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Leveraging the multi-country Ubuntu COVID-19 vaccine clinical trial as a platform for tuberculosis biomarker research in sub-Saharan Africa

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Background: CoVPN 3008 (Ubuntu), the largest study of COVID-19 mRNA vaccines in Africa, could serve as a platform for studying TB biomarkers, which have the potential to accelerate TB vaccine trials.

Methods: We enrolled adults ≥18 years living with HIV or another comorbidity associated with severe COVID-19 at 47 sites in East and Southern Africa. Enrolment data included medical history, physical exam, medications, SARS-CoV-2 serology and, for people with HIV (PWH), HIV viral load (VL) and CD4 count. We vaccinated at enrolment and month 6; SARS-CoV-2 seronegative participants were vaccinated also at month 1. Serum and stabilised whole blood (in Tempus tubes to preserve RNA) were collected at multiple timepoints. Peripheral blood mononuclear cells (PBMCs) were collected in a subset. Most participants completed 12 months of follow-up; some met exit criteria before month 12; a subcohort continued to 18 months.

Results: Data were collected on 14,001 participants enrolled between December 2021 and September 2022 (median age 39 years, 83% PWH, 69% SARS-CoV-2 seropositive, 12% with prior history of TB). Among 11,681 PWH, 17% had a CD4 count <350 cells/mm3, and 18.5% had HIV viraemia. Multiple vials of serial serum and whole blood samples were stored for >12,700 participants through month 7, for >10,500 through month 12, and for >2500 through month 18 (Figure 1). Serial PBMC samples were stored for >3000 participants at multiple timepoints.

Discussion: Ubuntu offers a unique opportunity to leverage a large, diverse, well-described, externally monitored cohort in a high TB- and HIV-burden setting with prospectively collected and stored blood samples to research TB biomarkers. Accurate predictive biomarkers of TB could reduce the size, duration, and cost of TB vaccine trials. An upcoming substudy will screen Ubuntu participants for subclinical or active TB and use stored samples from cases and TB-negative controls to investigate transcriptomic biomarkers of TB.

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Conflicts of Interest

None.

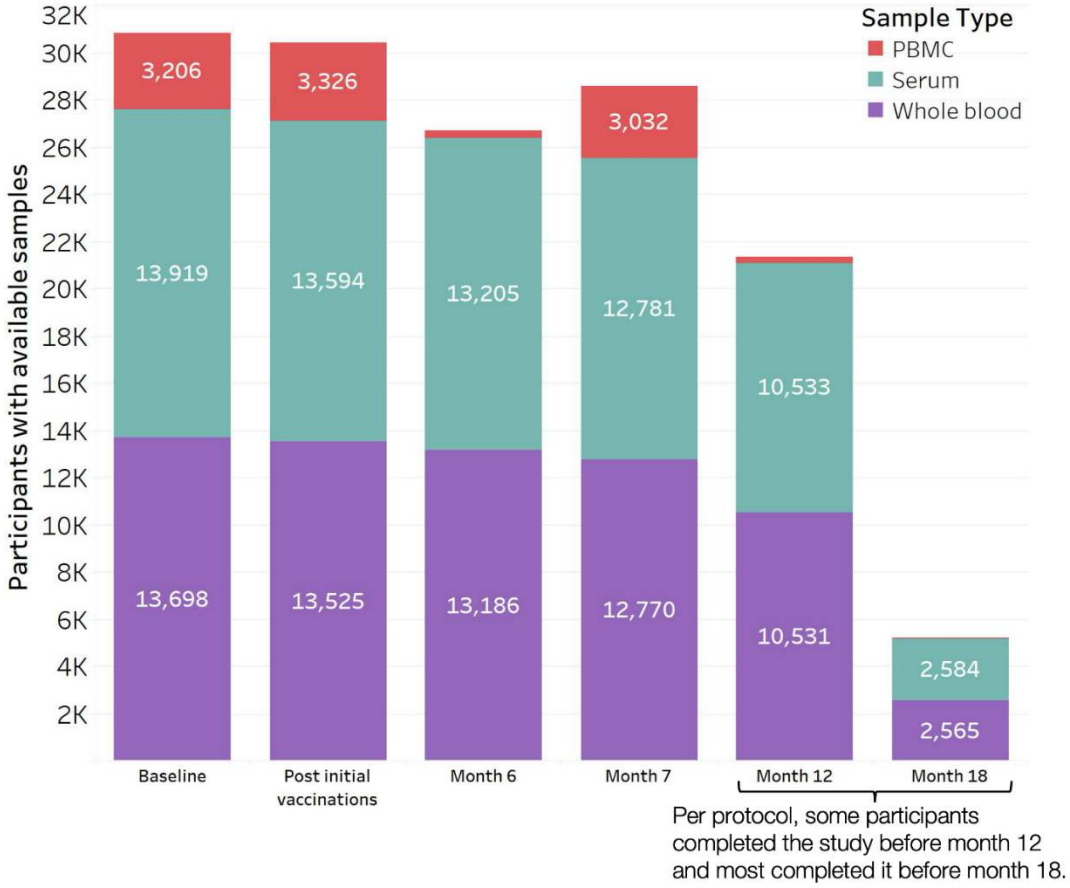

Figure 1. Serum, whole blood, and PBMCs collected at key timepoints during the study period. Serum (in Serum Separator tubes) and whole blood (in Tempus tubes) were scheduled to be collected at baseline, one month after the initial vaccinations (either at month 1 or 2, depending on the study group), at month 6, and one month post month 6 vaccination. Additionally, PBMCs (in Acid Citrate Dextrose tubes) were collected from three participant subsets: approximately 300 participants had PBMCs collected at all timepoints; approximately 3000 participants had PBMCs collected at baseline, one month after the initial vaccinations, and one month post month 6 vaccination; and all COVID-19 cases had PBMCs collected near diagnosis and at day 28.