# Implementing the Molbio Truenat platform and tuberculosis assays versus standard of care at primary care clinics for the detection and treatment of tuberculosis in Mozambique and Tanzania (TB-CAPT CORE): a cluster-randomised trial

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## Summary

**Background** To support access to life-saving tuberculosis testing and treatment, we evaluated whether placing portable, low complexity, WHO-recommended rapid molecular diagnostics at primary care clinics increased diagnoses and accelerated anti-tuberculosis treatment initiation compared to routine off-site testing.

**Methods** We conducted an open cluster-randomised trial of primary care clinics in Mozambique and Tanzania that provided tuberculosis diagnosis and treatment. Clinics were randomly assigned (1:1) to either on-site testing with Molbio Truenat MTB-Plus and RIF-Dx assays (intervention), or standard of care with referral-based testing using Xpert MTB/RIF Ultra (control). Adults (age ≥18 years) presenting to clinics with symptoms of presumptive pulmonary tuberculosis were eligible for inclusion if they could produce sputum and consented to participate. The primary outcome was the absolute number and proportion of participants with microbiologically confirmed tuberculosis who started treatment within 7 days of enrolment (their first visit), assessed among those with outcome data from follow-up calls (analysis population), among all enrolled participants who met eligibility criteria. This study is registered with ClinicalTrials.gov, NCT04568954.

**Findings** Between Nov 19 and Dec 3, 2020, 114 clinics were screened, of which 29 were randomly assigned and allocated to the intervention group (15 clinics) or control group (14 clinics). Between Aug 26, 2022 and June 16, 2023, 4034 participants (median age 42 years [IQR 32–55], 2156 [53·4%] female and 1878 [46·6 %] male, and 1281 [31·8%] living with HIV) were enrolled. 2534 and 2471 individuals were screened for eligibility in the intervention and control groups, respectively, with 2037 (80·4%) and 1997 (80·8%) participants enrolled; 47 participants were lost to follow-up. 302 (7·6%) of 3987 enrolled participants with outcome data had microbiologically confirmed tuberculosis. Among all enrolled participants, 147 (7·3% [95% CI 6·3–8·6]) of 2007 in the intervention group and 95 (4·8% [3·9–5·8]) of 1980 in the control group started treatment within 7 days (odds ratio [OR] 1·62 [95% CI 1·01–2·60]). Among those with microbiologically confirmed tuberculosis who were eligible for treatment, 147 (96·7%) of 152 in the intervention group and 95 (63·3%) of 150 in the control group started treatment within 7 days (OR 17·80 [95% CI 7·16–56·56]). The incidence rate ratios of starting treatment within 7 days were 1·52 (95% CI 1·12–2·07) for all enrolled participants and 1·48 (95% CI 1·35–1·63) for those with microbiologically confirmed tuberculosis who were eligible for treatment.

**Interpretation** This trial provides strong evidence supporting the placement of low complexity molecular tuberculosis diagnostics at primary care level, to enable same-day diagnosis and treatment initiation.

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For the Portuguese translation of the abstract see Online for appendix 1

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## Introduction

Tuberculosis remains a leading cause of death from a single infectious agent, despite being preventable and curable.[1] Accurate, timely diagnosis is crucial to prevent lung damage and transmission, yet 3·1 million of the estimated 10·6 million annual tuberculosis cases—and approximately 224 000 (60%) of those with multidrug-resistant tuberculosis—go undiagnosed.[1]

This diagnostic gap is largely due to limited access to testing and high attrition along the diagnostic pathway, which includes presentation to care, referral, sample collection, testing, result reporting, and treatment initiation.[2–6]

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## Research in context

### Evidence before this study

We searched PubMed on Jan 29, 2024, for systematic reviews and trials using (variations on and synonyms of) the search terms "tuberculosis" [AND] "point-of-care" [OR] "diagnostics" [OR] "Xpert MTB/RIF" AND "decentralisation" [OR] "primary care" [AND] "trial", with no date and language restriction. We found five cluster-randomised trials conducted in South Africa, Zambia, Zimbabwe, Malawi, and Uganda published between 2014 and 2021. Eligible populations were people presenting with symptoms suggestive of tuberculosis (n=3), people with symptoms suggestive of tuberculosis and living with HIV or at risk of drug-resistant tuberculosis (n=1), and people living with HIV initiating antiretroviral therapy regardless of symptoms (n=1). The intervention was Xpert MTB/RIF testing at primary health facilities in all trials, while the comparators differed across studies: on-site smear microscopy only (n=2), on-site smear microscopy and off-site culture (n=2), and on-site smear microscopy and off-site Xpert MTB/RIF testing. Most trials were comparing decentralised testing using a more sensitive diagnostic assay (Xpert MTB/RIF) to smear microscopy. Except for the trial conducted in Uganda, which implemented on-site Xpert MTB/RIF testing as part of a multicomponent intervention strategy to address health centre-level barriers, the comparator test performed in a central laboratory was culture. Although culture is more sensitive, its turn-around time is longer than molecular diagnostics.

All studies reported a reduced time to tuberculosis diagnosis and treatment initiation and a higher proportion of same-day treatment initiations in the intervention group compared with the control group. The two studies that reported on mortality did not find a significant difference between intervention and control participants.

### Added value of this study

To our knowledge, this is the first pragmatic trial which assesses the impact of decentralising molecular tuberculosis diagnostics to primary health clinics using the Truenat platform with MTB-Plus and MTB/RIF Dx assays (Truenat MTB assays). The Truenat platform has been specifically designed to be operated as a near point-of-care diagnostic solution in peripheral laboratories or primary health clinics with minimal infrastructure requirements. The features that make the Truenat platform conducive to decentralised use are its small size, battery operation, and reduced variability due to extreme heat and dust. The comparator group in this trial was optimised standard of care with off-site Xpert MTB/RIF Ultra testing with test cartridges, and sample and result transport was provided by the research team. All tuberculosis testing in intervention and control groups was performed by state staff. The proportion of participants who received a microbiological confirmation of pulmonary tuberculosis and started treatment within 7 days of presentation was significantly higher in intervention compared to control clinics. Among people with microbiologically confirmed pulmonary tuberculosis, the majority started tuberculosis treatment on the day of presentation in the intervention clinics. By contrast, same-day treatment initiation was rare in the control clinic. Importantly, a high proportion of people with *Mycobacterium tuberculosis* DNA not detected received their test results on the day of presentation, potentially allowing initiation of alternative non-tuberculosis treatments.

### Implications of all the available evidence

This study shows that decentralised molecular tuberculosis testing and same-day treatment initiation are feasible in high tuberculosis-burden countries across southern Africa. Although WHO has already endorsed the Truenat and MTB assays, other molecular diagnostics with similar performance and point-of-care potential are expected to come to the market soon. The GeneXpert platform has mainly been implemented in centralised laboratories as a hub-and-spoke model. However, many National Tuberculosis Programs are diversifying their diagnostic portfolios. Evidence generated by this trial will support decision making for considering decentralised molecular diagnostics for tuberculosis in countries with a high burden of tuberculosis.

