Lowering the Criterion for Impaired Fasting Glucose Is in Order

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Editor's comment: Because of the controversial nature of the new lowered criterion for IFG, I offered the Chairman of the Expert Committee an opportunity to respond to my commentary on the subject. I would only point out that Dr. Genuth's reference 8 shows an association between glycemia and cardiovascular disease (as have many other reports), but to date, five prospective studies, analyzed either singly or as a metanalysis, have been unable to demonstrate a beneficial effect of lowering glycemia on cardiovascular disease outcomes.

The title of the commentary by Davidson, Landsman, and Alexander (1) implies that any change in the diagnostic criterion for impaired fasting glucose (IFG) must have an obvious (to them) clinical benefit. But this is putting the cart before the horse; the cart of clinical benefit must be drawn by the workhorse of clinical science. The 1997 introduction of the IFG category was meant to emphasize that a gray zone of increased risk for developing diabetes existed between a "normal" and a clearly diabetic fasting plasma glucose (FPG) level. The 2003 report corrects the lower limit of IFG from 110 to 100 mg/dl because clinical science has advanced.

The data from four large cohorts followed observationally for up to 5 years has become available. This data could be used to select a scientifically better, lower cut point, which would give a combined maximum sensitivity and specificity for developing diabetes in the near term. Moreover, the Diabetes Prevention Program (DPP) (2) and Finnish Diabetes Study (3) have since shown us that the progression from an at-risk state (impaired glucose tolerance [IGT]) to diagnosed diabetes could be reduced by lifestyle changes, and the DPP, STOP-type 2 diabetes (4), and Troglitazone in Prevention of Diabetes (5) trials have shown that pharmacologic therapy could also reduce the risk of developing diabetes. It would be burying our clinical science heads in the sand to ignore these new analyses and new data. In the wake of an obesity (and physical inactivity) epidemic (6) and an ongoing diabetes epidemic (7), if 25% of the U.S. population in truth have IFG by the new definition, should they and we not know that they are at a much greater risk for diabetes by applying a simple test?

The authors have selected those reports that failed to find an independent relationship between FPG and cardiovascular disease or mortality as another argument against changing the cut point. But a carefully performed metanalysis of six studies encompassing 225,000 person-years of observation demonstrates a significant exponential relationship between FPG and cardiovascular disease events, beginning at an FPG of 75 mg/dl (8). Shall we ignore this analysis that was thought valid and important enough to be published in *Diabetes Care*?

The commentary also states that there is no evidence that a diagnosis of IFG would improve the likelihood of patient success in following a lifestyle modification treatment program. But medicine does not establish diagnostic criteria for any disease based on the likelihood of adherence to treatment. Even so, we have learned from the DPP that being identified as at risk by virtue of having IGT (most also had IFG) induced 50% of the participants to achieve a weight loss goal ≥7% at 6 months and 38% to achieve that weight loss at their most recent DPP visit (2). In addition, 74% met the goal of at least 150 min of physical activity per week by 6 months and 58% at the most recent visit. Achieving these goals unquestionably required strenuous efforts and highly motivated clinic treatment teams. But it worked! Together, these lifestyle changes resulted in a 58% reduction in the risk of progression to diabetes (2). Whether such results can be obtained outside of a clinical trial setting is unclear, but why should we skeptically dismiss them as being unattainable "in real life?" We should not so quickly conclude that IFG/IGT can be ignored simply because a lifestyle intervention may be difficult to implement and sustain in some patients.

Finally, the commentary raises the frequently heard argument that identifying persons at risk for diabetes only puts them at further risk—the risk of being denied health insurance or employment. It is time to stop submitting to such putative or real pressures. Instead, we should use our data and analyses that support scientifically credible diagnostic criteria to make insurers responsible for providing the means to prevent, or at least delay, diabetes through lifestyle modifications. For our part, we should continue to seek improved criteria that will identify more precisely those individuals from the high-risk groups of IFG and IGT who will actually develop diabetes if left untreated.

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Abbreviations: DPP, Diabetes Prevention Program; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; FPG, fasting plasma glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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