

CASE AND COMMENTARY: PEER-REVIEWED ARTICLE

What Are the Most Ethically Salient Implications of Epigenetic Age Testing?

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Abstract

This commentary on a case considers how clinicians should help patients interpret results of tests that might be personally meaningful but not clinically actionable. Tests of biological age, for example, can easily lead to patient misunderstandings that can increase risks of psychological harm and make age-related discrimination seem justifiable. This commentary suggests that companies offering epigenetic testing should be more transparent about these tests' reliability and limitations.

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Case

AA is a healthy 56-year-old patient who ordered a direct-to-consumer test online that is a measure of biological age. These so-called “epigenetic clock” tests estimate the likelihood of developing age-related conditions (eg, cancer, cardiovascular disease, and Alzheimer’s disease) and predict one’s risk of death.

AA received the test’s results, which state that he is “biologically 65-years-old.” AA follows up on the manufacturer’s recommendations to begin courses of the company’s brain health and cellular repair supplements. AA has questions, too, and follows up with Dr B, his primary care physician.

AA is worried about his accelerated so-called biological age relative to his chronological age and his reportedly higher risk of age-related diseases and death. “Do I really have so little time, Dr B? Can you help me live healthier and longer? Can you help me age less or more slowly?” Dr B considers how to respond.

Commentary

When we age, our DNA changes. These changes happen on the genetic level through telomere shortening, genetic mutation accumulation, and mitochondrial dysfunction. Other changes are epigenetic, which means that what changes is the way our genes are expressed in our bodies and how well they do the work they are meant to do. That work

consists of creating proteins that are needed for what we consider the normal functioning of a cell, tissue, or organ and creating them when they are needed and not when they are not needed. The older we get, the less reliable those epigenetic biological processes tend to become.¹ This so-called epigenetic drift increases the likelihood of infections (such as pneumonia and COVID-19) and age-related diseases (such as cancer or heart and lung diseases), which in turn puts us at a higher risk of dying.² Yet gene expression is influenced not only by genetic factors, but also by environmental conditions and lifestyle choices like what we eat and how physically active we are, which is why 2 people of the same chronological age can be very different in terms of how well their bodies function on various levels. This is what is commonly referred to as a person's epigenetic or biological age: biologically, we do not all age at the same rate. Some people age faster than we would expect on the basis of their chronological age, some age more slowly.

In this commentary, we question the empirical validity of biological age testing and highlight some of the ethical questions arising from it. Patients and the public can easily misunderstand the significance of biological age tests, which increases the risk of psychological harm and makes age-related discrimination appear justifiable. To mitigate these risks, companies offering epigenetic testing need to be clearer about how the tests work, how reliable they are, and what they can and cannot show.

“Biological Age” Is a Fiction

A person's biological age can be assessed in various ways. The most common tests, known as “epigenetic clocks,” measure DNA methylation patterns. Methylation is a process that is responsible for the activation and silencing of particular genes. Other tests focus on different biomarkers, such as the length of telomeres. While these tests have been shown to be fairly reliable indicators of a person's risk of developing certain age-related diseases,³ we should be very clear that they cannot tell us how old we “really” are, as is frequently claimed in the media.⁴ The number that those tests come up with and that we are led to believe is our actual age is in fact fictitious because it entirely depends on what biomarkers and what method of computation are being used, which, in the absence of any consensus about what markers and methods *should* be used, undermines the very concept of a person's biological age.⁵

Although biological age is widely treated as a reality, there is no such thing as a particular person's biological age. This is why we are likely to get a different result if we take a different kind of test,⁶ and, even if the same kind of test is applied, the result also depends on the type of tissue that is used as the source material, as well as the size of the sample. Your heart might then turn out to be “older” or “younger” than your liver.⁷ In fact, those tests don't measure how old our cells are or how old the cells in particular parts of our body are. Our cells are in fact never older than we are (though some of them are chronologically younger), and our age depends on when we were born and nothing else. So, if, like patient AA, we are 56 years old and told that our biological age is actually 65, then all that can possibly mean is that whatever parts of our bodies have been tested are in a worse state than is to be expected for someone our age and that this state is more commonly found in someone who is 9 years older, which is, of course, still a good reason for AA to be concerned about the state of his health and possibly make some changes in his life.

Fiction as Legal Reality

Having this kind of information can no doubt be helpful. Since some of the damage that is measured in these tests is reversible, and since further damage can possibly be prevented or slowed with the right treatment, they can be useful tools for identifying health risks and potential remedies, such as lifestyle changes, pharmacological interventions, or even cellular reprogramming.⁸ But to frame the results of these tests as the discovery of one's biological age—especially if biological age is presented and promoted as one's "actual" age—is highly misleading and has far-reaching potential consequences if taken literally. Some bioethicists have already argued that people should be given the right to have their assumed biological age, rather than their documented chronological age, officially recognized as their legal age if there is a difference between them to prevent unjust age discrimination.⁹

This argument has not been accepted by any courts yet, but the more we get used to thinking of our purported biological age as our real age, the more likely it becomes that it will eventually be regarded as a fact **demanding legal recognition**. But legally recognizing one's biological age as one's actual age would almost certainly also affect the opportunities one has in life. Would someone who is clinically assessed as younger than what their date of birth indicates have to wait until they have reached biological pension age before being able to access their pension? Would someone who is assessed as older find it more difficult to get health or life insurance, find a romantic partner, or even access clinical interventions?