Studies from many countries in southern Africa have reported substantial bottlenecks along diagnostic pathways.[2,3,7–9] Locating diagnostics at primary care clinics could eliminate the need for sample and result transport, potentially enabling same-day treatment initiation.

Although Xpert MTB/RIF, endorsed by WHO in 2011,[10] revolutionised tuberculosis and rifampicin resistance detection, its impact has been limited.[11–14] High costs and operational requirements (eg, stable electricity, temperature control, and dust-free environments) have confined its use to centralised laboratories in hub-and-spoke models.[15–18]

Encouragingly, the tuberculosis diagnostic pipeline is now stronger than ever. Investments during the COVID-19 pandemic period are now driving innovation in platforms and sample types.[19] New molecular and point-of-care diagnostics are emerging that might be deployed in primary care clinics or even in communities. Portable battery-operated molecular testing platforms, such as the Molbio Truenat platform (endorsed by WHO in 2020), offer the potential to further decentralise molecular testing.[20]

Here, we present the results of the TB-CAPT CORE trial, which evaluated whether availability of decentralised (ie, on-site) molecular testing with Molbio Truenat for people with presumptive pulmonary tuberculosis, combined with rapid communication of results, could lead to a greater proportion and number of individuals with microbiologically confirmed pulmonary tuberculosis initiating tuberculosis treatment within 7 days compared with standard of care in Mozambique and Tanzania.

## Methods

### Study design and clusters

We conducted a cluster-randomised trial at primary care clinics (hereafter referred to as clinics) in Tanzania (n=15) and Mozambique (n=14).

Clusters were clinics in Mozambique and Tanzania within the catchment area of the four African research institutions (appendix 2 pp 7–10). Clinics were eligible if they provided tuberculosis diagnosis and treatment, notified at least one person with tuberculosis per month in 2018–19, and did not have a GeneXpert instrument on site (appendix 2 p 27).

All adults presenting to trial clinics with symptoms of presumptive pulmonary tuberculosis were assessed for eligibility. Inclusion criteria for recruitment were symptoms suggestive of pulmonary tuberculosis, as defined by national tuberculosis treatment guidelines in each country; ability to provide a sputum sample; aged 18 years or older; and willingness and ability to provide informed consent. Exclusion criteria were circumstances that raised doubt about free and informed consent, a diagnosis of tuberculosis or current receipt of anti-tuberculosis therapy, serious illness requiring hospital admission, and previous enrolment in the trial. Full eligibility criteria are listed in appendix 2 (p 27).

The study protocol is available in appendix 2 (p 34) and has been published previously.[21] The trial protocol was approved by the following institutional review boards: Ifakara Health Institute, National Institute for Medical Research, Centro de investigação de Saúde de Manhiça, Instituto Nacional de Saúde and the National Bioethics Committee for Health in Mozambique (reference: 217/CNBS/21), and the National Health Research and Ethics Committee in Tanzania (reference: NIMR/HQ/R.8c/Vol.I/2323). This study is registered at ClinicalTrials.gov, NCT04568954. Only adults (aged 18 years or older) who signed written informed consent were enrolled in the study. An independent scientific advisory committee periodically reviewed the conduct of the trial and approved all changes of the protocol.

A list of protocol deviations is provided in appendix 2 (p 26). At Instituto Nacional de Saúde, follow-up calls were initially only conducted for participants diagnosed with tuberculosis. This resulted in 778 of 1031 participants in the analysis population with a protocol deviation, attributed to either a missed follow-up or contact occurring outside of the follow-up windows. At Centro de investigação em Saúde de Manhiça, Instituto Nacional de Saúde, and National Institute for Medical Research, the number of participants in the analysis population who were classified as having a protocol deviation due to attempted contact outside the follow-up windows were as follows: three of 869 at Centro de investigação de Saúde de Manhiça, 90 of 1195 at Instituto Nacional de Saúde, and two of 892 at National Institute for Medical Research. No other key deviations were identified or reported.

### Randomisation and masking

Clinics were randomly assigned (1:1) to intervention or control groups using a stratified, restricted randomisation procedure. Stratification was based on site (Centro de investigação de Saúde de Manhiça, Instituto Nacional de Saúde, Ifakara Health Institute, and National Institute for Medical Research) and clinic size, defined by the mean number of presumptive tuberculosis cases per quarter (Q1 2018–Q2 2020), resulting in eight strata. Within each stratum, all balanced allocations (ie, equal numbers of clusters per group) were generated using SAS (version 9.4), effectively functioning as fixed block sizes equal to the number of clinics in each stratum. Allocations were further restricted to ensure a 5% or higher difference in expected tuberculosis diagnosis between groups. From 154 166 eligible combinations, a random sample of 10 000 was drawn using a fixed seed (281345214), and the final allocation was selected on Dec 3, 2020, using seed 93657873. Randomisation was performed by an independent statistician not involved in site selection or implementation. Allocation was concealed from implementing staff until enrolment and stratification of clusters were complete. Eligible clinics were nominated by national programmes, assessed for eligibility, and enrolled by the trial team; final assignment to groups followed the pregenerated allocation list. Due to the nature of the intervention, clinic staff, participants, and research staff taking the informed consent, administering the baseline questionnaire, and doing the follow-up calls were not masked to group assignment. However, data analysts were masked to group assignment, with blinded datasets until the database lock.

See Online for appendix 2

### Procedures

In intervention clinics, Truenat platforms (Molbio Diagnostics, Goa, India) were installed and facility-based laboratory staff were trained on Truenat assays before study initiation. During the intervention, sputum samples were tested with Truenat MTB Plus and, when positive, reflex-tested with Truenat MTB-RIF Dx for rifampicin resistance. Tests took 1 h, and participants were asked to wait for results to enable same-day treatment initiation.

In control clinics, staff received refresher training on national tuberculosis diagnosis and treatment guidelines. Sputum samples were processed per standard procedures, including off-site Xpert testing and on-site smear microscopy in parallel in some clinics. Site assessments revealed operational issues (eg, sputum container stockouts and delays in sample transport) leading to occasional referral of patients instead of samples. To address this issue, sputum containers were stocked throughout, and samples were collected at least twice weekly. Off-site laboratories received Xpert MTB/RIF Ultra cartridges for sample testing.

After obtaining written informed consent from participants, a paper questionnaire captured sociodemographic data, including self-reported information on sex, symptom

duration, medical history, and household characteristics. Race and ethnicity data were not collected. Participants provided a sputum sample for on-site or off-site testing. When participants were unable to expectorate, they received a container for next-day submission; those still unable to produce sputum were excluded.

Contact details, including those of a trusted informant, were collected. Follow-up calls were made at 7–21 days (call one) and 60–90 days (call two) after enrolment. When participants could not be reached after three attempts, the trusted informant was contacted or a home visit was conducted.

