BILL & MELINDA GATES MEDICAL RESEARCH INSTITUTE

TBV02-E01

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

Alemnew Dagnew, MD, MSc, MVPCD, MPH

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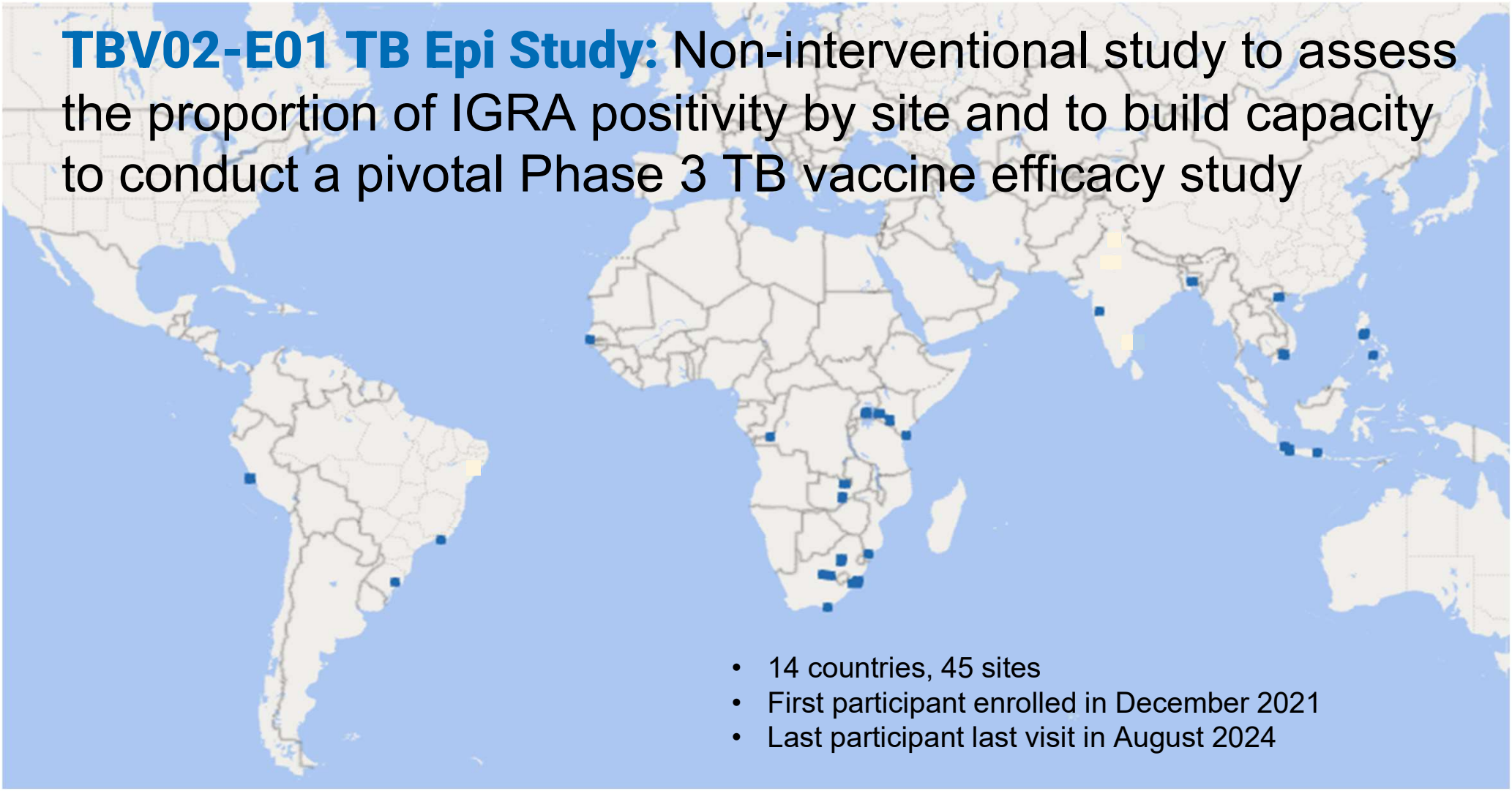
TBV02-E01 TB Epi Study: Non-interventional study to assess the proportion of IGRA positivity by site and to build capacity to conduct a pivotal Phase 3 TB vaccine efficacy study



