Response to Comment on: Chauhan et al. (2010) Impact of Common Variants of *PPARG*, *KCNJ11*, *TCF7L2*, *SLC30A8*, *HHEX*, *CDKN2A*, *IGF2BP2*, and *CDKAL1* on the Risk of Type 2 Diabetes in 5,164 Indians. Diabetes;59:2068–2074

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We read with interest the letter by Gupta and Ebrahim (1) complimenting our article (2) published recently in *Diabetes*. As mentioned rightly by the authors, there have not been many well-powered association studies on type 2 diabetes in the Indian population; hence this collaborative effort, even though as a replication of established genome-wide association study (GWAS) signals, is indeed exemplary. While thanking the authors for acknowledging our contribution, we believe that the issue raised by them of spurious association because of population stratification has limited scientific basis.

The issue of population stratification in Indians is an ever-unanswered question. The authors have based their arguments on the "landmark study" of Reich et al. (3) and on the Indian Genome Variation Consortium (IGVC) study (4). It would be appropriate to remind the authors that Reich et al. analyzed 1 million SNPs in not more than 4–5 samples in each Indian population in a total sample size of ~150. The IGVC, which evaluated more samples with ~400 markers (not neutral) (4) and reported genetic heterogeneity in Indians, also stated that the effect of population stratification in disease association studies may be small if case subjects and control subjects are both drawn from the same cluster. Moreover, a study by Rosenberg et al. (5) reports that false positives arising because of genetic heterogeneity in the diverse Indian population could be smaller than expected.

Along similar lines, Gupta and Ebrahim have themselves suggested that "consideration of recruitment strategies based on endogamy in a defined geographic area would be one means of conducting genetic association studies in India without introducing population stratification." This is precisely what has been done in the present study. Further, we did perform a multiple dimensional scaling based on 608 unlinked markers in the Delhi study (as suggested by one of the reviewers), which indicated that all the samples were indeed derived from one Indo-European cluster.

Above all, Gupta and Ebrahim, even when questioning the validity of the associations reported by us, admit that these are "highly plausible given the high priors for these SNPs from studies in other populations," and such studies have no problem. We still agree that population stratification remains an important consideration, but a preliminary ongoing GWAS in a subset of the samples reveals that adjustments for possible stratification based on principal components have yielded results similar to those reported.

We hope our joint effort paves the way for more collaboration among South Asian and sub-Saharan researchers themselves, rather than researchers from abroad.

ACKNOWLEDGMENTS

No potential conflicts of interest relevant to this article were reported.

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DOI: 10.2337/db10-0868