At follow-up, participants were asked per a standardised script, whether they had been diagnosed with "tuberculosis in their sputum" and whether treatment had started. We recorded responses for treatment start date and clinic. Tuberculosis diagnosis and treatment initiation were verified using off-site test results, treatment registers, and tuberculosis cards. Self-reported tuberculosis category, treatment status, and start date were cross-checked with clinical records.

### Outcomes

The primary outcome was the absolute number and the proportion of participants with microbiologically confirmed tuberculosis who started tuberculosis treatment within 7 days of their first visit, among all enrolled and eligible participants. Additional details regarding all predefined primary and secondary outcomes, whether these were analysed and reported in the manuscript, and information on subgroup analyses are summarised in appendix 2 (pp 22–24).

Secondary outcomes reported here are the time to microbiological confirmation of tuberculosis (up to 60 days from enrolment) among all enrolled and eligible participants; the proportion of participants treated for tuberculosis within 60 days who were either microbiologically or clinically confirmed, among those with microbiological confirmation and among those with clinical confirmation; the number and proportion of participants with signs and symptoms of pulmonary tuberculosis who started tuberculosis treatment with microbiological confirmation within 60 days, among all enrolled and eligible participants; the number and proportion of participants with signs and symptoms of pulmonary tuberculosis starting tuberculosis treatment without microbiological confirmation within 7 and 60 days among all enrolled and eligible participants; the number and proportion of enrolled participants with signs and symptoms of pulmonary tuberculosis initiating tuberculosis treatment (regardless of confirmation status) within 7 and 60 days among all enrolled and eligible participants; the time to tuberculosis treatment initiation among those with microbiological confirmation and all enrolled participants (censored at 60 days); and the number and proportion of enrolled participants with ongoing treatment status at 60 days among those diagnosed with tuberculosis either clinically or microbiologically, and separately among those with clinical diagnosis and among those with microbiological confirmation. Due to minimal variation in this outcome, analysis of ongoing treatment status was not conducted; and prevalence of current cough, limited appetite, and weakness at 60 days from enrolment (although prevalence of cough at 60 days was analysed, data on limited appetite and weakness were unavailable). Several economic outcomes were prespecified but not analysed in this study; these included patient-incurred costs, number of lost working days, unit costs of diagnosis and treatment, and the incremental cost-effectiveness ratio. These secondary outcomes were assessed separately in a dedicated cost-effectiveness analysis and are reported elsewhere.[22]

We also report here the prespecified additional outcomes around operational characteristics: Truenat platform and tuberculosis assay non-determinate test result rates, and the rate of Truenat platform failure are reported here.

### Statistical analysis

The sample size calculation was based on the proportion of participants with microbiologically confirmed pulmonary tuberculosis who initiated treatment within 7 days of their first visit among all enrolled and eligible participants. The study used a matched-pair cluster randomised design, with clinics as the unit of randomisation.

The number of clusters per group ($N_{cp}$) was estimated using the formula 7·14 for matched cluster randomised trials,[23] in which the adjustment constant for matched design (A) is 2, cluster size (*CS*) is 150, and coefficient of variation ($CV_m$) is 0·25. The proportions ($p_{intervention}$ and $p_{control}$) were derived as:

$$p = prev \times sens \times \left(1 - LTFU_{diag}\right) \times \left(1 - LTFU_{pretreat}\right)$$

where *prev* is the prevalence of tuberculosis in the target population, *sens* is the diagnostic sensitivity, $LTFU_{diag}$ is the proportion of participants lost to follow-up at diagnosis, and $LTFU_{pretreat}$ is the proportion of participants lost to follow-up before treatment.

Assumptions included a tuberculosis prevalence of 12% (based on the clinic-level positivity being 10-20%), sensitivity of 70% (control) and 89% (intervention), diagnostic loss to follow-up of 10% (control) and 2% (intervention), and pretreatment loss to follow-up of 20% (control) and 10% (intervention). This resulted in $p_{control}$=0·060 and $p_{intervention}$=0·093.

To detect a 3% absolute difference with 80% power and a 5% significance level, 13 cluster pairs (26 clinics; 3900 participants) were required. To account for recruitment and cluster size uncertainties, 28 clinics (4200 participants) were initially targeted. To mitigate the risk of under-recruitment due to COVID-19, the number of randomised clinics was increased to 30. An additional six clinics were added, bringing the total number of clusters to 36, as back-up capacity for an eventuality for clinic replacement or addition if under-enrolment was observed. Ultimately,

these additional six clinics were not required, thus not included in the study. One clinic was excluded after randomisation due to ineligibility. The populations defined for analysis were intention to treat (ITT; ie, all participants randomly assigned to their respective groups); the analysis dataset (participants in the ITT population with partial outcomes [ie, data available for follow-up call one or follow-up call two]); per protocol (ie, including participants who fulfil the protocol in terms of eligibility, interventions, and outcome assessment without any major protocol deviation); and the protocol deviation dataset (ie, including participants listed in protocol deviations reported to the institutional review board and remaining analysis dataset participants with follow-up call attempts outside of the specified time periods).

The statistical analysis plan (appendix 2 pp 95–122) and all post-hoc deviations from the statistical analysis plan (appendix 2 pp 3–4) are provided. All statistical analyses were conducted using the R statistical software (version 4.3.1). Primary and secondary analyses were prespecified to be conducted on the analysis dataset and per-protocol populations. Descriptive analysis of baseline characteristics was used to identify imbalances between study groups at the clinic level. Baseline characteristics at the clinic level and separately at the individual level are summarised, as number and proportion of total, or as median proportion with IQR, as indicated, in table 1.

Cough duration, smoking status, diabetes status, and previous tuberculosis treatment were added post hoc to the initial statistical analysis plan, to better understand group balance and inform covariate choices (appendix 2 pp 3–4). The sample flow was reported from the ITT population. p values were adjusted using the Benjamini-Hochberg method.

A sensitivity analysis assessed protocol deviation (appendix 2 pp 27–28).

No formal safety analysis was conducted, as the study procedures did not involve investigational products or interventions beyond routine clinical care.

Absolute effects were reported using Wilson's score method for differences in proportions (PropCIs, diffscoreci) and bootstrapping for group-wise medians (boot, boot).

All models were initially fitted with prespecified covariates (ie, trial group, country, sex, age, and HIV status), which were retained, removed, added (ie, previous tuberculosis treatment) or changed (ie, institution instead of country) based on statistical significance as baseline characteristics and model stability based on z-test, likelihood ratio tests, and Akaike information criterion. The exclusion of some prespecified variables (ie, HIV status and previous tuberculosis treatment) from the primary analysis was performed to reduce the risk of overfitting and convergence issues after the data were made available and therefore decided post hoc to the initial statistical analysis plan (appendix 2 pp 3–4). Estimates from the full models, the variables retained in the reduced models, and their respective diagnostics are presented in appendix 2 (pp 11–13, 17).