- 14 countries, 45 sites
- First participant enrolled in December 2021
- Last participant last visit in August 2024

Inclusion/exclusion criteria

Inclusion criteria

- Capable of giving signed informed consent and informed assent
- Between 15 and 34 years of age
- Participants who agree to stay in contact with the study site for the duration of the study

Exclusion criteria

- History of active TB within the last 24 months
- History of previous administration of an experimental *Mtb* vaccine
- Unstable/uncontrolled chronic condition according to the judgment of the investigator

Objectives and endpoints

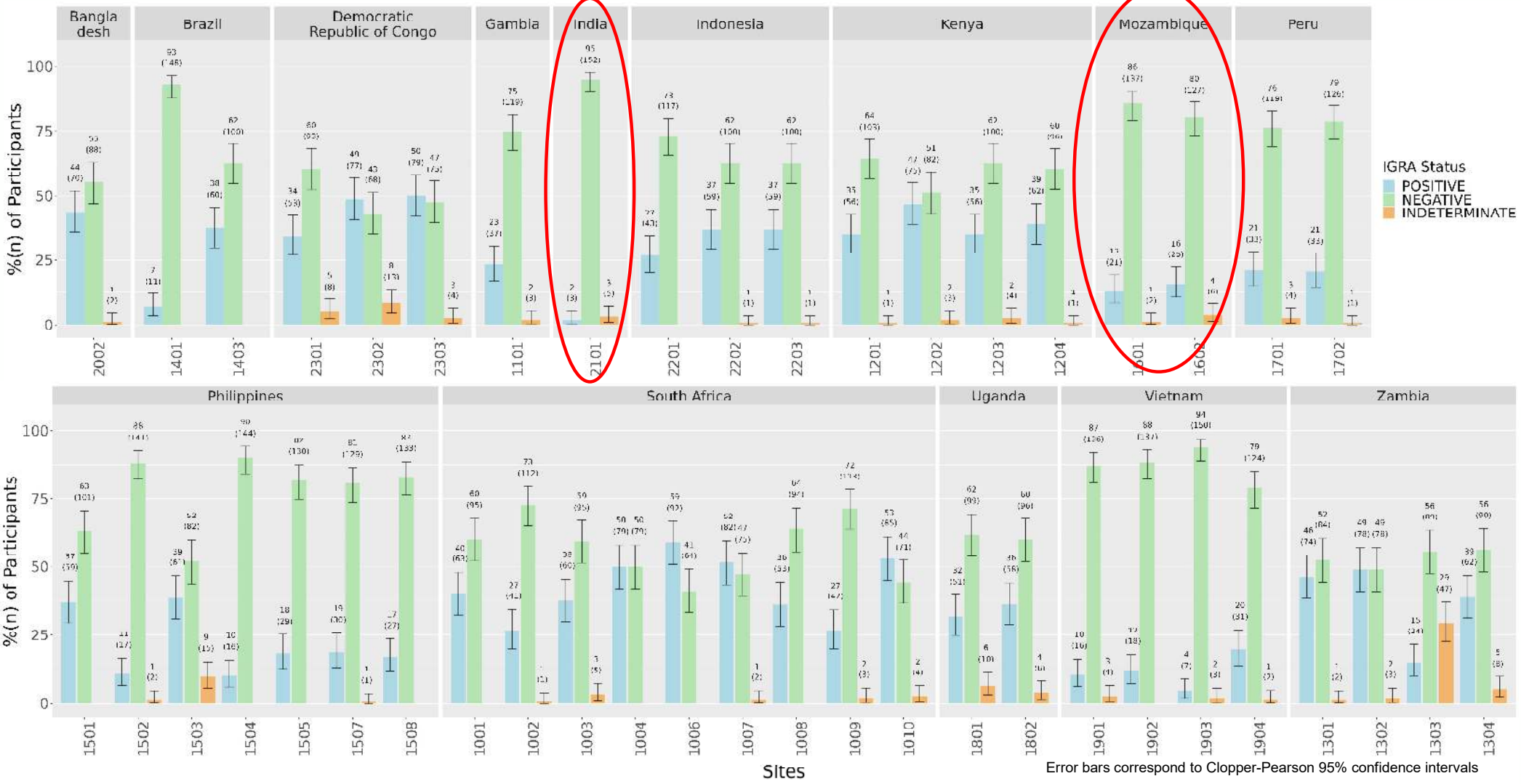
Primary	
• To describe the proportion of IGRA positivity by site	• IGRA status (positive/negative/indeterminate) at screening
Secondary	
• To assess the association of age with the proportion of IGRA positivity by site • To describe the overall incidence of suspected and laboratory-confirmed pulmonary TB (disease)	• IGRA status (positive/negative/indeterminate) at screening • Suspected pulmonary TB during the study follow-up period • Laboratory-confirmed pulmonary TB during the study follow-up period
Exploratory	
• To describe changes in the proportion of IGRA positivity by site • To describe the association between IGRA IFNγ concentration at screening and progression to pulmonary TB	• IGRA status (positive/negative/indeterminate) at Month 12 vs. screening • IGRA IFNγ concentration at screening and time to suspected pulmonary TB during the study follow-up period • IGRA IFNγ concentration at screening and time to laboratory-confirmed pulmonary TB during the study follow-up period
Other exploratory endpoints may include, but are not limited to, assessing transcriptomic, proteomic, or metabolomic profiles, antibodies, and *Mtb* markers.	

