Closing the gap, increasing access, provide adequate therapy
TB-CAPT (Close the gap, increase Access, Provide adequate Therapy) will provide evidence for impactful implementation of tuberculosis (TB) and TB/HIV co-infection diagnostic strategies, including drug-susceptibility testing, through a series of trials in Tanzania, Mozambique, and South Africa.
Timely and appropriate diagnosis and treatment is the key to reduce TB mortality, morbidity, and prevent transmission. However, 40% (4.2 million) of the 10.6 million people with TB and two-thirds of those with multi-drug resistant (MDR) TB remain undiagnosed. The main reasons are inaccessibility of diagnostics and attrition during the diagnostic process. Improved systematic delivery and access to quality diagnostic testing, at healthcare centres closer to patients’ homes would have a significant impact in decreasing the “missing millions” who die due to undiagnosed TB or are diagnosed very late. There is an urgent need for TB tools and diagnostic technologies that can not only detect disease but can also identify strains that are resistant to the TB medications that are available.

TB-CAPT includes two clinical trials in Tanzania and Mozambique, and a validation study in South Africa that evaluate the impact of diagnostic interventions on outcomes, including the effects of expanding TB testing strategies for people living with HIV (PLHIV). The trials have been designed to consider local epidemiology, as well as existing infrastructure, to compare new strategies with current standards of care.
TB-CAPT CORE TRIAL:
A pragmatic, randomized, controlled trial that assesses the impact of point-of-care implementation of the Molbio MTB assays using the Truenat system on TB diagnosis and treatment initiation in peripheral health clinics in Tanzania and Mozambique.

A total of 4,028 participants (2,031 in the intervention arm, 1,997 control arm) were enrolled in the trial between August 2022 and June 2023. In the intervention clinics, Molbio Truenat platforms were placed at facilities (N=15). During the intervention period sputum samples underwent testing with Truenat MTB Plus and, if positive, extracted DNA was reflex tested using the Truenat MTB-RIF Dx assay. Participants were asked to wait until Truenat TB testing was completed to facilitate same-day treatment initiation. In the control clinics (N=14), sputum samples collected from participants were investigated according to the standard procedures, which included off-site Xpert testing in all clinics and on-site smear microscopy in some clinics. The overall prevalence of microbiologically confirmed clinical TB was 7.5% across both arms, with men having a higher prevalence (11.2%) than women (4.2%). A total of 149 (7.3%, 95% confidence interval [CI] 6.3%–8.6%) participants started microbiologically confirmed TB treatment within 7 days of their first visit to the health centre in the intervention arm compared to 96 (4.8%, 95% CI 3.9%–5.9%) participants in the control arm. In the intervention arm, 126 (82.9%) of 152 participants diagnosed with microbiologically confirmed TB started...
Placement of molecular diagnostics in primary healthcare centres (PHCs) is feasible, reduces TB treatment delays, and increases the number of microbiologically confirmed TB diagnoses. Same-day TB treatment initiation is achievable in PHCs.
Routine respiratory specimens from 763 participants (May 2021 – Feb 2022), processed and tested with Xpert MTB/RIF Ultra, were stored in sample reagent buffer at 2–8°C. If rifampicin-resistant, the residual specimen was assessed for volume adequacy (≥2 ml) and Xpert MTB/XDR tested, with storage time recorded. A second specimen was used for routine and reference standard testing. Xpert MTB/XDR yielded a full set of valid resistance detection results in 639 (84%) compared with 507 (66%) for routine testing (p<0.0001). Median turnaround time for finalized results was 23 hours for Xpert MTB/XDR and 15 days for routine testing (p<0.0001). While 748 (98%) specimens were ≥2 ml, only 102 (13%) were stored for ≤4 hours. By reference standard (combined phenotypic and genotypic testing [whole genome sequencing]), 284/394 (72%) were isoniazid-resistant and 55/380 (14%) were fluoroquinolone-resistant. Xpert MTB/XDR sensitivity was 94% (95% CI 91–97) for isoniazid and 95% (85–99) for fluoroquinolone resistance detection. Specificity was 98% (94–100) and 100% (98–100), respectively.

- Reflex Xpert MTB/XDR testing performed well and is feasible in high throughput centralized laboratories.
- Turnaround times for resistance detection dramatically decreased from weeks to hours.
Recruitment of hospitalized HIV-positive adults is ongoing for the EXULTANT trial. As of October 2023, a total of 803 participants have been enrolled from 7 hospitals, associated with 4 research institutions across Tanzania and Mozambique. The primary objective is to investigate the effect of an expanded TB screening strategy among HIV-positive patients admitted to hospital (including Ultra on sputum, stool and urine, and AlereLAM on urine, performed regardless of presence of TB symptoms) on the proportion of bacteriologically confirmed TB cases starting treatment within 72 hours of enrolment, compared to Ultra testing (on sputum / any tissue) and AlereLAM (on urine) in only those patients who are symptomatic for TB or fulfill WHO testing recommendations. A number of secondary and exploratory objectives will assess the impact of this screening strategy on 2-month all-cause mortality, and evaluate the diagnostic yield of additional non-sputum based testing in this population.
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