A generalised linear model (appendix 2 pp 21–23) with log link and Poisson distribution was used, with the number of successes (ie, participants diagnosed with microbiologically confirmed pulmonary tuberculosis and initiating treatment within 7 days) per clinic as the response. Robust standard errors were calculated to account for potential distribution violations, and 95% CIs were derived accordingly. Incidence rate ratios (IRRs) were obtained by exponentiating fixed-effect coefficients. The application of log link, the calculation of robust standard errors, and the choice of reporting of IRRs was done post hoc to the initial statistical analysis plan (appendix 2 pp 3–4).

Differences in proportions were analysed using a generalised linear mixed model (appendix 2 pp 21–23), with trial group, age group, sex, and research institution as fixed effects. A random intercept for clinic nested within the trial group accounted for clustering. Odds ratios (ORs) and 95% CIs were calculated by exponentiating the fixed-effect coefficients from the full generalised linear mixed model, incorporating both fixed and random effects.

As planned, a subgroup analysis of the primary outcome was conducted among participants with microbiologically confirmed pulmonary tuberculosis. Using treatment initiation within 7 days as a binary outcome, a generalised linear mixed model was fitted as aforementioned. Due to extreme proportions, 95% CIs were estimated via the profile likelihood method.

For the primary and secondary outcomes, additional subgroup analyses were prespecified by sex and gender (if the data were available), HIV status, institution, country, asset index, and age category if there was a strong difference observed in the descriptive statistics. For the primary outcome, no notable differences were observed in the distribution of the primary outcome across age categories, and data for the country setting variables were missing for 90% of participants. Additionally, subgroup analysis by asset index was not done because it was determined to be of limited relevance to the main analysis outcomes. As a result, subgroup analyses were not conducted for these variables. Although a substantial variation in the primary outcome regardless of group was observed by institution, ($\chi^2$=45·069, p<0·001), the small number of outcome occurrences (within institutional subgroups [ie, eight of 529 occurrences and 12 of 363 occurrences in one of the institutions]) precluded meaningful subgroup analyses. Instead, the institution was included as a covariate in all model adjustments. For the secondary outcomes, only the outcome of time to bacterial confirmation of tuberculosis (up to 60 days) from enrolment was assessed by microbiological confirmation status, while all other subgroup analyses were not done in order to limit multiplicity and avoid over-interpretation of the exploratory findings, especially due to the limited power of the comparisons.

Secondary binary outcomes were analysed using the same methods as primary outcomes. Initially, mixed-effects Cox proportional hazards models (appendix 2 pp 21–23) were used, with clinic-level clustering via random intercepts.

| | Clinic-level characteristics | | Individual-level characteristics | |
|---|---|---|---|---|
| | Intervention (n=15) | Control (n=14) | Intervention (n=2007) | Control (n=1980) |
| Research institution | | | | |
| Mozambique | | | | |
| Centro de Investigação em Saúde de Manhiça | 3 (20·0%) | 3 (21·4%) | 420 (20·9%) | 449 (22·7%) |
| Instituto Nacional de Saúde | 5 (33·3%) | 3 (21·4%) | 625 (31·1%) | 406 (20·5%) |
| Tanzania | | | | |
| Ifakara Health Institute | 4 (26·7%) | 4 (28·6%) | 599 (29·9%) | 596 (30·1%) |
| National Institute for Medical Research | 3 (20·0%) | 4 (28·6%) | 363 (18·1%) | 529 (26·7%) |
| On-site HIV care and treatment services available | 15 (100%) | 14 (100%) | .. | .. |
| Tuberculosis notifications per month in 2019 | 61·0 (34·5–155·5) | 76·5 (21·5–177·3) | .. | .. |
| Distance to Xpert laboratory, km | 11·0 (6·6–19·0) | 16·0 (5·0–25·0) | .. | .. |
| Participants | 147·0 (123·0–150·0) | 149·5 (141·0–150·0) | .. | .. |
| Setting† | | | | |
| Urban | 8·2% (0·0–9·3) | 3·9% (0·7–8·4) | 108 (5·4%) | 83 (4·2%) |
| Rural | 0·7% (0·0–9·6) | 6·0% (1·2–9·6) | 85 (4·2%) | 112 (5·7%) |
| Missing | 90·0% (90·0–90·7) | 90·0% (89·9–90·1) | 1814 (90·4%) | 1785 (90·1%) |
| Sex | | | | |
| Male | 40·0% (36·5–54·2) | 43·2% (39·7–56·4) | 919 (45·8%) | 932 (47·1%) |
| Female | 60·0% (45·8–63·5) | 56·8% (43·6–60·3) | 1088 (54·2%) | 1048 (52·9%) |
| Age | | | | |
| Median | 42·1 (40·5–45·3) | 41·7 (40·7–45·6) | 42·2 (32·0-55·0) | 42·7 (32·0-55·2) |
| 18–30 years | .. | .. | 459 (22·9%) | 464 (23·4%) |
| 30–40 years | .. | .. | 476 (23·7%) | 453 (22·9%) |
| 40–50 years | .. | .. | 433 (21·6%) | 438 (22·1%) |
| ≥50 years | .. | .. | 639 (31·8%) | 625 (31·6%) |
| Cough duration, days* | 18·5 (14·0–21·0) | 21·0 (14·0–21·0) | 18 (14–30), n=2006 | 18 (14–30), n=1979 |
| Self-reported smoking | | | | |
| Yes | 9·3% (4·6–18·0) | 9·6% (7·2–12·6) | 289 (14·4%) | 301 (15·2%) |
| No | 90·0% (81·6–93·1) | 89·0% (85·0–92·0) | 1697 (84·6%) | 1662 (83·9%) |
| Unknown | 0·8% (0·0–1·9) | 0·7% (0·0–1·2) | 21 (1·0%) | 17 (0·9%) |
| Self-reported diabetes | | | | |
| Yes | 2·0% (0·4–3·0) | 1·8% (0·8–3·0) | 41 (2·1%) | 39 (2·0%) |
| No | 96·6% (94·4–98·1) | 96·1% (94·8–98·6) | 1921 (95·7%) | 1891 (95·5%) |
| Unknown | 0·0% (0·0–3·2) | 1·0% (0·2–2·4) | 45 (2·2%) | 50 (2·5%) |
| HIV status | | | | |
| Positive | 26·2% (14·4–41·7) | 37·3% (25·2–43·0) | 560 (27·9%) | 708 (35·8%) |
| Negative | 49·3% (39·5–58·5) | 49·7% (42·0–57·7) | 983 (49·0%) | 995 (50·2%) |
| Unknown or not tested | 17·5% (10·8–26·2) | 9·9% (7·8–19·5) | 464 (23·1%) | 277 (14·0%) |
| Self-reported previous tuberculosis treatment | | | | |
| Yes (any time) | 4·6% (1·7–12·2) | 10·7% (2·8–13·8) | 146 (7·3%) | 206 (10·4%) |
| Yes (within the past 2 years) | .. | .. | 30 (1·5%) | 33 (1·7%) |
| Yes (>2 years ago) | .. | .. | 89 (4·4%) | 152 (7·7%) |
| Yes (period unknown) | .. | .. | 27 (1·4%) | 21 (1·1%) |
| No | 92·0% (87·5–97·6) | 87·9% (85·3–95·0) | 1840 (91·7%) | 1752 (88·4%) |
| Unknown | 0·0% (0·0–1·0) | 0·7% (0·0–2·5) | 21 (1·0%) | 22 (1·1%) |

Data are n (%) or median prevalence (IQR). *One participant in the intervention group reported no cough; one participant in the control group had an unknown cough status. †Proportions represent median values across clinics and may not sum to 100% as each category median was calculated independently from clinic-level data.

