Response to Comment on: Maruthur et al. Does Genetic Ancestry Explain Higher Values of Glycated Hemoglobin in African Americans? Diabetes 2011;60:2434–2438

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We appreciate the interest of Dagogo-Jack (1) in our study of genetic ancestry and HbA_{1c} in African Americans (2). We interpret his major concerns as follows: *1*) HbA_{1c} values may have a glucose-independent genetic component and *2*) in our study, adjustment for glucose did not fully account for HbA_{1c} values $\geq$6.5%.

Our goal was to evaluate if differences in genetic ancestry might explain differences in HbA_{1c} between individuals of African and European ancestry observed in previous studies. Although the heritability of HbA_{1c} approaches 60% in twin studies (3) and "glucose-independent" genetic loci for HbA_{1c} have been found in populations of European descent (4), our results indicate that genetic loci accounting for the heritability of HbA_{1c} are not likely to be population-specific or have large population differences.

After accounting for fasting glucose, we observed a prevalence of undiagnosed diabetes of 4.4% defined by HbA_{1c} $\geq$6.5% (2), but as in prior studies, including that cited by Dagogo-Jack (5), adjustment for glucose was based on a single measurement and should be distinguished from average glucose (6). The within-person variability of a single glucose measurement is substantially higher than that of HbA_{1c} (7). Thus, we cannot conclude that individuals shifted from the diabetes to the nondiabetes category in our analysis had normal glucose homeostasis. Single HbA_{1c} and glucose measures communicate different information about glucose homeostasis in an individual. The availability of only a single glucose measure is a limitation of many epidemiological studies of glucose homeostasis, and the discrepancy between measures alone does not establish HbA_{1c} as an inferior test.

We agree that our analyses cannot provide a definitive explanation for the black-white difference in HbA_{1c}, but we feel strongly that there is little to suggest a strong genetic ancestral determinant of this difference. Our results support current recommendations for the use of HbA_{1c} to diagnose diabetes in all ethnic groups (8).

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