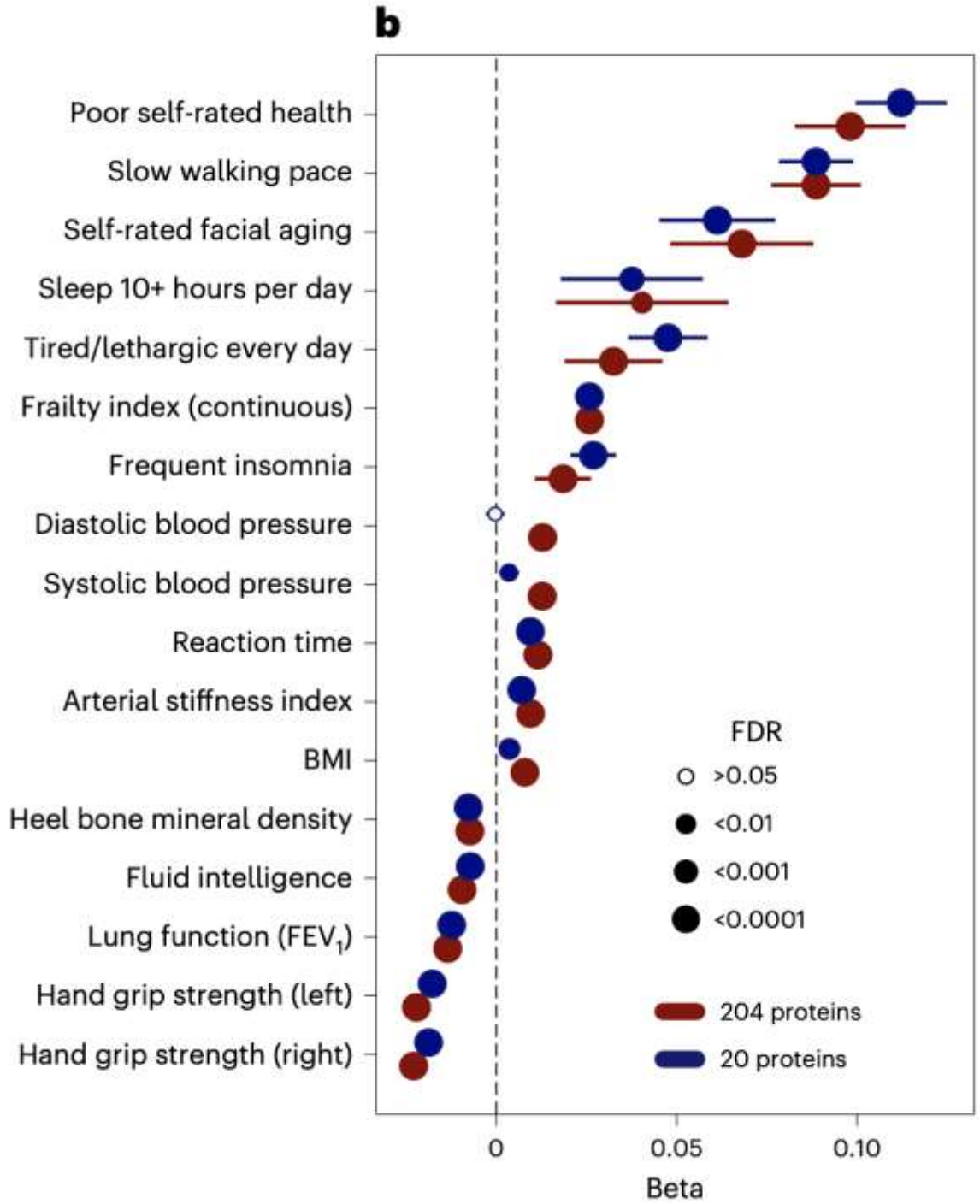
The one true clock is not **age**, but our health

ProtAgeGap



Should we screen people with protein age gaps more frequently for chronic conditions


