

1	Table of Contents	
2	Supplementary Table 1: Reference standard definitions	2
3	Definitions	3
4	Microbiological reference standard	3
5	Extended microbiological reference standard	3
6	Composite reference standard	3
7	Supplementary Results	5
8	Bacterial load in study Ultra and routine Xpert.....	5
9	Drug susceptibility results of study Ultras on FNABs	5
10	Supplementary Figure 1: Spaghetti and box and whiskers plots showing FNAB Ultra	
11	internal positive control quantitative information (SPC CT). (A) Study SPC CTs vs.	
12	routine SPC CTs.....	6
13	Supplementary Figure 2: Quantitative information of Ultra (IS6110/IS1081, rpoB) and	
14	Xpert (rpoB) compared with bacillary load (MGIT960 liquid culture TTP).....	7
15	Supplementary Table 2: Non-head-to-head and head-to-head diagnostic accuracy	
16	analyses of Xpert and Ultra using a microbiological reference standard (MRS), extended	
17	microbiological reference standard (eMRS) and composite reference standard (CRS) for	
18	the detection of Mycobacterium tuberculosis complex DNA.....	8
19	Supplementary Table 3: Study Ultra-positive patients who were culture- and cytology-	
20	negative, with information on their Ultra semi-quantitation category, previous TB status,	
21	TB treatment initiation status and patient’s status after at least 12-weeks of follow-up	9
22	Supplementary Table 4: Diagnostic accuracy of Ultra on urine measured using the	
23	microbiological reference standard (MRS) in a head-to-head analysis stratified by HIV	
24	status.....	11
25	Supplementary Table 5: Diagnostic accuracy analyses (non-head-to-head top, head-to-	
26	head bottom) of routine Xpert and study Ultra (excluding traces) on FNABs using a MRS	
27	stratified by HIV status	Error! Bookmark not defined.
28	Supplementary Table 6: Non-head-to-head and head-to-head diagnostic accuracy	
29	analyses of Xpert and Ultra using a microbiological reference standard (MRS), extended	
30	microbiological reference standard (eMRS) and composite reference standard (CRS) for	
31	the detection of Mycobacterium tuberculosis complex DNA, excluding trace positive Ultra	
32	results	12
33	Supplementary Table 7: Diagnostic accuracy analyses (non-head-to-head top, head-to-	
34	head bottom) of routine Xpert and study Ultra (reclassifying traces as negative) on FNABs	
35	using a MRS stratified by HIV status	Error! Bookmark not defined.
36	Supplementary Table 8: Non-head-to-head and head-to-head diagnostic accuracy	
37	analyses of Xpert and Ultra using a microbiological reference standard (MRS), extended	
38	microbiological reference standard (eMRS) and composite reference standard (CRS) for	

39 the detection of Mycobacterium tuberculosis complex DNA, reclassifying trace positive
40 Ultra results as negative 14
41

42 **Supplementary Table 1:** Reference standard definitions

	MRS*	eMRS†	CRS‡
Site of disease fluid			
Xpert	✘	✔	✔
MGIT960 Culture	✔	✔	✔
Cytology	✔	✔	✔
Non-site-of disease fluid			
Smear	✘	✔	✔
Xpert	✘	✔	
Ultra	✘	✔	✔
MGIT960 Culture	✘	✔	✔
Treatment information			
TB treatment initiated	✘	✘	✔
Response to treatment self-reported by patient	✘	✘	✔
Case definitions			
Reference standard positive (Definite TB cases)	Any MRS test positive	Any eMRS test positive	Any eMRS test positive/or TB treatment was initiated and response to treatment documented
Reference standard negative (Non-TB patients)	No MRS test positive	No eMRS test positive	No eMRS test positive and patient not initiated on treatment
Probable TB patients	N/A	N/A	No eMRS test positive, but treatment initiated
Unclassifiable	No positive MRS test and site-of-disease fluid culture contaminated or not done	No positive eMRS test and site-of-disease fluid culture contaminated or not done	No positive eMRS test and site-of-disease fluid culture contaminated or not done, or treatment not initiated

43 Abbreviations: Composite reference standard, CRS; Extended reference standard, eMRS; MGIT960 culture,
 44 Mycobacteria Growth Indicator Tube 960; Microbiological reference standard, MRS; Smear, smear microscopy;
 45 Ultra, Xpert MTB/RIF Ultra; Xpert, Xpert MTB/RIF.

46

47

48

49

50 **Definitions**

51 Microbiological reference standard

52 For the microbiological reference standard (MRS), a definite TB case was defined as a fine
53 needle aspirate (FNAB) being culture-positive or cytology-positive and a non-TB patient was
54 defined as being FNAB culture and cytology negative. Patients were unclassifiable if they had
55 no positive MRS test and the site-of-disease culture was either contaminated or not done or
56 cytology was not done.

