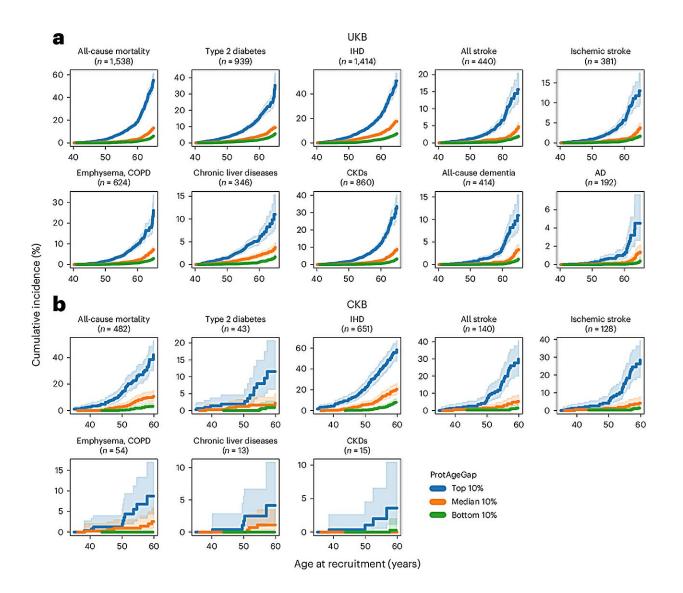


Proteins carried in the blood offer new insights into aging and age-related disease risk

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Proteomics age clock stratifies people into divergent age-specific mortality and



disease risk trajectories. Credit: *Nature Medicine* (2024). DOI: 10.1038/s41591-024-03170-9

Chronological age is the most important factor determining risk of disease and death in adults. However, life expectancy can vary considerably among individuals with similar chronological age.

In this study, the researchers used data from 51,408 participants across three large <u>population</u> studies to develop the most powerful clock to date that captures biological age and predicts the risk of premature death and numerous diseases. They analyzed nearly 3,000 proteins in <u>blood</u> <u>samples</u> from participants in the UK Biobank study to develop a machine learning model that uses 204 proteins to estimate a person's biological age.

The study, "<u>Proteomic aging signatures predict disease risk and mortality</u> <u>across diverse populations</u>," is published in *Nature Medicine*.

This <u>protein</u>-based biological age model was also shown to be able to accurately estimate the biological age of participants in the other two studies, the China Kadoorie Biobank, and FinnGen (based in Finland), who have a very different genetic makeup and lifestyles compared with people living in the UK.

The researchers compared the participants' chronological age with their biological age based on blood proteins to calculate the "protein age gap" as a biological indicator of how fast a person is aging. Within UK Biobank, they could link the protein age gap to a wide range of health outcomes to see if it could reliably predict age-related physical and mental well-being, risk of <u>disease</u> and death.



Key findings:

- The protein age gap was shown to differ by up to 12 years between two people with the same chronological age;
- A person's protein age gap is associated with changes in aging and physical/mental well-being, including physical frailty, handgrip strength, renal function, bone density, cognitive function, and telomere length (a marker of aging that can be measured based on your DNA);
- The protein age gap was shown to be able to accurately predict those at high and low risk of premature death and 18 major diseases, including dementia, heart disease, liver and kidney diseases, and various cancers;
- The protein-based biological age clock was able to reveal major pathways that are the key players in aging and risk of multimorbidity (having two or more conditions simultaneously).

The study provides the largest and most comprehensive evidence to date demonstrating that the protein age gap is associated with numerous agerelated diseases and premature death, which represents an unprecedentedly powerful instrument compared to previous biological age clocks. The clock also sheds light on the proteins that are driving the risk of multimorbidity, which together with aging already imposes a major pressure on the NHS and global health services.

Professor Cornelia van Duijn, St Cross Professor of Epidemiology at Oxford Population Heath and senior author who has led the team, said, "This is the most powerful biological aging clock developed to date that outperforms all previous clocks in identifying those who age faster and experience more ill-health from aging. The number of diseases the protein-based age clock has been able to accurately predict is unprecedented."



Many of the previous studies on biological age have been conducted but none have reached the breadth and depth of the present study, spanning populations with different genetic ancestry and geographic backgrounds and predicting a wide a range of age-related disorders and premature death.

Dr. Austin Argentieri, lead author on the paper at Oxford Population Health and Research Fellow at Massachusetts General Hospital and the Broad Institute of MIT and Harvard, said, "Developing robust proteinbased aging clocks that predict future risk of many diseases and generalize to diverse population groups is a key step in developing effective preventative health strategies that can be used to monitor risk of age-related diseases.

"As technology develops and the cost of proteomic analysis drops, this will further support the development of precision medicine approaches that can be put to widespread use to help people live longer and more healthily."

Professor Zhengming Chen, Richard Peto Professor of Epidemiology at Oxford Population Health, UK Principal Investigator for the China Kadoorie Biobank study, and one of the senior co-authors on the paper, said, "Having been tested and validated in diverse populations, the protein-based age clock can be considered for rapid clinical translations in different populations to inform lifestyle interventions (such as smoking cessation, weight loss), routine health check-up schemes, and clinical trials."

Chronological age simply tells the passage of time rather than the aging of our body's functions. For some people, their biological 'clock' is ticking faster than others and they age faster. Others may age more slowly than expected based on their <u>chronological age</u>. This may be due to differences in their genetic makeup, lifestyles, and living



environments.

In order to gain better insight into who is aging more quickly or more slowly, researchers have previously developed biological age clocks using various biological and clinical indicators.

In the future, protein-based <u>biological age</u> clocks could be used to study the relationships between genetics and environment and the impact that these relationships have on aging, in turn delivering key insights into how we age and our likelihood of developing disease across our lifespan.

More information: Proteomic aging signatures predict disease risk and mortality across diverse populations, *Nature Medicine* (2024). DOI: <u>10.1038/s41591-024-03170-9</u>

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