SUPPLEMENT

	Churchyard et al., 2015	Penn-Nicholson et al., 2021	Dorman et al., unpublished	Dorman et al., 2018	Theron et al., unpublished	Mupfumi et al., 2014
Study sites eligible for inclusion*	South Africa	Ethiopia, India, Papua New Guinea, and Peru	Kenya, South Africa, and Uganda	Belarus, Georgia, India, and South Africa	South Africa	Zimbabwe
Analytic population, n	4001	1411	906	870	777	390
Individuals with treatment initiation, n (primary outcome)	130	22	61	23	4	66
Alternative outcome, n	20	19	61	23	1	16
Age category, n 18 – 30 years 31 – 40 years	1322 1134	370 275	263 282	206 214	340 267	80 174
41 years and above	1545	766	361	450	170	136
Male, n	1444	784	459	522	300	171
Individuals with history of prior TB, n	613	192	223	255	107	49
Reported cough None Yes	759 3242	0 1411	0 906	48 822	566 211	200 190
Reported night sweats None Yes	2254 1747	829 582	310 596	433 437	618 159	188 202
Reported fever None Yes	2219 1782	629 782	275 631	360 510	742 35	161 229
HIV Negative Positive, not on ART Positive, on ART Unknown	1203 1246 624 928	703 0 28 680	429 64 412 1	318 100 67 385	0 0 777 0	0 61 329 0
Individuals with abnormal chest X-ray result, n	NA	196	NA	250	NA	NA
Year of data collection	2012	2019 – 2020	2018 – 2020	2016	2017 – 2020	2011 – 2012
Initial TB tests used for diagnoses**	SSM, Xpert	Xpert, Xpert Ultra	Xpert, Xpert Ultra	Xpert	Xpert Ultra	SSM, Xpert

 Table S1. Demographic and clinical characteristics of participants, by study.

	Pereira et al., 2020	Hanrahan et al., 2015	Mishra et al., 2020	Luetkemeyer et al. 2016	Bjerrum et al., 2020	Agizew et al., 2019
Study sites eligible for inclusion*	Brazil	South Africa	South Africa	Brazil, South Africa	Ghana	Botswana
Analytic population, n	147	168	212	280	121	5838
Individuals with treatment initiation, n (primary outcome)	0	5	0	28	6	132
Alternative outcome	0	2	0	28	2	33
Age category, n 18 – 30 years	24	25	68	54	33	2099
31 – 40 years	12	66	48	92	42	2248
4 I years and above	76	11	90	134	40	1491
Individuals with history of prior TB, n	0	0	87	36	9	624
Reported cough None Yes	0 147	22 146	12 200	15 265	66 55	4793 1045
Reported night sweats None Yes	0 147	128 40	62 150	116 164	82 39	5321 517
Reported fever None Yes	49 98	132 36	186 26	134 146	60 61	5340 498
HIV Negative Positive, not on ART Positive, on ART Unknown	144 3 0 0	24 38 104 2	170 42 0 0	110 170 0 0	0 38 83 0	0 5838 0 0
Individuals with abnormal chest X-ray result, n	NA	10	NA	NA	NA	NA
Year of data collection	2018 – 2019	2011 – 2013	2016 – 2018	2012 – 2013	2013 – 2014	2012 – 2014
Initial TB tests used for diagnoses**	Xpert Ultra	Xpert	SSM, Xpert, Xpert Ultra	SSM	Xpert	SSM. Xpert

Table S1 (continued). Demographic and clinical characteristics of participants, by study.

* Data from countries with high income and low TB burdens were not considered for inclusion. ** Diagnostic tests performed solely for research purposes, which were not part of routine practice in the setting, were excluded.

Country	Adjusted odds ratio of treatment initiation, compared to cross-country average (95% Credible Intervals)
Belarus	0.56 (0.12, 2.04)
Botswana	0.55 (0.26, 1.17)
Brazil	0.33 (0.12, 0.83)
Ethiopia	0.57 (0.16, 1.80)
Georgia	0.48 (0.17, 1.17)
Ghana	1.15 (0.42, 3.00)
India	0.97 (0.46, 2.12)
Kenya	2.14 (0.92, 5.09)
Papua New Guinea	1.34 (0.42, 3.93)
Peru	0.95 (0.31, 2.68)
South Africa	0.36 (0.18, 0.72)
Uganda	7.01 (3.43, 15.16)
Zimbabwe	2.88 (1.32, 6.34)

Table S2. Odds ratios of TB treatment initiation following negative diagnostic test result:country random effects from primary analysis.

