Table 1: Study Designs of Clinical Trials with Primary or Secondary Aims to Estimate Impact of Xpert on Patient Outcomes

Study Name[a]	Setting	Design	Randomization level	Sample Size	Study population inclusion criteria (main criteria)	Standard of Care	Intervention	Patient Outcome Questions Addressed
TB-NEAT[9]	South Africa, Zimbabwe, Zambia, and Tanzania	Pragmatic, randomized, two-arm parallel-group, multicenter trial.	Individual	1,502 patients with presumptive TB.	Patients: ≥18 years old; presenting to primary care TB clinics; ≥1 TB symptom as defined by WHO (i.e., presumptive TB patient*); spontaneous sputum expectoration possible; no prior TB treatment in last 60 days.	Same-day, onsite sputum smear microscopy by laboratory technician (one spot sputum/patient). One spot for culture.[b]	Nurse-performed point-of-care Xpert MTB/RIF at the clinic (one spot sputum per patient). Reference standard was liquid culture [b]	- Primary: Tuberculosis-related morbidity (measured with the TB score and the Karnofsky performance score (KPS) among culture-positive patients who had begun anti-tuberculosis treatment. - Other: diagnostic yield, time from sample collection to TB treatment, TB treatment initiation rates, empiric TB treatment, LTFU before TB treatment, TB treatment outcomes, and mortality.
XTEND[10,20,29]	South Africa	Pragmatic, two-arm, parallel, cluster-randomized trial.	Cluster (a TB lab with 2 clinics per lab)	20 labs, 2 clinics per lab, and 4,656 patients with presumptive TB.	Laboratories and their clinics: not part of other Xpert evaluations; did not already have GeneXpert; complied with current SOC TB diagnostics; not likely to be closed. Patients: ≥18 years old; not on TB treatment; had been asked to and were able to provide a sputum specimen (i.e., presumptive TB patient); local resident.	Sputum smear microscopy by laboratory technician (two spot sputa/patient).	Xpert MTB/RIF performed at the laboratory by technicians (one spot sputum/patient).	- Primary: Mortality at 6 months from enrollment. - Other: diagnostic yield, time from sample collection to TB treatment, TB treatment initiation rates, empiric TB treatment, LTFU before TB treatment.
Brazil Stepped Wedge[11,21]	Brazil	Stepped-wedge cluster-randomized trial	Cluster (primary care lab)	14 labs, 24,227 presumptive TB patients among whom 4,640 patients started TB treatment.	Primary care labs: all 11 labs in one city (Rio de Janeiro), and 3 labs in Manaus, purposefully selected with criteria not specified. Patients: All patients who provided sputa for TB diagnostic work up were eligible (i.e., presumptive TB patients).	Sputum smear microscopy by laboratory technician (one or two spot sputa/patient).	Xpert MTB/RIF performed at the laboratory by technicians (one spot sputum/patient).	- Primary: Laboratory-confirmed TB case notification rate; time from sample collection to TB treatment initiation - Other: TB treatment initiation rates, empiric TB treatment, TB treatment outcomes.
Zimbabwe RCT[14]	Zimbabwe	Pragmatic, randomized, two-arm parallel-group, trial.	Individual	424 patients starting ART.	Patients: Symptomatic and asymptomatic HIV-infected patients initiating ART; ≥18 years old; no prior ART; not receiving TB treatment; produced at least 1 sputum sample (spontaneous or with induction)	Sputum smear microscopy (two spot sputa/patient).	Xpert MTB/RIF performed at the laboratory by technicians (two spot sputa/patient).	- Primary: % of patients who died or developed incident TB (composite outcome) during ART within 3 months of randomization. - Other: diagnostic yield, time from sample collection to TB treatment, TB treatment initiation rates, empiric TB treatment, TB incidence, LTFU after ART start.
South Africa Single Clinic CRT[12]	Khayelitsha, SA	Single clinic, pragmatic, two-phase, crossover, cluster-randomized trial.	Cluster (one primary healthcare clinic randomized on weekly basis to each arm)	51 weeks randomized; 1,985 presumptive TB patients randomized among whom 492 started TB treatment.	Cluster: Purposefully chosen clinic. Patients: Presumptive TB patients; ≥18 years old; not receiving TB treatment for 3 days or more; all presumptive TB patients included in the intention to treat (ITT) while the per protocol analysis excluded 40 of 1,985 patients unable to produce sputa.	On site lab sputum smear microscopy (two spot sputa/patient).	On site Xpert (one spot sputum/patient).	Primary outcome: % of bacteriologically-confirmed TB cases not starting TB treatment within 3 months of randomization. Secondary outcomes: diagnostic yield, time from sample collection to TB treatment, TB treatment initiation rates, empiric TB treatment, TB treatment outcomes, and 6-month mortality.
Uganda Pre-post trial[13]	Kampala, Uganda	Single clinic, prospective pre-post study.	Not randomized	477 hospitalized presumptive TB patients among whom 252 started TB treatment.	Patients: ≥18 years old; presumptive TB patient; not receiving TB treatment; patients with insufficient or absent sputa were excluded from analysis (29 of 525 initial enrollees excluded for this reason); patients who died within 3 days of hospital admission, excluded from analysis.	On site lab fluorescent smear microscopy (two spot and one morning sputum/patient). Remainder for culture.[b]	On site Xpert (one spot sputum/patient). One spot and the morning sputum sent for culture.[b]	Primary outcome: Not specified. Other: time from sample collection to TB treatment, TB treatment initiation rates, empiric TB treatment, TB treatment outcomes, LTFU after hospital admission, and 2-month mortality.

