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A global epidemiologic study assessing interferon gamma release assay positivity in populations with high tuberculosis burden

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Background: Tuberculosis (TB) vaccine efficacy trials evaluating prevention of disease must be feasible in size and duration and would ideally take place at clinical trial sites that enroll from communities with the highest incidence rates. In preparation for the Phase 3 trial of the investigational M72/AS01E-4 vaccine, we conducted a multi-country study, using interferon gamma release assay (IGRA) positivity as a proxy for expected incidence of TB.

Methods: We enrolled 7167 participants aged 15 to 34 years from communities with a high burden of TB at each of 45 sites in 14 countries (approximately 160 per site): Bangladesh, Brazil, Democratic Republic of Congo, The Gambia, India, Indonesia, Kenya, Mozambique, Peru, The Philippines, South Africa, Uganda, Vietnam, and Zambia. This study is ongoing, but here we present data pertaining to the primary and first secondary objectives, describing IGRA status by site at the time of enrollment, IGRA status by age (categorized by ages 15-24 and 25-34 years), and association of age with the proportion of participants with IGRA positivity using logistic regression models.

Results: The proportion of participants with IGRA positivity varied considerably across countries and sites (Figure). When participants were categorized by age, IGRA positivity generally tended to be higher in the older age category (25-34 years). Notably, at 12 (27%) of the 45 sites, IGRA positivity was higher in the older age category compared to the younger one (with the 95% CIs of the odds ratios excluding one). At 9 (20%) of the 45 sites, IGRA positivity increased with age (with the 95% CIs of the odds ratios excluding one) when age was treated as a continuous variable.

Conclusion: IGRA positivity varied among different countries and sites. Hence, identifying areas of high IGRA positivity will be crucial for sites participating in TB vaccine efficacy trials, including the Phase 3 trial of the M72/AS01E-4 vaccine candidate.

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Conflicts of Interest

None

Error bars correspond to Clopper-Pearson 95% confidence intervals