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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Maruthur et al. (1) showed that European genetic admixture is inversely related to HbA_{1c} levels among African Americans, although admixture explained less than 1% of the variance in HbA_{1c}. Others have reported that genetic factors account for ~60% of the variance in HbA_{1c} (2). For unclear reasons, African Americans express higher HbA_{1c} levels than Caucasians with similar blood glucose values (3,4). Genetic loci that are unique to HbA_{1c} (and not necessarily shared by blood glucose) have been identified by several researchers, but specific data are lacking in African Americans (5–7). Admixture analyses, which are inherently superficial, may not provide the definitive genetic data needed to clarify black/white differences in HbA_{1c}. Thus, it is premature to downplay biological differences in the etiology of ethnic disparity in HbA_{1c}, or to attribute the latter to nebulous "downstream factors" (1).

Maruthur et al. report that adjusting for genetic ancestry had a minimal effect on HbA_{1c}-based diagnosis of diabetes—after accounting for fasting glucose—and conclude that their findings support the use of HbA_{1c} for diagnosis of diabetes in African Americans. That conclusion is unsupported by their data: the prevalence of diabetes decreased from 11% (using $HbA_{1c} \geq 6.5\%$) to 4.4% (based on fasting glucose) (1). Thus, 60% of African Americans, who had normal fasting glucose levels, were misdiagnosed with diabetes using the recommended HbA_{1c} cutoff.

The diagnostic use of HbA_{1c} assumes a degree of concordance with blood glucose values that is simply not supported by evidence (4,8). Therefore, it is desirable for clinicians to obtain confirmatory blood glucose levels when screening for diabetes or prediabetes, particularly among African Americans (4).

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