Objectives/endpoints for the current analyses are in red.

Demographics across the 14 countries

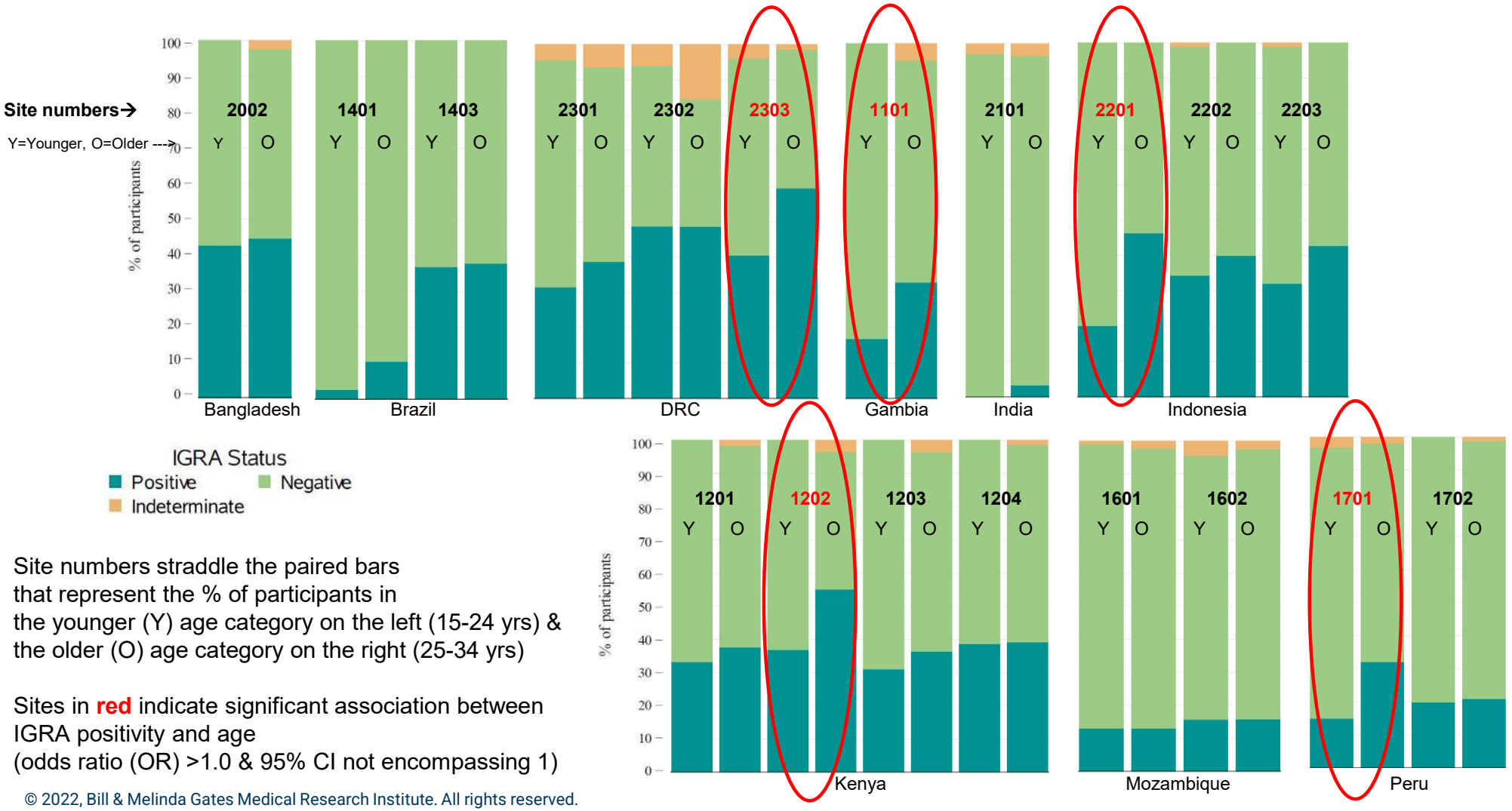
- The mean age of participants ranged from 22 years in Mozambique to 25 years in India.
- The percentage of participants in the older age category (25-34 years) ranged from 28% in Mozambique to 56% in India.
- The percentage of female participants varied from 31% in India to 68% in The Gambia.
- None of the participants in Bangladesh and India were healthcare professionals; the highest percentage of healthcare professionals was 15% in Brazil.
- The countries with higher percentage of participants classified as underweight were The Gambia (21%), Indonesia (19%), South Africa (18%) and Democratic Republic of Congo (16%).
- The highest percentage of participants with a positive HIV test result was 11% in South Africa.