***Table 1:*** **Baseline characteristics at the clinic and individual level (analysis dataset)**

Schoenfeld residuals were used to assess the proportional hazards assumption. A strong violation in the group variable (ie, the main variable of interest) prompted the use of linear mixed-effects regression for time-to-event outcomes related to treatment and diagnosis. As the specific alternative approach was not prespecified in the statistical analysis plan, this constitutes a post-hoc analysis (appendix 2 pp 3–4). Relative effects were obtained by exponentiating the group coefficient. 95% CIs were computed using the Wald method.

As post-hoc analyses, we aimed to assess the number and proportion of participants who received their test result on the day of presentation and who initiated treatment on the day of presentation. However, for participants who received their test result on the day of presentation, we did not perform this post-hoc analysis because same-day receipt of results was only captured in the intervention group. In the control group, only the date the clinic received the laboratory result was recorded, not the date the result was communicated to the participant. This differential ascertainment prevents a valid between-group analysis, so we did not report same-day result receipt.

### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

## Results

Between Nov 19 and Dec 3, 2020, of 114 clinics screened, 36 were eligible and randomised to intervention and control groups; 30 were selected for trial implementation (including six back-ups). One clinic was excluded at trial initiation due to the unexpected presence of a GeneXpert instrument. Of the 29 clinics included, 15 were randomly assigned to the intervention and 14 to the control (figure). No participants were screened or enrolled at the six back-up clinics. Between Aug 26, 2022, and June 16, 2023, 5005 individuals who accessed the study clinics during the study were assessed for eligibility. Of those, 4034 (80·6%) were enrolled in the trial (figure). 47 participants were lost to follow-up and excluded from the outcome analysis. All efforts to contact these participants or their informants after enrolment were unsuccessful. Hence, the primary outcome data were not available. Among these participants, the sputum results from samples submitted at enrolment were tested for *Mycobacterium tuberculosis* DNA, with no detection in 26 (87%) of 30 in the intervention group and 15 (88%) of 17 in the control group, detection in two (7%) in the intervention group and two (12%) in the control group, and unknown status in two (7%) in the intervention group due to an invalid result. No loss to follow-up was reported among participants with microbiologically confirmed pulmonary tuberculosis at 2–3 months after enrolment.

Baseline clinic-level and participant-level characteristics are summarised in table 1 and given in detail by clinic cluster in appendix 2 (pp 7–8). The characteristics were broadly balanced between groups regarding setting, availability of HIV services, and patient demographics (table 1). Median age, sex distribution, and other participant-level indicators showed minimal variation. 4034 participants were enrolled (median age 42 years [IQR 32–55]), with a balanced sex distribution (2156 [53·4%] female and 1878 [46·6%] male), and 1281 [31·8%] were living with HIV.

The proportion of participants with HIV positivity and previous tuberculosis treatment was higher in control clinics than in intervention clinics, but both factors were accounted for in the adjusted analyses.

302 (7·6%) of 3987 participants in the analysis dataset were diagnosed with microbiologically confirmed pulmonary tuberculosis. Among all enrolled participants, 147 (7·3% [95% CI 6·3–8·6]) of 2007 in the intervention group and 95 (4·8% [3·9–5·8]) of 1980 in the control group were initiated on tuberculosis treatment within 7 days of presentation (table 2), an absolute difference of 2·53% (95% CI 1·05–4·03). The odds of receiving a microbiological confirmation and initiating treatment within 7 days were higher (OR 1·62 [95% CI 1·01–2·60], intraclass correlation coefficient [ICC]=0·07) in the intervention group compared with the control group (table 2). Median time to treatment initiation in the intervention group was 0·0 days (IQR 0·0–0·0), compared with 5·0 days (IQR 3·0–10·0) in the control group, reflecting an absolute difference of 5·0 days (95% CI 4·0–7·0).

Among participants with microbiologically confirmed pulmonary tuberculosis (152 [7·6%] of 2007 participants in the intervention group and 150 [7·6%] of 1980 participants in the control group), 96·7% (147 participants) in the intervention group and 63·3% (95 participants) in the control group started treatment within 7 days of presentation, yielding an absolute difference of 33·38% (95% CI 25·30–41·72). Among those diagnosed with microbiologically confirmed tuberculosis, the odds of starting treatment within 7 days were higher in the intervention group compared with control group (OR 17·80 [95% CI 7·16–56·56], ICC=0·03). The IRRs of starting treatment for microbiologically confirmed tuberculosis within 7 days were 1·52 (95% CI 1·12–2·07) and 1·48 (95% CI 1·35–1·63) when comparing intervention and control clinics in all participants and those with microbiologically confirmed tuberculosis, respectively.

Among participants with microbiologically confirmed tuberculosis, same-day treatment was also substantially higher in the intervention clinics (125 [82·2%] of 152 participants) compared with in the control clinics (five [3·3%] of 150 participants; post hoc; table 3). The absolute difference in time to microbiological confirmation of tuberculosis between the intervention and the control groups was 3 days (relative effect 0·52 [95% CI 0·47–0·56], ICC=0·10; table 2).

Regarding time to tuberculosis treatment initiation, a significant interaction between study group and tuberculosis diagnosis category (microbiological *vs* clinical) was observed (likelihood ratio test $\chi^2$=25·98, df=2, p<0·0001). Therefore, analyses were conducted separately within each diagnostic subgroup (decided post hoc; appendix 2 p 3). Time to treatment initiation for microbiologically confirmed tuberculosis also differed significantly between the intervention group and the control group, with an absolute difference of 5 days (relative effect 0·49 [95% CI 0·44–0·54], ICC=0·06; table 2). Among those clinically diagnosed with pulmonary tuberculosis (30 [1·5%] of 2007 in the intervention group *vs* 62 [3·1%] of 1980 in the control group),

