REPLY: Low Asian Enrollment in Cardiometabolic Studies and the Importance of Trial Context

Dr Pendyal believes our main finding, that only 8% of all participants from seminal cardiometabolic trials in the last 10 years are Asian, needs context.[1] We maintain that the only context needed is that cardiometabolic disease is prevalent worldwide, and 60% of the global burden exists among Asians and the Asia-Pacific region,[1] indicating a marked underrepresentation in seminal cardiometabolic evidence. Dr Pendyal's suggestion still reveals a concerning narrative. Of the 51 trials conducted solely in North America/Canada in our data set, only 0.4% (n = 2,410 of 599,937) of the enrolled participants identified as Asian, whereas the representative local population would be closer to 7%. The majority of our included trials were conducted in multiple regions in which an average of 7.5% of all participants identified as Asian. Thus, our data suggests that all sites can enhance diversity by attempting to enroll a population that more closely resembles their local demography; however, a global, coordinated, and system-based approach focused on building capacity in the APAC region will be needed to more meaningfully (and sustainably) enhance Asian and APAC regional enrollment.

We were cautious not to suggest any observed variation in therapeutic effectiveness by race is a solely biological phenomenon—indeed, we wrote "the degree to which the complex and dynamic construct of race and ethnicity can be practically disentangled from inextricable environmental, socioeconomic, genetic, and biological forces remains to be seen."[2] We agree that disaggregation beyond racial umbrella terms is important; however, clinical trials rarely report socioeconomic factors that would have allowed us to undertake such an analysis suggested by Dr Pendyal. Of note, we specifically point out in our paper that even disaggregation into key subgroups such as East Asian and South Asian was performed in only 11% of the trials. Nevertheless, our aim was not to focus on the complex area of racial subgroup analysis, which ultimately may benefit more from pharmacogenomic and precision medicine approaches. Instead, we hoped to spotlight the importance of achieving racial and geographic trial diversity, which promotes fairness, trust, equity, and generalizable biomedical insights.[3]

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

REFERENCES

1. Azzopardi R, Nicholls SJ, Nerlekar N, et al. Asia-Pacific investigators and Asian enrollment in cardiometabolic trials: insights from publications between 2011 and 2020. *JACC: Asia*. 2023;3(5):724–735.

2. Zhao D. Epidemiological features of cardiovascular disease in Asia. *JACC Asia*. 2021;1:1–13. https://doi.org/10.1016/j.jacasi.2021.04.007

3. Schwartz AL, Alsan M, Morris AA, Halpern SD. Why diverse clinical trial participation matters. *N Engl J Med*. 2023;388:1252–1254. https://doi.org/10.1056/NEJMp2215609