IGRA status at Screening, by site



Error bars correspond to Clopper-Pearson 95% confidence intervals

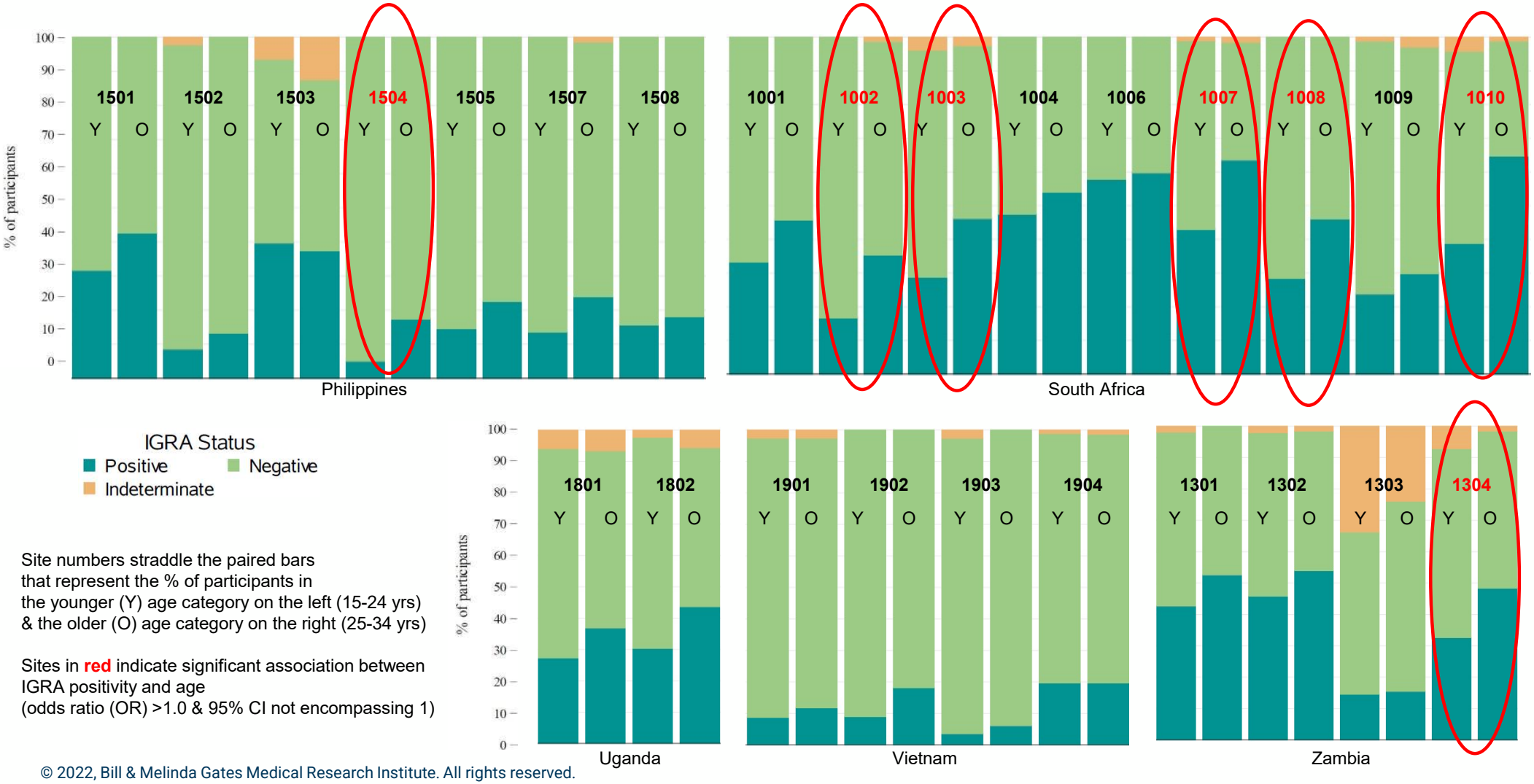
IGRA status at each site by age category: Younger (15-24 yrs) and Older (25-34 yrs, 1 of 2