Breast cancer
(n=252)
Lung cancer
(n=165)
Prostate cancer
(n=311)
Colorectal cancer
(n=176)
Non-Hodgkin lymphoma
(n=77)
Pancreatic cancer
(n=48)
Leukemia
(n=40)
Esophageal cancer
(n=45)
Ovarian cancer
(n=45)
Liver cancer
(n=32)
Brain cancer
(n=29)
Hodgkin lymphoma
(n=11)
Cumulative incidence (%)
ProtAgeGap
Top 10%
Median 10%
Bottom 10%


b
Poor self-rated health
Slow walking pace
Self-rated facial aging
Sleep 10+ hours per day
Tired/lethargic every day
Frailty index (continuous)
Frequent insomnia
Diastolic blood pressure
Systolic blood pressure
Reaction time
Arterial stiffness index
BMI
Heel bone mineral density
Fluid intelligence
Lung function (FEV1)
Hand grip strength (left)
Hand grip strength (right)
FDR
>0.05
<0.01
<0.001
<0.0001
204 proteins
20 proteins
0
0.05
0.10
Beta

leading DNAm clocks, including the Horvath clock[22],
DNAm PhenoAge[23] and DunedinPACE[24] (E

Table 1 | Loci emerging from GWAS of discrete and continuous lifespan-related phenotypes in human studies

			Replication		
Closest gene(s)	**Discrete phenotypes**	**Continuous phenotypes**	**Within publication**	**Between publications**	**Associations with age-related diseases**
APOE[141–145]	Age ≥99th percentile;age ≥90 years; age ≥100 years; parental age ≥90th percentile	Parental lifespan; age attained by parents	Yes	Yes	Multiple
CHRNA3 and *CHRNA5*[143,144]	Parental age ≥90th percentile	Parental lifespan; age attained by parents	Yes	No	Cancer
LPA[143,144]	Parental age ≥90th percentile	Parental lifespan; age attained by parents	Yes	No	Multiple
CDKN2A/B (*CDKN2B-AS1*)	Parental age ≥90th percentile	Parental lifespan; age attained by parents	Yes	No	Multiple
USP42[141]	Age ≥99th percentile	None	Yes	No	None
TMTC2[141]	Age ≥99th percentile	None	Yes	No	None
IL6[145]	Age ≥100 years	None	No	No	Inflammatory
ANKRD20A9P[145]	Age ≥100 years	None	No	No	None
LINC02227[142]	Age ≥90 years	None	Yes	No	Cardiovascular
FOXO3A[146]	Age ≥90 years	None	Yes	No	None
RAD50 and *IL13*[147]	Age ≥90 years	None	Yes	No	None
MC2R[143]	Parental age ≥90th percentile	None	Yes	No	None
USP2-AS1[143]	Parental age ≥90th percentile	None	Yes	No	None
HLA-DQA1 and *HLA-DRB1*[143,144]	None	Parental lifespan; age attained by parents	Yes	No	Inflammatory
ATXN2[143]	None	Age attained by parents	No	No	Multiple
FURIN[143]	None	Age attained by parents	No	No	Cardiovascular
EPHX2[143]	None	Age attained by parents	No	No	Cancer
PROX2[143]	None	Age attained by parents	No	No	None
CELSR2 and *PSRC1*[143]	None	Age attained by parents	No	No	Cardiovascular

We included only studies that showed one or more genome-wide significant associations with lifespan-related phenotypes ($P < 5 \times 10^{-8}$), with the exception of the *RAD50* and *IL13* locus ($P = 5.42 \times 10^{-7}$), which was based on the number of linkage disequilibrium-independent markers on the genotyping array (Immunochip) used in the study[147]. We excluded studies that were based on results from cohorts that were also included in more recent and larger studies. 'Within publication' refers to replication of a locus in different cohorts within the same publication. 'Between publications' refers to replication of a locus in different cohorts from different publications.

Genetic predictors of age

References

- Wikipedia
- Our World in Data

- What will you do with your time on this earth