Table 4: Limitations of Clinical Trials Designed to Estimate Xpert Impact on Patient Outcomes

Study	Design							Conduct	Health System Weaknesses			
	Study Population Not Exclusively a WHO Priority Population (reason)		Restricted to Outpatients	Not a Randomized Trial	No Blinding to TB Diagnostic used	Higher Rates of Empiric TB Treatment in Microscopy Arm	Not Powered to Detect a Morbidity or Mortality Difference	Anticipated Morbidity or Mortality Difference Possibly Too Large (i.e., possibly underpowered)	LTFU of Enrollees Restricted Key Outcome Ascertainment	% of Study Enrollees Not Knowing their HIV status	% of HIV-positive Enrollees on ART (ART coverage)	High LTFU of Microbiologically-Confirmed TB Patients before TB Treatment[j]	High LTFU of TB patients during TB Treatment
TB-NEAT[9]	✓	(40% HIV - negative)	✓	X	✓	✓	X	✓[a]	✓[b]	<1%[i]	26%	✓	✓
XTEND[10,29]	✓	(50-55% HIV-negative)	✓	X	✓	✓	X	✓[a]	X[c]	21-27%	33%	✓	NA
Brazil Stepped Wedge[11,21]	✓	(90-92% HIV-negative)	✓	X	✓	X	✓	N/A	✓[d]	>50%	NA	NA	✓
Zimbabwe RCT[14]	X	(100% HIV-positive)	✓	X	✓	X	X	✓[a]	✓[e]	0%	100%	NA	NA
South Africa CRT[12]	✓	(40-41% HIV-negative)	✓	X	✓	✓	✓	N/A	NA	18%	NA	NA	✓
Uganda Pre-post[13]	✓	(24% HIV-negative)	X	✓	✓	✓	✓	N/A	✓[f]	0%	NA	NA	✓
SA ICU trial[15]	✓	(70% HIV-negative)	X	X	✓	✓	✓	N/A	X[g]	15%	31%	NA	NA
Pre-Post trial, Indonesia[16]	X	(100% DR TB suspects)	✓	✓	✓	X	✓	N/A	✓[h]	NA	NA	✓	NA

Abbreviations: "✓", stated study limitation applies to this study; "X", study limitation does not apply; WHO, World Health Organization; TB, tuberculosis; LTFU, loss to follow-up; HTC, HIV testing and counselling; NA, not available; N/A, not applicable, SA, South Africa; SOC, standard of care; DR, drug resistant

[a] See text for discussion

[b] 20% loss to follow-up (LTFU) of culture-confirmed TB cases.

[c] Although LTFU before TB treatment was 16% among microbiologically confirmed TB patients, investigators ascertained vital status of nearly all study enrollees (+-99%) by study end.

[d] High incidence of LTFU (about 16% in both SOC and intervention phase)

[e] 17% (70/424) of ART enrollees LTFU before 6 months.

[f] 7% of study enrollees (32/477) LTFU before study end.

[g] Less than 4% were LTFU at 90 days.

[h] Missing data on 2nd line treatment initiation was very high both pre-Xpert (52.4%) and post-Xpert (31.0%). Based on available data, missing data on TB treatment initiation seems equivalent to LTFU before second-line TB treatment initiation. Overall missing data (probable LTFU) before second-line TB treatment was 42% (267/634) among rifampicin resistant cases.

[i] Study enrollees were offered HIV testing and counseling at study enrollment.

[j] Data points are presented in Table 3