Site numbers straddle the paired bars that represent the % of participants in the younger (Y) age category on the left (15-24 yrs) & the older (O) age category on the right (25-34 yrs)

Sites in **red** indicate significant association between IGRA positivity and age (odds ratio (OR) >1.0 & 95% CI not encompassing 1)

IGRA status at each site by age category: Younger (15-24 yrs) and Older (25-34 yrs, 2 of 2



Site numbers straddle the paired bars that represent the % of participants in the younger (Y) age category on the left (15-24 yrs) & the older (O) age category on the right (25-34 yrs)

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Association between IGRA status and age

- For 12 (27%) of 45 sites, the odds of having a positive IGRA status was higher among the older participants (25-34 yrs) than among the younger participants (15-24 yrs) with OR >1.0 & 95% CI that do not encompass 1.
- For 33 (73%) of 45 sites, the OR for the association between IGRA status and age category (25-34 yrs vs 15-24 yrs) encompasses 1

Conclusions

- As expected, IGRA positivity varied by country and across sites within countries.
- When participants were categorized by age, IGRA positivity generally trended higher in the older age category (25-34 years).
- For 12 (27%) of 45 sites, the odds of having a positive IGRA status was higher among the older participants (OR >1.0 & 95% CI do not encompass 1)
- We succeeded in selecting high TB burden sites for this study, as many of the sites had high IGRA positivity
- The data allowed data-driven site-selection for the M72/AS01$_{E-4}$ Phase 3 trial, as well as site-specific adjustment of recruitment strategies.

Authors

BILL & MELINDA GATES MEDICAL RESEARCH INSTITUTE

Alemnew F. Dagnew
Linda L. Han
Lisa Schlehuber
Justine Sunshine
Amy Cinar
Michael Dunne
Alexander C. Schmidt

Deepali Gaikwad, Department of Pulmonary Medicine, PCMC'S PGI YCM Hospital, Pune, Maharashtra, India.

Alberto L Garcia-Basteiro
ISGlobal
Barcelona Institute for Global Health
Hospital Clínic - Universitat de Barcelona

Tarcela Gler, De La Salle Medical and Health Sciences Institute, Cavite, Philippines.

Sri Rezeki Hadinegoro, Department of Child Health Faculty of Medicine University of Indonesia, Jakarta, Indonesia.

Willem Hanekom
AHRI AFRICA HEALTH RESEARCH INSTITUTE

Javier R. Lama, Asociacion Civil Impacta Salud y Educación, Lima, Peru.

Monde Muyoyeta, Center for Infectious disease Research in Zambia (CIDRZ), Lusaka, Zambia

Sissy Musala
PNLT - RDC

Videlis Nduba
KENYA MEDICAL RESEARCH INSTITUTE KEMRI

Valeria Cavalcanti
INI Instituto Nacional de Infectologia Evandro Chagas

Tapash Roy
IRD Bangladesh

Jayne Sutherland
UKRI MRC Unit The Gambia
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Sofia Viegas
INSTITUTO NACIONAL DE SAÚDE MOÇAMBIQUE

Anne Wajja
MRC/UVRI and LSHTM Uganda Research Unit
UKRI Medical Research Council
Uganda Virus Research Institute
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Timothy Walker, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

Gates MRI TB Epi Study Group

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Thank you