

Most accurate test to date developed to measure biological aging

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A team of European researchers has developed a new test that can accurately measure biological aging in a clinical setting. The discovery was made while studying patients for the aging effects of chronic kidney



disease.

The <u>new test</u> is an <u>epigenetic clock</u>—a type of biochemical assessment that looks at DNA to understand how well the body is aging in contrast to its <u>chronological age</u>—and is the first of these cutting-edge tests to be proven to perform accurately in a <u>clinical setting</u>, in both healthy and unhealthy tissue.

The work was led by a partnership between the University of Glasgow and the Karolinska Institutet, Stockholm, and is published in the *Journal of Internal Medicine* as part of a study into the aging effects of chronic kidney disease and its associated treatments. It is titled "Epigenetic clocks indicate that kidney transplantation and not dialysis mitigates the effects of renal aging."

The research team studied more than 400 patients with chronic kidney disease in Sweden alongside around 100 matched population controls, to better understand the impact on aging of the disease, including during dialysis treatment and after kidney transplant.

To do this, researchers used a range of tests including blood biomarkers, skin autofluorescence and epigenetic clocks. The team used the clocks to measure the change in biological age of around 47 patients one year after kidney transplantation, or one year after the start of their dialysis treatment, as well as how the healthy tissue in 48 controls aged by comparison.

The results showed that for patients with chronic kidney disease, their biological clock is ticking faster than the average person's. This continues to be the case even after dialysis treatment. Indeed, patients' biological clocks were only shown to slow down following a kidney transplant.



However, while the epigenetic clocks all showed a similar picture, the research team found that none of the current clocks could be shown to be accurate in a clinical setting, and all were found to be inaccurate to differing degrees when tested in healthy tissue over time.

To address this, the team developed a new, more accurate epigenetic clock—the Glasgow-Karolinska Clock—that works on healthy and unhealthy tissue. The results from this new clock matched what doctors saw in patients with chronic kidney disease, and also appeared to accurately assess healthy tissue too. This study is the first real-world test of epigenetic clocks in a normal aging setting, and against clinical parameters.

As the body ages, a series of factors lead to epigenetic changes and loss of a chemical tag (DNA methylation) from your DNA. This is often associated with a range of disease common to aging, such as chronic kidney disease, cancer and heart disease. Epigenetic clocks have been proposed as a "gold standard" for measuring age accurately, beyond a person's biological age, as they are able to measure methylation tags on DNA.

Professor Paul Shiels, lead author of the study for the University of Glasgow, said, "This study is the first time in a clinical setting that we can accurately report on the extent of biological as opposed to chronological aging in chronic kidney disease patients. Our findings, using the new Glasgow-Karolinska Clock—show that not only are these patients aging faster than people in the general population, their accelerated aging only slows down once they have had a transplant. Treatment with dialysis does not appear to impact this process.

"This is also the first clinical test of epigenetic clocks, and the discovery that most are inaccurate when compared with <u>medical evidence</u> has led us to develop a new more accurate test which can accurately measure



methylation tags on DNA of both healthy and unhealthy tissue. We have proven it is accurate to the high standards of a clinical setting.

"Methylation tagging of DNA is impacted by what we eat and also out gut microbiome. As a result, this new clock has real potential to be able to evaluate lifestyle interventions, including diet, that could benefit the public and help to address issues such as health inequalities."

Peter Stenvinkel, professor at Karolinska Institutet, said, "I found the new tool to estimate effects of interventions on <u>biological age</u> of much interest. The tool could be used to study treatment strategies in patients with end-stage <u>kidney</u> disease—a group subjected to premature aging."

More information: Epigenetic clocks indicate that kidney transplantation and not dialysis mitigates the effects of renal ageing, *Journal of Internal Medicine* (2023). DOI: 10.1111/joim.13724, onlinelibrary.wiley.com/doi/10.1111/joim.13724

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