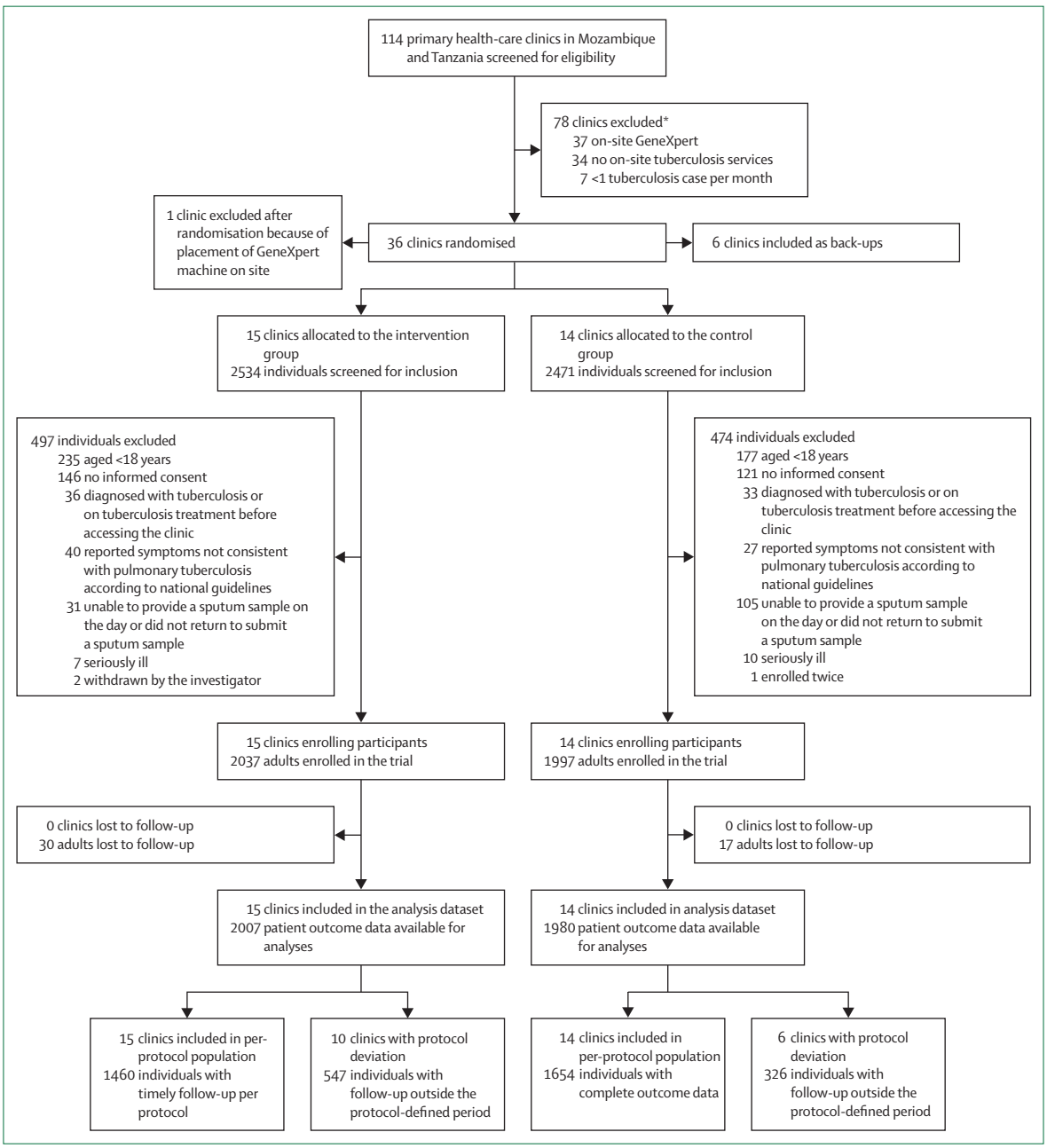


***Figure:*** **Flow diagram of clusters and individuals through the phases of the TB-CAPT CORE trial**
*Primary care clinics within the catchment area of the enrolling institutions in Mozambique and Tanzania were evaluated on the basis of the number of presumptive tuberculosis cases reported between 2018 and 2019 to ensure sufficient participant recruitment during the trial's enrolment phase. Clinics were excluded when they had low patient volumes (fewer than one person with tuberculosis per month), had no on-site tuberculosis treatment services, or already had on-site GeneXpert testing available.

time to treatment initiation differed by 4 days in the intervention clinics compared with the control clinics (relative effect 0·62 [95% CI 0·49–0·78], ICC=0·07; table 3).

The odds of receiving a microbiological confirmation for pulmonary tuberculosis and initiating treatment by 60 days did not significantly differ between groups (OR 1·02 [95% CI 0·66–1·58], ICC=0·06), and this finding was consistent when analysing absolute numbers per clinic (table 2). Similarly, the odds of receiving microbiological confirmation by 60 days and starting treatment at any time (OR 1·05 [95% CI 0·67–1·64], ICC=0·07, adjusted p=0·86) or the odds of receiving a clinical confirmation by 60 days and starting treatment (0·57 [0·24–1·33], ICC=0·18, adjusted p=0·29) did not significantly differ between groups (appendix 2 pp 16–18).

Among those clinically diagnosed with tuberculosis (ie, without microbiological confirmation; table 2), the intervention did not significantly affect the proportion of

| | Intervention | Control | Absolute difference (95% CI) | Point estimate (95% CI) | Adjusted p value |
|---|---|---|---|---|---|
| **Primary outcome: proportion of people with confirmed and treated pulmonary tuberculosis at 7 days** | | | | | |
| All enrolled* | 147/2007; 7·3% (6·3–8·6) | 95/1980; 4·8% (3·9–5·8) | 2·53% (1·05–4·03) | OR 1·62 (1·01–2·60) | 0·095 |
| All microbiologically confirmed pulmonary tuberculosis | 147/152; 96·7% (92·5–98·6) | 95/150; 63·3% (55·4–70·6) | 33·38% (25·30–41·72) | OR 17·80 (7·16–56·56) | <0·0001† |
| **Primary outcome: number of people with confirmed and treated pulmonary tuberculosis at 7 days** | | | | | |
| All enrolled | | | | | |
| Median rate per clinic per 100 participants (IQR) | 6·0 (4·2–8·1) | 4·2 (2·3–5·2) | 1·84 (–0·49 to 4·69) | IRR 1·52 (1·12–2·07) | 0·024‡ |
| All microbiologically confirmed pulmonary tuberculosis | | | | | |
| Median rate per clinic per 100 participants (IQR) | 100·0 (93·6–100·0) | 68·6 (50·0–82·1) | 31·40 (16·92 to 50·00) | IRR 1·48 (1·35–1·63) | <0·0001† |
| **Secondary outcome: time to microbiological confirmation of pulmonary tuberculosis** | | | | | |
| All microbiologically confirmed pulmonary tuberculosis | | | | | |
| Median days to diagnosis (IQR)§ | 0·0 (0·0–0·0) | 3·0 (2·0–6·0) | 3·0 (3·0 to 4·0) | Relative effect 0·52 (0·47–0·56) | <0·0001† |
| **Secondary outcome: time to treatment of pulmonary tuberculosis** | | | | | |
| All microbiologically confirmed pulmonary tuberculosis | | | | | |
| Median days to treatment (IQR)§ | 0·0 (0·0–0·0) | 5·0 (3·0–10·0) | 5·0 (4·0 to 7·0) | Relative effect 0·49 (0·44–0·54) | <0·0001† |
| All clinically confirmed pulmonary tuberculosis | | | | | |
| Median days to treatment (IQR)§ | 3·5 (1·0–7·0) | 7·5 (2·0–15·8) | 4·0 (0·0 to 7·0) | Relative effect 0·62 (0·49–0·78) | 0·011‡ |
| **Secondary outcome: proportion of people with confirmed and treated pulmonary tuberculosis at 60 days** | | | | | |
| All enrolled* | 150/2007; 7·5% (6·4–8·7) | 145/1980; 7·3% (6·3–8·6) | 0·15% (–1·48 to 1·78) | OR 1·02 (0·66–1·58) | 0·93 |
| **Secondary outcome: number of people with confirmed and treated pulmonary tuberculosis at 60 days** | | | | | |
| All enrolled* | | | | | |
| Median rate per clinic per 100 participants (IQR) | 6·4 (4·2–8·5) | 5·1 (4·0–9·2) | 1·25 (–3·81 to 3·15) | 1·02 (0·68–1·53) | 0·93 |