	Adjusted odds ratio of treatment initiation (95% Credible Intervals)
Age category	
18 – 30 years	Ref
31 – 40 years	1.30 (0.53–3.26)
41 years and above	1.47 (0.71–3.25)
Sex	· · ·
Female	Ref
Male	1.00 (0.56–1.83)
History of prior TB	
None	Ref
Yes	0.64 (0.28–1.39)
Unknown	0.50 (0.10–1.91)
Reported cough	
None	Ref
Yes	1.26 (0.22–9.67)
Reported night sweats	
None	Ref
Yes	1.14 (0.60–2.18)
Reported fever	
None	Ref
Yes	0.68 (0.36–1.27)
HIV	
Negative	Ref
Positive, not on ART	1.03 (0.17–5.44)
Positive, on ART	1.28 (0.27–5.51)
Unknown	0.58 (0.27–1.15)
Chest X-ray	
Normal	Ref
Abnormal	6.89 (3.29–14.42)
Unknown	0.69 (0.16–2.54)
Diagnostic test	
Sputum Smear	
	-
Xpert	- Ref
Xpert Xpert Ultra	- Ref 0.77 (0.05–16.03)

Table S3. Odds ratios of TB treatment initiation following negative diagnostic test result: secondary analysis for datasets including chest x-ray results.

	Adjusted odds ratio of treatment initiation, compared to
Study	cross-study average
-	(95% Credible Intervals)
Churchward at al. 2015	0.53
Churchyard et al., 2015	(0.20, 1.50)
Penn-Nicholson et al. 2021	0.85
	(0.27, 2.57)
Dorman et al unnublished	3.77
Dorman et al., unpublished	(1.30, 11.00)
Dorman et al. 2018	0.70
Bornan et al., 2010	(0.28, 1.77)
Theron et al unnublished	1.14
	(0.30, 4.05)
Munfumi et al. 2014	4.97
	(1.76, 15.56)
Pereira et al 2020	0.27
	(0.02, 1.67)
Hanrahan et al. 2015	1.30
	(0.25, 9.72)
Mishra et al. 2020	0.10
	(0.01, 0.48)
Luetkemever et al. 2016	1.18
	(0.45, 3.21)
Bierrum et al. 2020	1.68
	(0.51, 5.79)
Agizew et al. 2019	0.87
Ayizew et al., 2019	(0.34, 2.33)

Table S4. Odds of TB treatment initiation following negative diagnostic test result: study random effects from alternative model specification.

Search terms for Embase (Elsevier, embase.com).

Advanced Search:

Source: Embase subset (from 1974 to present)

Date: Publication years from 2010 - 2022

1) 'tuberculosis'/de OR 'lung tuberculosis'/de OR tuberculosis:ab,ti,kw

2) 'molecular diagnostics'/de OR 'molecular diagnosis'/de OR 'Mycobacterium tuberculosis test kit'/de OR 'polymerase chain reaction system'/de OR 'xpert'/de OR 'xpert ultra'/de OR 'xpert mtb rif ultra'/de OR 'sputum analysis'/de OR ('sputum smear'/de AND 'microscopy'/exp) OR 'sputum culture'/de OR genexpert:ab,ti,kw OR xpert:ab,ti,kw OR 'smear microscopy':ab,ti,kw OR 'sputum microscopy':ab,ti,kw

3) 'clinical trial'/de OR 'controlled clinical trial'/de OR 'randomized controlled trial'/exp OR 'diagnostic accuracy'/de OR 'diagnostic test accuracy study'/de OR 'evaluation study'/de OR 'clinical trial':ab,ti,kw OR random*:ab,ti,kw OR accuracy:ti,ab,kw OR evaluation:ab,ti,kw

1 AND 2 AND 3

NOT ('chapter'/it OR 'conference abstract'/it OR 'conference paper'/it OR 'conference review'/it OR 'editorial'/it OR 'review'/it)

Search terms for MEDLINE/PubMed (National Library of Medicine, NCBI)

("Tuberculosis"[Mesh:NoExp] OR "Tuberculosis, Pulmonary"[Mesh] OR tuberculosis[tiab]) AND ("Molecular Diagnostic Techniques"[Mesh:NoExp] OR ("Sputum"[Mesh] AND "Microscopy"[Mesh]) OR genexpert[tiab] OR xpert[tiab] OR smear microscopy[tiab] OR sputum microscopy[tiab]) AND ("randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR "random allocation"[mesh] OR "clinical trial"[pt] OR "evaluation study"[pt] OR "clinical trial"[tiab] OR random*[tiab] OR accuracy [tiab] OR evaluation[tiab]) AND 2010[pdat]: 2022[pdat]. Hierarchical Bayesian logistic regression model.

