COMMENTS AND RESPONSES

International Expert Committee Report on the Role of the A1C Assay in the Diagnosis of Diabetes

Response to Kilpatrick, Bloomgarden, and Zimmet

We appreciate the comment by Kilpatrick et al. (1) regarding the International Expert Committee report on the diagnosis of diabetes with the A1C assay (2). The Committee considered all of the limitations of the A1C assay for populations in which it is not available or is currently too expensive, as well as for individuals in whom the assay may be misleading. On the basis of these recognized limitations, the Committee emphasized the use of the currently recommended glucose tests and criteria in such populations or individuals. We did not "breeze over" any of the relative advantages or disadvantages of the A1C assay as a means of diagnosis; rather, the Committee considered the sum total of current evidence regarding the A1C assay in coming to its recommendations. The Committee concluded that overall, the A1C assay has merit for the diagnosis of diabetes.

Although Kilpatrick et al. suggest a number of limitations of the A1C assay that are well supported by data, they have, in our opinion, exaggerated others. For example, whether A1C levels are elevated disproportionately to the mean glucose levels in some racial groups is far from established (3). In addition, the higher A1C levels in older populations (4), which Kilpatrick et al. suggest may lead to "overdiagnosis," may very well have biological significance. Finally, many of the previously identified interfering factors can be addressed by using commonly available specific A1C assays (www.ngsp.org), and most of the clinical factors that may interfere with interpretation of the A1C should be easily recognizable in the course of usual clinical care. Such factors will interfere with the use of the A1C assay whether for management or diagnosis.

The unreferenced assertion by Kilpatrick et al. that measures of glucose are "superior to A1C" in predicting risk is unsupported by any analyses of which we are aware. The one example they cite from the recent study by Sabanayagam et al. (5), which examined the relationship between measures of glycemia and retinopathy, in fact showed a nominally higher area under the curve receiver operating characteristic for the relationship of A1C with mild and moderate retinopathy (0.899 and 0.904, respectively) than for random glucose (0.849 and 0.863, respectively). The authors did not present a statistical comparison of the areas under the curve.

Our main argument regarding the comment by Kilpatrick et al., however, is with their assumption that glucose measurements are the gold standard for diagnosing diabetes. The International Expert Committee was more open-minded regarding this issue, acknowledged that there was no gold standard, and examined the relative merits of various measures of glycemia. This allowed us to weigh the A1C assay against measures of glucose. Kilpatrick et al. conveniently ignore the well-recognized limitations of glucose measurements such as high intraindividual biological variability, preanalytic instability, and the inconvenience of timed samples for patients, all of which favor the A1C assay for diagnosis (2).

The International Expert Committee has recommended using the A1C assay for the diagnosis of diabetes and identifying those at high risk for diabetes. When the assay is unavailable or uninterpretable, we recommend using glucose testing. Although we expect further debate, we hope that our recommendations will stimulate the international community to consider using A1C in the diagnosis of diabetes.

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