# Response to Letter to the Editor: "One-Hour Postload Hyperglycemia: Implications for Prediction and Prevention of Type 2 Diabetes"

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We appreciate the opportunity to respond to the comments by Hulman *et al.* regarding our review (1). It is important to remind that the current fasting and 2-hour postload plasma glucose (2hPG) cut-points for diagnosing type 2 diabetes (T2DM) and prediabetic conditions, such as impaired fasting glucose and impaired glucose tolerance (IGT), were justified "largely because at approximately that point the prevalence of the microvascular complications considered specific for diabetes (nephropathy and retinopathy) increased dramatically" (2). By contrast, 1-hour postload plasma glucose (1hPG) threshold was studied for identifying individuals at increased risk to develop T2DM. The 1hPG value of 155 mg/dL (8.6 mmol/L) was recognized as the best predictor of T2DM in both Caucasians and Mexican-Americans (3, 4). Importantly, several prospective studies using this 1hPG cut-point have been published so far, thus allowing us to perform a meta-analysis showing that individuals with 1hPG $\geq$ 155 mg/dL have an increased risk to develop T2DM (1). Because there is a continuum of risk of future T2DM across the spectrum of fasting glucose and 2hPG, it is not surprising that studies in various ethnic populations have identified different 1hPG cut-points varying from 144 mg/dL (8.0 mmol/L) in Koreans (5) to 160 mg/dL (8.9 mmol/L) in Europeans (6). Remarkably, in the study by Paddock *et al.* (7), the cut-points that maximized the sum of sensitivity and specificity at 5 years for predicting T2DM were 148 mg/dL (8.2 mmol/L) for 1hPG and 124 mg/dL (6.9 mmol/L) for 2hPG, with the latter being lower than 140 mg/dL (7.8 mmol/L) cut-point recommended by the World Health Organization and all scientific societies worldwide. These data confirm that the choice of 1hPG cut-point predicting T2DM is necessarily arbitrary and driven by the need to identify a 1hPG cut-off that represents the lower limit of a range of glucose values associated with a progressively greater risk of developing T2DM and a reasonable compromise in terms of sensitivity and specificity. Thus, as in the case of the diagnostic criteria for IGT ranging from 140 to 199 mg dL (7.8 to 11 mmol/L), it is reasonable that 155 mg/dL cut-point for 1hPG may represent the lower limit of a range of glucose levels associated with T2DM risk.

Hulman *et al.* argue that it "is questionable in a time when multivariable prediction models are available and easily calculated" to search for a glycemic parameter during the oral glucose tolerance test able to identify at-risk individuals. However, it is noteworthy that 1hPG alone outperformed the prediction model of multiple clinical risk factors including age, gender, body mass index, T2DM family history in the Botnia study (4) and Malmö Prevention Project (6), and the addition of 1hPG to clinical prediction models did significantly improve their predictability (3,4).

We agree with Hulman *et al.* that more interdisciplinary collaborations are necessary to answer unresolved

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questions including: (i) What is the 1hPG cut-point for diagnosing T2DM analogous to the 2hPG > 200 mg/dL (11.1 mmol/L)? (ii) Should the 1hPG replace the 2hPG for classifying prediabetes and T2DM?

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