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Better definition of 'pre-diabetes' can help identify those at risk for long-term complications

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Defining pre-diabetes based on hemoglobin A1C, a common test that determines a long-term average blood sugar level, is the most accurate predictor of who will go on to develop long-term complications from diabetes, new Johns Hopkins Bloomberg School of Public Health research suggests.

Professional organizations do not agree on how to define pre-diabetes, a condition that indicates a patient is likely to develop type 2 diabetes and its potential complications in the near future. For example, the American Diabetes Association recommends using hemoglobin A1C or glucose levels to diagnose pre-diabetes, while the World Health Organization recommends physicians use glucose only.

What they do agree on, however, is that people who are at high risk of developing diabetes can reduce that risk substantially through lifestyle modifications such as moderate weight loss, increased exercise and diet modifications. Some groups also recommend the use of a medication called metformin to help reduce diabetes risk. The issue is figuring out the best way to identify people with pre-diabetes, researchers say.

Their findings are published Nov. 15 in the *Lancet Diabetes & Endocrinology*.

"The goal is to figure out who is at the highest risk of not only

developing diabetes but of developing its serious complications including kidney disease, cardiovascular disease and even death," says study leader Bethany Warren, a PhD student in the Department of Epidemiology at the Bloomberg School. "Hemoglobin A1C appears to be the tool that is best able to do that."

Another set of criteria used to define pre-diabetes uses a fasting glucose test (taken after the patient hasn't eaten for eight hours) or a two-hour glucose test, which uses the fasting test while also checking the blood two hours again after consuming a sugary drink. The researchers found no difference between the two glucose measures, but did find that they identified more people as having pre-diabetes than hemoglobin A1C, even though fewer of them would go on to develop complications from diabetes. Glucose measures look at current levels in the blood as opposed to hemoglobin A1C, which looks at a longer-term average of glucose exposure over the prior two to three months.

"When someone is told they have pre-diabetes, we hope it will cause them to make changes to their habits in order to prevent the development of diabetes and its complications," says the study's senior author Elizabeth Selvin, PhD, MPH, a professor in the Bloomberg School's Department of Epidemiology. "Being identified as having pre-diabetes can also make it easier to receive weight loss and nutritional counseling as well as reimbursement for these services. Intensive lifestyle changes and weight loss can reduce the risk of diabetes, so it is critically important we identify those persons who are at high risk. At the same time, we also don't want to over-diagnose people. Using the hemoglobin A1C test allows us to more accurately identify those persons at highest risk."

For their study, the researchers used data from the Atherosclerosis Risk in Communities Study, which followed the health of a large middle-aged population over decades. The researchers analyzed fasting glucose and

hemoglobin A1C levels of 10,844 adults between 1990 and 1992 and followed them over the course of up to 22 years to see how likely they were to develop diabetes, kidney disease and cardiovascular disease or to die of all causes. They also analyzed fasting and two-hour glucose levels of 7,194 adults who were tested between 1996 and 1998 and followed them for up to 16 years, looking for the same outcomes.

A hemoglobin A1C level of 6.5 percent means a person has diabetes. The researchers compared two cut-off points for hemoglobin A1C to define pre-diabetes. The American Diabetes Association's definition of pre-diabetes uses hemoglobin A1C values of 5.7 to 6.4 percent, while a group called the International Expert Committee considers hemoglobin A1C levels of six to 6.4 percent to be pre-diabetes.

They found that using an A1C-based definition, those identified as having pre-diabetes were 50 percent more likely to develop kidney disease, twice as likely to develop cardiovascular disease and 60 percent more likely to die from any cause compared to those with normal A1C. The associations were not as strong when glucose tests were used to identify people with pre-diabetes.

"This is important information for physicians and it is also important information for professional organizations," Selvin says. "Coming to a global consensus on how to define and diagnose pre-diabetes would really help move the field forward – and help patients all over the world."

More information: Bethany Warren et al. Comparative prognostic performance of definitions of prediabetes: a prospective cohort analysis of the Atherosclerosis Risk in Communities (ARIC) study, *The Lancet Diabetes & Endocrinology* (2016). DOI: 10.1016/S2213-8587(16)30321-7

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