Setting the Record Straight

Even if being told that one's biological age considerably exceeds one's chronological age has no legal implications (yet), many patients will struggle to interpret this claim correctly—namely, as a shorthand for a probabilistic assessment of possible future health problems and resulting life expectancy. Clinicians confronted with a patient who has received a test result seemingly providing a scientific confirmation of **accelerated biological aging** need to be sensitive to the emotional impact that this piece of information is likely to have on that patient and do everything they can to mitigate it by following well-established guidelines for crisis management following a medical diagnosis.¹⁰ All illnesses are, to a certain extent, crises of meaning that disturb the ill person's understanding of their world,¹¹ but what is usually most disturbing is an illness that we know—or are being told—will drastically reduce our life expectancy, as happens to AA in the case described above. To be diagnosed as suffering from a terminal illness is bound to come as a shock to any patient and is likely to upend their entire life. To be told that one is actually much older than one thought one was might well have a similar effect because it makes death appear more imminent. In both cases, the time we think we have left in our lives has suddenly shrunk considerably.

Even if the biological age test that AA took was not clinically indicated, it is still within the remit of Dr B's responsibilities to make sure that AA fully understands the results, which do not entail that he will develop morbidity or die earlier than would be expected on the basis of his chronological age. Rather, they merely indicate that certain aspects of his physical condition make it more likely that particular health hazards lie in store for him in the future if not addressed. This explanation should then lead to a discussion of what, exactly, was measured in the biological age test taken by AA and what can be done to prevent the underlying conditions it revealed from compromising AA's health and well-being later.

Balancing Innovation and Trust

However, for this discussion to be possible, Dr B would have to know exactly how the test results were generated, which is harder to determine than it should be because of the proprietary nature of current epigenetic clocks and the economic incentives that accompany them. This problem is both an informational and an ethical one, which can only be solved through greater transparency. Experts outside of the commercial venture are prevented from impartially analyzing the algorithms via a peer-review process, and other independent developers are not allowed to dig into the code to check for flaws and biases. Not only does this secrecy make monopolies more likely and innovation less likely,¹² but many potential users will also find it difficult to trust a technology that is largely protected from public scrutiny,¹³ and rightly so. The lack of transparency makes it easier for commercial companies offering epigenetic testing to manipulate the results and provide false positives to sell products that might or might not work. Even if the companies are honest, the suspicion that those companies might offer solutions to problems that wouldn't exist if they had not first created them will not go away until epigenetic testing companies adopt a business model that permits closer external scrutiny of their algorithms. Companies must also give consumers all the information they need to justify their trust that the risk scores provided are accurate and that the recommended supplements and interventions will actually help them. And because companies' success as businesses ultimately relies on the trust of consumers, they would do well to open-source all or part of the epigenetic testing algorithms to gain ideas from the wider community on how to improve the reliability of the score provided, potentially foster innovation via collaboration, and discover and develop new talent or partnerships. In the meantime, clinicians like Dr B should follow existing guidelines regarding the interpretation of direct-to-consumer genetic and genomic testing results, such as the American College of Physicians' position paper, "Ethical Considerations in Precision Medicine and Genetic Testing in Internal Medicine Practice."¹⁴

Conclusion

Biological age is a fiction that should, at the very least, be clearly identified as such by **clinicians** when discussing biological age tests with patients to prevent them from becoming confused, upset, or falsely flattered about results purporting to show that their biological age differs from their chronological age. Taking this step would also prevent patients from misinterpreting their supposed biological age as their "real" or "actual" age, with its potentially far-reaching legal implications. Epigenetic testing can, of course, reveal potential or existing health problems and provide valuable information that can be used to improve a patient's health and lifespan. Yet to fully realize the potential of epigenetic clocks in an ethically responsible way, researchers, regulators, and developers must prioritize transparency, accountability, standardization. By open sourcing their algorithms, or parts of them, while maintaining ownership of their platform or tools, companies would be able to balance technological and scientific innovation with the need for accountability and trust. Regulators could support this move by creating a framework to categorize the efficacy of interventions for particular biomarkers and defining and mandating the use of standards to calculate biological age.

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Editor's Note

The case to which this commentary is a response was developed by the editorial staff.

Citation

AMA J Ethics. 2025;27(12):828-833.

DOI

10.1001/amajethics.2025.828.

Conflict of Interest Disclosure

Contributors disclosed no conflicts of interest relevant to the content.

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