Scientists devise a more accurate way to gauge blood sugar averages in diabetes

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Combining the power of advanced math with tests commonly used to measure blood sugar, scientists from Harvard Medical School and Massachusetts General Hospital have created a new model that more

accurately accounts for long-term blood sugar fluctuations in people with diabetes. The disease affects more than 422 million people worldwide, according to the World Health Organization and more than 29 million Americans, according to the Centers for Disease Control and Prevention.

By factoring in the age of each patient[1]s red blood cells, the new method offers a more precise, individualized gauge of three-month blood sugar averages and reduces in half the error rate of the most commonly used ' but sometimes inaccurate ' test known as A1C. Findings of the study are described Oct. 5 in *Science Translational Medicine*.

"What we currently deem the gold standard for estimating average blood glucose is nowhere as precise as it should be," said senior investigator John Higgins, an associate professor of systems biology at HMS and a clinical pathologist at Massachusetts General Hospital. "Our study not only pinpoints the root of the inaccuracy but also offers a way to get around it."

The A1C test led to notable off-target estimates in about a third of more than 200 patients whose test results were analyzed as part of the research. The team found these inaccuracies stemmed entirely from individual variations in the life span of a person[1]s red blood cells.

In a final step, the scientists calculated new, age-adjusted estimates and tested their predictive accuracy by comparing them to actual blood sugar levels measured directly via continuous glucose monitors ' wearable devices that read a person[1]s blood sugar every five minutes.

Incorporating the new model into existing tests, the researchers said, could lead to more precise diagnosis, monitoring and better-tailored treatments.

Estimating a person[1]s three-month blood sugar average is the best

indicator of disease control and the most accurate predictor of looming complications, according to experts. Persistently elevated blood sugar can, over time, damage the heart, brain, kidneys, eyes, nerves and other organs.

Because blood sugar varies by the hour and even by the minute, capturing "an average" to account for fluctuations over an extended period is a far better indicator of disease status than taking a "snapshot" measurement at one time.

To estimate blood sugar averages, physicians use the A1C test as a proxy. The A1C measures so-called glycated hemoglobin ' the amount of sugar soaked up by red blood cells over an extended period of time.

The test, however, is somewhat imprecise. As little as 15 milligrams of glucose per deciliter of blood could signal the difference between high normal values in a person without diabetes and low abnormal values in someone with the disease. The A1C test can lead to identical readings for people with average blood sugar levels that differ by as much as 60 mg/dl. At the same time, people with similar blood sugar levels can end up having widely divergent results. Researchers are not sure what fuels this discrepancy, but the age of red blood cells has recently emerged as a prime suspect.

"Like a water-soaked sponge that[1]s been sitting on the kitchen sink for days, older red blood cells tend to have absorbed more glucose, while newly produced red blood cells have less because they haven[1]t been around as long," Higgins said.

Thus, the researchers said, two people with the same amount of sugar in their blood but could end up with different results on their A1C test depending on the average lifespan of their red blood cells.

To eliminate the influence of age-related variation, the HMS team developed a formula that factors in the life span of a person's red blood cells. The formula is based on several values, including directly measured glucose levels, and, crucially, on earlier findings by Higgins' team showing that in each person, the lifespan of red blood cells is tightly regulated, within 1 percent or so. Next, researchers compared the age-adjusted blood sugar estimates to estimates derived from the standard A1C test and then to readouts of glucose levels measured directly by continuous glucose monitors.

The standard A1C test provided values that were significantly off target ' by 15 mg/dl or more ' in one out of three patients. By factoring in red blood cell age, however, the scientists reduced the error rate to 1 in 10.

For example, using the standard A1c test, one patient's glycated hemoglobin levels measured at 8.1 percent, leading to an estimated blood sugar level of 186 mg/dl. When the researchers factored in the person's red blood cell age ' 45 days ' the estimate went up to 209 mg/dl. Compared with the actual glucose levels measured by a continuous glucose monitor ' 210mg/dl ' the age-adjusted estimate was off by a mere point. By contrast, the standard estimate was off by 24 points.

Incorporating the age-adjusted formula into current A1C testing approaches would significantly boost the accuracy of glucose estimates, the researchers said. Under the new model, patients could wear a glucose monitor for a few weeks to have their blood sugar tracked as a baseline, also allowing physicians to calculate the average age of a person[1]s red blood cells before having the monitor removed.

"Physicians treating recently diagnosed patients would immediately know what a patient[1]s red blood cell age is," Higgins said. "The patient's test results can then be adjusted to factor in the red blood cell age and get a result that more accurately reflects the actual levels of blood sugar,

allowing them to tailor treatment accordingly."

More information: "Mechanistic modeling of hemoglobin glycation and red blood cell kinetics enables personalized diabetes monitoring," *Science Translational Medicine*, stm.sciencemag.org/lookup/doi/ … scitranslmed.aaf9304

Provided by Harvard Medical School