For the main analysis we fit the following regression model:

 $TREAT \sim Binomial (n = trials(1), p)$

 $logit (p) = \beta_0 + \beta_{Age_cat}Age_{cat} + \beta_{Sex}Sex + \beta_{TB_{hist}}TB_{hist} + \beta_{cough}Cough + \beta_{sweat}Sweat + \beta_{Fever}Fever + \beta_{HIV}HIV + \beta_{Diag_{test}}Diag_{test} + \beta_{year}Year + b_{country}$

Where:

- TREAT is the binary outcome variable indicating whether or not an individual initiated TB treatment.
- *p* is the probability of receiving treatment.
- *Age_{cat}*, *Sex*, *TB_{hist}*, *Cough*, *Sweat*, *Fever*, *HIV*, *Diag_{test}*, and *Year* are exposure variables as defined in Table 2.
- *b_{country}* represents the country random effect term.

All analyses were performed using the "brms" package (v.2.19.0) in R (v.4.2.3). We adopted the default prior distributions available in this package, with all main effects given prior student-*t* distributions with 3 degrees of freedom and a scale parameter of 10, and the random effects standard deviation given a half student-*t* prior with 3 degrees of freedom. The approach uses an extension of Hamiltonian Monte Carlo to sample from the posterior distribution of the regression model parameters (24–26). During the sampling process, 4,000 posterior samples were generated and convergence was assessed using Gelman-Rubin statistic (i.e., potential scale reduction factor (PSRF)). PSRF values for all parameters were observed to be 1.00, confirming convergence (39). The reported coefficient estimates (aOR) in **Table 2** represent the posterior

means for each parameter and equal-tailed 95% credible intervals (95% CI). Secondary analyses and alternative model specifications were performed using a similar approach.

Description of individual studies included in analysis.

The XTEND study was a pragmatic cluster-randomized trial conducted in South Africa assessing 6-month mortality of clinic attendees randomly allocated testing with Xpert MTB/RIF or sputum smear microscopy (6). Penn-Nicholson et al. conducted a prospective multi-center diagnostic accuracy study conducted in four countries (Peru, India, Ethiopia and Papua New Guinea) to assess the performance of the Truenat TB assays compared to Xpert MTB/RIF (40). Dorman et al. conducted a prospective multi-center diagnostic accuracy study in eight countries (South Africa, India, Georgia, and Belarus) assessing sensitivity and specificity of Xpert Ultra compared to Xpert (32). Dorman et al. subsequently conducted the Ultra 2 study in three countries (South Africa, Uganda, Kenya), incorporating the same study procedures as used in the Ultra study (32), with improvement in stability of the initial Ultra assay (Dorman et al., unpublished). Theron and the study team conducted a prospective diagnostic accuracy study in South Africa focusing on people living with HIV (PLHIV) attending clinics to start antiretroviral therapy (ART). The preliminary findings were published in the Union Conference. Mupfumi et al. conducted a pragmatic randomized control trial in Zimbabwe, examining the impact of Xpert on ART-associated TB and patient outcomes (10). Pereira et al assessed the diagnostic accuracy of Xpert Ultra in Brazil (41). Hanrahan et al. conducted a prospective cohort study in South Africa to investigate the effects of placement of Xpert at the point of care (POC) (42). Mishra et al. conducted a two-cohort diagnostic accuracy study in South Africa (43). Luetkemeyer et al. conducted a longitudinal multicenter study in the US, Brazil and South Africa to evaluate the Xpert assay (44). Bjerrum et al. conducted a diagnostic accuracy study of LAM studies among PLHIV in Ghana (45). Lastly, Agizew et al. conducted a stepped-wedge cluster randomized trial comparing TB treatment outcomes of SSM and Xpert among PLHIV in Botswana (46).