SA ICU RCT[15]	South Africa, Cape Town	Prospective cohort at 4 ICUs with nested individual RCT sub-study.	Individual	341 ICU patients with presumptive TB, of whom 242 randomized.	Patients: ≥18 years old; presumptive TB patient; mechanically ventilated; tracheal aspirate obtained for all enrollees. RCT sub-study: Enrolled during 2010-12 before Xpert became SOC.	1.5-7.5 mL of tracheal secretions sent for blinded smear microscopy.	1.5-7.5 mL of tracheal secretions sent for blinded Xpert.	Primary: % of culture-positive TB patients started on TB treatment at 48 h after enrolment. Other: Diagnostic yield, , time from sample collection to TB treatment, TB treatment initiation rates, empiric TB treatment, and mortality at various time points after randomization.
Indonesia Pre-post trial[16]	Java, Indonesia	Pre-post trial at three provincial public hospitals in Indonesia.	Not randomized	975 patients at risk of drug-resistant TB pre-Xpert and 1,442 post-Xpert	Patients: Any age, at risk of MDR-TB, according to Indonesian guidelines.	1 sputum for microscopy and 1 for culture. If positive culture, first-line DST.	1 sputum sample sent for Xpert, one sputum sample for culture. If positive culture, first-line DST.	Primary: TB case detection rates (diagnostic yield), RR TB detection rates among TB cases (RR TB diagnostic yield), RR TB treatment initiation rates, and time to RR TB treatment initiation.

Abbreviations: RCT, randomized clinical trial; SA, South Africa, ICU, intensive care unit; TB, tuberculosis; ART, antiretroviral therapy; WHO, World Health Organization; SOC, standard of care; MTB, Mycobacterium tuberculosis; RIF, Rifampicin resistant; RR, rifampicin resistant; DST, drug susceptibility testing; LTFU, loss to follow-up

[a]If the trial did not have an official name, it is referred to by a combination of the country it was conducted in and the trial design.

[b]Diagnostic algorithms varied across studies. Only in two studies, marked with [b] was a specimen supposed to be sent for culture for all enrollees. Chest x-ray was a diagnostic tool available to clinicians if deemed necessary, in all studies.