Data are n/N; % (95% CI) unless otherwise specified. Other secondary endpoints are reported in the appendix 2 (pp 19–21). IRR=incidence rate ratio. OR=odds ratio. *All enrolled refers to all participants included in the analysis dataset. †Adjusted p≤0·001. ‡Adjusted p≤0·05. §Time to diagnosis and treatment was censored at 60 days.

***Table 2:*** **Absolute and relative effect sizes for primary and major secondary endpoints from the analysis dataset participants**

participants starting treatment initiation by 7 days (OR 0·97 [95% CI 0·31–3·07], ICC=0·28, adjusted p=0·97) or 60 days (0·57 [0·24–1·38], ICC=0·20, adjusted p=0·32). This finding was consistent when analysing absolute numbers per clinic (IRR 1·27 [95% CI 0·58–2·79], adjusted p=0·63 for 7 days and 0·50 [0·23–1·10], adjusted p=0·15 for 60 days; appendix 2 pp 16–18).

Among all participants, the proportion of participants with signs and symptoms of pulmonary tuberculosis initiating treatment, regardless of microbiological diagnosis within 7 days (OR 1·47 [95% CI 0·88–2·45], ICC=0·10, adjusted p=0·23) or 60 days (0·87 [95% CI 0·56–1·36], ICC=0·08, adjusted p=0·61) did not significantly differ between groups (appendix 2 pp 16–18). The IRRs of starting treatment for tuberculosis among participants with signs and symptoms of tuberculosis, regardless of microbiological confirmation within 7 days and 60 days were 1·42 (95% CI 1·01–2·00, adjusted p=0·091) and 0·84 (0·62–1·14, adjusted p=0·36), respectively.

Effect estimates were similar in the per-protocol population (data not shown) across all analyses. Baseline characteristics at group, clinic, and individual level for the per-protocol population are summarised in appendix 2 (pp 5–6, 9–10).

Symptoms, health status, and proportion of people reporting to have received treatment at the follow-up call number one were similar among intervention and control participants (appendix 2 p 19). The prevalence of cough did not differ significantly between groups at 60 days from enrolment (OR 0·72 [95% CI 0·38–1·38], ICC=0·14, adjusted p=0·41; appendix 2 pp 16–18).

In subgroup analyses, there was no evidence that the intervention effect on the primary outcomes differed according to sex, HIV status, or country (appendix 2 p 19). Results were similar in the per-protocol population (appendix 2 p 21).

Nine participants died while receiving tuberculosis treatment: four participants were diagnosed with microbiologically confirmed pulmonary tuberculosis (one in the intervention group and three in the control group) and five were diagnosed clinically (three in the intervention group and two in the control group).

For 137 (6·7%) of 2037 sputum samples, DNA extraction errors were observed on the initial test in the intervention group. Most of these errors (112 [84·8%] of 132) were resolved when the DNA extraction was repeated using the same sputum sample (appendix 2 p 21).

Of the 2012 samples for which DNA extraction was successful, 1796 (89·3%) revealed actionable results on the Truenat MTB Plus chip (*Mycobacterium tuberculosis* [MTB] detected: n=143; MTB not detected: n=1653) and 191 (9·5%)

| | Intervention | Control |
|---|---|---|
| **Treatment initiation** | | |
| Participants with confirmed pulmonary tuberculosis | n=152 | n=150 |
| Same day | 125 (82·2%) | 5 (3·3%) |
| Within 7 days of presentation | 147 (96·7%) | 95 (63·2%) |
| Within 60 days of presentation | 150 (99·0%) | 145 (97·0%) |
| Participants with clinical pulmonary tuberculosis | n=30 | n=62 |
| Same day | 4 (13·3%) | 4 (6·5%) |
| Within 7 days of presentation | 25 (83·3%) | 31 (50·0%) |
| Within 60 days of presentation | 30 (100·0%) | 61 (98·4%) |
| **Treatment outcomes** | | |
| Participants with confirmed pulmonary tuberculosis | n=150 | n=145 |
| On tuberculosis treatment | 147 (98·0%) | 137 (94·5%) |
| Transfer out | 2 (1·3%) | 5 (3·4%) |
| Death | 1 (0·7%) | 3 (2·1%) |
| Loss to follow-up | 0 | 0 |
| Participants with clinical pulmonary tuberculosis | n=30 | n=61 |
| On tuberculosis treatment | 26 (86·7%) | 58 (95·1%) |
| Transfer out | 0 | 1 (1·6%) |
| Death | 3 (10·0%) | 2 (3·3%) |
| Loss to follow-up | 1 (3·3%) | 0 |

Data are n (%).

***Table 3:*** **Treatment initiation and treatment outcomes among participants diagnosed with tuberculosis**

results were invalid. 25 (1·2%) of 2012 analysis runs were aborted due to an error and no result was obtained. 192 tests were repeated using the same DNA eluate, resulting in an additional 127 (66·1%) actionable results (MTB detected: n=6; MTB not detected: n=121).

143 (96·0%) of 149 DNA eluates in which MTB was detected were reflexed to the Truenat MTB-RIF Dx chip: 92 (64·3%) results were actionable (rifampicin resistance: n=3; rifampicin resistance not detected: n=89). No actionable result was obtained for 51 DNA eluates (indeterminate: n=46; error: n=5; appendix 2 p 18). In the control group, 134 participants with MTB detected by GeneXpert underwent rifampicin resistance testing. Among these, six (4·5%) had rifampicin-resistant tuberculosis, 123 (91·8%) had no resistance detected, and five (3·7%) had indeterminate results (appendix 2 p 25).

## Discussion

In this cluster-randomised trial conducted among adults with presumptive tuberculosis attending 29 primary care clinics in Mozambique and Tanzania, we found that the placement of the Truenat platform with MTB Plus and MTB-RIF Dx assays at clinics combined with rapid communication of results and same-day tuberculosis treatment initiation led to a 1·5-times higher proportion of people starting treatment for microbiologically confirmed tuberculosis within 7 days after presentation compared with control clinics. Time to treatment was halved, with 82·2% of confirmed cases in the intervention group starting treatment on the day of presentation, compared with just 3·3% in the control group.

