PRESS RELEASE

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NUS Medicine researchers develop a better and more accurate biological ageing clock

Singapore, 9 June 2025 — Researchers from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) have developed an improved biological ageing clock, *LinAge2*, that offers doctors a practical and more accurate way to assess how quickly a person is ageing – and what can be done to slow it down.

The new algorithm-powered tool builds on earlier clinical ageing clocks known as PCAge and LinAge. These older models, derived from blood and urine tests and health questionnaires, demonstrated strong predictive capability for long-term mortality and functional decline. PCAge, in particular, outperformed standard cardiovascular risk scores and could forecast ageing trajectories well before the onset of disease. This approach was adapted and integrated for clinical use, which paved the way for LinAge2's enhancements in accuracy, interpretability, and ease of use.

Published in *npj Aging*, LinAge2 not only outperformed other clinical models but also surpassed leading epigenetic clocks in predicting long-term mortality and health outcomes. Key findings include:

- **More accurate mortality prediction**: LinAge2 performed better than chronological age and biological ageing clocks in indicating likely mortality within 10 and 20 years
- **Links to functional health**: Individuals with lower LinAge2 biological age walked faster, had better cognitive scores, and were more likely to be independent in daily living.
- **Actionable insights**: The model identifies specific health issues — such as smoking or metabolic syndrome — that accelerate ageing, enabling tailored interventions.

“Chronological age tells us how many years we’ve lived, but it doesn’t reflect our actual health risks,” said Associate Professor Jan Gruber, senior author of the study and principal investigator at the Department of Biochemistry and Healthy Longevity Translational Research Programme (TRP) at NUS Medicine. “That’s where biological ageing clocks, like LinAge2, come in — they’re computational algorithms that integrate clinical data into a single measure of biological age. LinAge2 captures how fast a person is really ageing inside, which can help inform personalised treatment strategies, lifestyle interventions, and ultimately extend healthy years of life.”

To develop LinAge2, the team analysed data from the US National Health and Nutrition Examination Survey (NHANES), a large public dataset containing routine health information from thousands of participants. This included physical examination results, blood test values, and mortality records, allowing researchers to trace long-term health outcomes. They then applied a mathematical technique known as principal component analysis (PCA) to extract key health patterns and estimate a person's biological age — a measure of physiological ageing rather than just the number of years lived.

The research team tested LinAge2's ability to predict both mortality and functional health, such as gait speed, cognitive performance, and independence in daily activities. Compared to popular DNA-based ageing clocks like PhenoAge DNAm and GrimAge2, LinAge2 consistently demonstrated stronger predictive power. The model was further refined by removing complex lab tests, adjusting for gender differences, and ensuring results were not skewed by extreme values. A visual tool was also developed to help users identify which specific health factors are accelerating ageing, making LinAge2 an accessible and actionable resource for clinicians and researchers.

LinAge2 was co-developed with clinician collaborator Dr Fong Sheng, Consultant in Geriatric Medicine at the Ng Teng Fong General Hospital. He added, "Our long-term vision is to embed tools like LinAge2 into everyday medical practice, which doctors can use during check-ups, to help them tailor treatment plans based on a person's true biological condition and not just their age in years. By identifying who is ageing faster inside, we can help patients act early to slow it down through lifestyle changes, medical treatments, or preventive care. This can lead to better quality of life and longer healthspan, not just life expectancy."

To advance clinical integration, the researchers are working with Singapore-based healthtech provider NOVI Health to incorporate LinAge2 as part of its healthy longevity programme. The researchers aim to validate the model across more diverse populations and explore its application in monitoring responses to healthspan interventions, such as lifestyle modifications, dietary adjustments, and/or medications. This work will further the development of evidence-based healthy longevity treatments in clinical practice.

A/Prof Gruber added, "It is our hope that validation of LinAge2 in various cohorts and populations will bring us closer to a future of preventive, personalised, and proactive medicine — where we address ageing itself, not just the diseases it causes."

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Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments, and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, research centres of excellence, corporate labs and more than 30 university-level research institutes focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research, and cybersecurity.

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About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

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Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2025 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2025).

For more information about NUS Medicine, please visit https://medicine.nus.edu.sg/

About the National Medical Research Council (NMRC)

The NMRC was established in 1994 to oversee research funding from the Ministry of Health and support the development and advancement of biomedical research in Singapore, particularly in the public healthcare clusters and medical schools. NMRC engages in research strategy and planning, provides funding to support competitive research grants and core research enablers, and is responsible for the development of clinician scientists through awards and fellowships. The council's work is supported by the NMRC Office which is part of

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