These findings align with the XPEL-TB trial in Uganda, which evaluated a multicomponent intervention, including decentralised testing, workflow optimisation, and performance feedback.[24] Although XPEL-TB did not significantly increase the proportion of confirmed cases treated within 14 days, it did increase the rate of treatment initiation by 56% and improved diagnostic timeliness. The discrepancy between proportions and rates might reflect higher numbers of patients evaluated in the intervention group. Unlike our study, XPEL-TB included an active implementation strategy,[25,26] which might have facilitated greater testing uptake. Our trial, conducted without such enhancements and during the COVID-19 pandemic, still showed substantial gains.

Our trial and XPEL-TB are among the few studies that have compared decentralised molecular testing with off-site diagnostics of similar performance. Other studies have used smear microscopy or culture as comparators, making it difficult to isolate the effect of decentralisation from differences in test sensitivity or processing time.[3,11,13,27] All these studies, including ours, reported reduced time to treatment initiation with decentralised testing models.

In our trial, in the intervention group, 182 participants were diagnosed with pulmonary tuberculosis, of whom 152 were microbiologically confirmed and 30 (16·5%) were clinically diagnosed. In the control group, 212 were diagnosed, with 150 microbiologically confirmed and 62 (29·2%) clinically diagnosed—similar to 2023 regional data from Africa (31%),[1] but lower than 2022 data from Maputo City, Mozambique (46%).[28] This lower rate might reflect training of clinic staff across all clinics on national diagnostic algorithms and exclusion of participants unable to produce sputum or requiring hospital admission. Notably, time to treatment initiation was shorter for those with clinical diagnoses than in those with microbiological diagnoses, and the control group had nearly twice as many clinical diagnoses as the intervention group. This finding suggests clinicians might have felt more confident withholding empirical treatment when rapid, reliable test results were available. Similar patterns were observed in South Africa and Nepal after the introduction of Xpert MTB/RIF, with declines in empirical treatment and case notifications.[29,30] Qualitative studies also show that patients value timely, accurate diagnoses. However, little is known about the experiences of those who receive negative results during tuberculosis work-up—a perspective that remains underexplored.[30]

Although DNA extraction and Truenat assay error rates were low, non-actionable results were common, mostly due to invalid assays. Additionally, one in three MTB-positive samples tested with MTB-RIF Dx yielded indeterminate rifampicin resistance results, probably due to low sample input (6 µL) and the higher detection threshold of the

single-copy rpoB target, which might particularly affect patients with low bacillary burden.[20] Repeat or second-sample testing might resolve this issue and result in more actionable results, but adds cost and delays treatment.

Our trial had several limitations. A protocol deviation led to delayed outcome ascertainment for a substantial number of participants, although primary outcomes were still available for most and validated using tuberculosis registers (presumptive and treatment). Per-protocol and analysis dataset results were consistent, suggesting minimal effects on study outcomes. As participants, researchers, and clinic staff were not masked to group assignment, ascertainment bias cannot be excluded. However, outcome assessors were trained to conduct standardised telephone interviews, and tuberculosis diagnoses were confirmed through registers and clinic notes. The similar prevalence of microbiologically confirmed tuberculosis in both groups makes systematic under-reporting in the control group less likely. Follow-up calls 7–21 days after presentation might have reduced pretreatment loss to follow-up, potentially underestimating the intervention effect. Under routine conditions, pretreatment loss to follow-up is often higher—for instance, a systematic review from the pre-Xpert era reported a pooled rate of 18% in African studies.[31] A trusted informant (such as a family member or caregiver) was contacted to collect follow-up information when participants could not be reached directly. Although this strategy helped minimise loss to follow-up, it might have introduced recall or reporting bias, particularly for time-sensitive outcomes such as the timing of treatment initiation or symptom resolution. This approach could have affected the accuracy and consistency of outcome ascertainment across participants. Additionally, our research team supported sample transport for control clinics, which might have shortened the time to diagnosis and further attenuated the intervention effect.

The trial was conducted during the COVID-19 pandemic, which caused substantial delays in initiation and introduced uncertainty around health-care access and utilisation. Randomisation was based on 2019 tuberculosis notification data, as data from 2020 and 2021 were considered unrepresentative due to pandemic-related disruptions. To account for this uncertainty, the number of clinics included was increased from 28 to 30. One control clinic was excluded before enrolment on discovery of an existing on-site GeneXpert instrument; it was not replaced. Instead, enrolment was closely monitored across groups in each country for imbalances. Six additional clinics were randomised as back-ups in case of low recruitment, site closures, or unexpected GeneXpert availability.

This trial highlighted the feasibility and clinical deployment of a low-complexity point-of-care molecular tuberculosis diagnostic at primary care in high tuberculosis-burden settings. Future studies are needed to provide evidence of such approaches on long-term patient outcomes and health system sustainability.

#### Contributors

KK, AP-N, SGS, and MR contributed to trial conceptualisation and methodology development. CK, MC, JH, DN, DE, PM, IS, AL, MS, HT, CaM, AM, and SV contributed to participant enrolment, collection of data, and specimen testing management. FR and LL contributed to database management. BE and MW conducted the statistical analysis with input from KK. KK, BE, MW, FR, and LL verified the underlying data. KK wrote the original draft of the manuscript, which was reviewed by CK, MC, VL, JH, IS, BE, AG-B, FR, MW, LL, DN, DE, PM, NEN, ChM, AL, MS, HT, CaM, AM, SV, ET, MR, and AP-N. BE and MW led the revision of the manuscript in close collaboration with KK, contributing substantially to the writing and restructuring of revised versions. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

#### Declaration of interests

CK is an Academic Editor at *PLOS Global Public Health* and has received grants from the European & Developing Countries Clinical Trials Partnership, Unitaid, the European Union, the 5% Initiative, the German Federal Ministry of Education and Research, the French National Agency for Research on AIDS and Viral Hepatitis, the United States Agency for International Development, the Medical Research Foundation, Janssen Pharmaceuticals, and the Bill & Melinda Gates Foundation. AG-B is Associate Editor of *BMJ Global Health* and *The International Journal of Tuberculosis and Lung Diseases;* serves on the advisory board of BioNTech (paid) and the ERA4TB (unpaid); has been Chair of the TB Group at the European Respiratory Society (2000–23); has received grants from The European & Developing Countries Clinical Trials Partnership, National Institutes of Health, European Research Council, and The Gates Medical Research Institute; has been paid honoraria for lecturers at the annual Spanish Association of Nursing and Vaccines; and received support from the Gates Foundation to attend meetings related to tuberculosis vaccines. AP-N has received grants from The European & Developing Countries Clinical Trials Partnership, European Union, the Bill and Melinda Gates Foundation, Unitaid, and the RIGHT Foundation. KK has received grants from The European & Developing Countries Clinical Trials Partnership, Wellcome Trust, the Bill and Melinda Gates Foundation, and the UK Medical Research Council. All other authors declare no competing interests.

#### Data sharing

The dataset has been made available in the Dryad data repository, accessible at https://doi.org/10.5061/dryad.b8gtht7qx. The data has been shared under the public domain CC0 licence waiver.

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