57 Extended microbiological reference standard

58 For the extended microbiological reference standard (eMRS), a definite TB case was defined
59 as a FNAB or any other body fluid being culture-, smear-, routine Xpert- or Ultra- positive and
60 a non-TB case was defined as FNAB and other body fluids being culture-, smear-, Xpert-and
61 Ultra- negative. Patients were considered unclassifiable if they had no positive eMRS test and
62 the site-of-disease culture was either contaminated or not done.

63 Composite reference standard

64 For the composite reference standard (CRS), a definite TB case was defined as a FNAB or any
65 other body fluid being culture-, smear-, Xpert- or Ultra- positive or TB treatment was initiated
66 and response to treatment is documented; a probable-TB case was defined as a FNAB or any
67 other body fluid being culture-, smear-, Xpert- or Ultra- positive or the patient being initiated
68 on TB treatment after the 12-week follow up; and a non-TB case was defined as FNAB and
69 other body fluids being culture-, smear-, Xpert-and Ultra- negative, and the patient was not
70 initiated on TB treatment, and the patient was diagnosed with an alternative disease. Patients
71 were unclassifiable if they had no positive eMRS test and the site-of-disease culture was either
72 contaminated or not done, and treatment was not initiated.

73 **Supplementary Results**

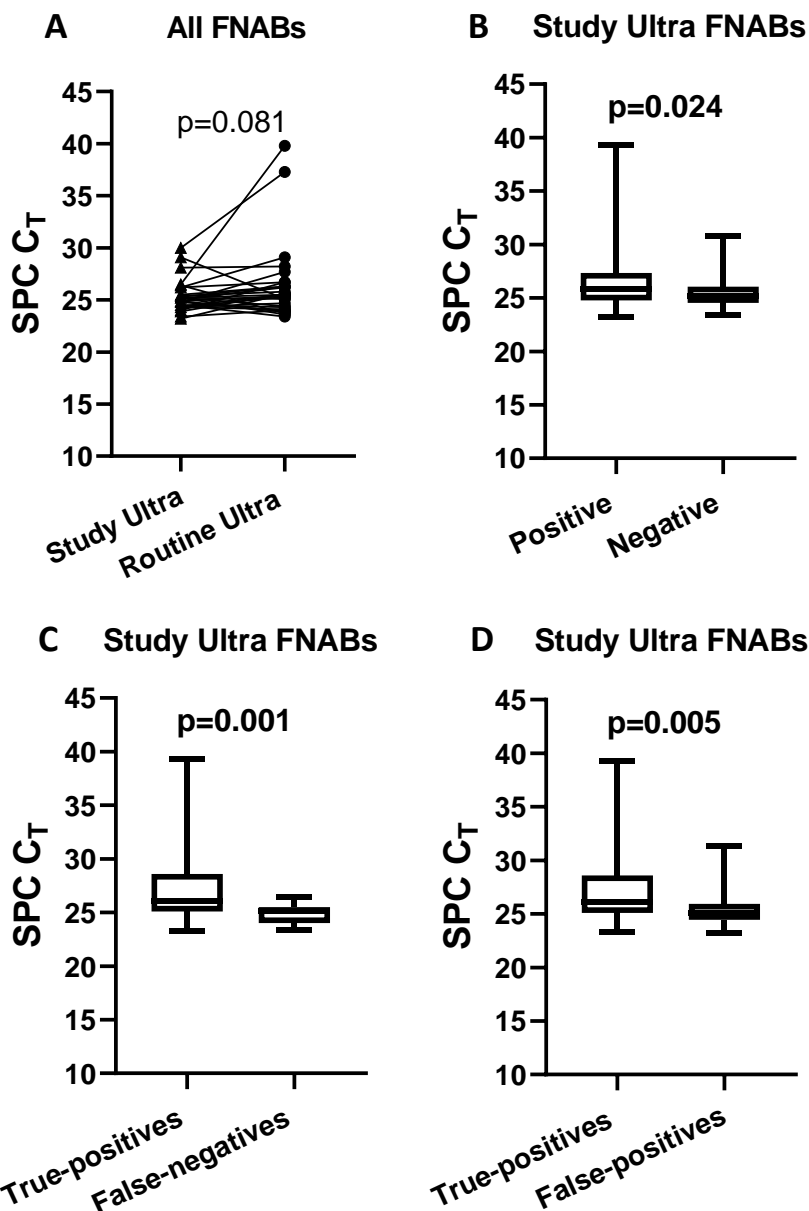
74 Bacterial load in study Ultra and routine Xpert

75 No correlations were observed between study Ultra quantitation (IS6110/IS1081 C_T and *rpoB*
76 C_{Tmin}) and culture time-to-positivity (TTP) and routine Xpert quantitation (*rpoB* C_{Tmin}) and
77 culture TTP (**Supplementary Figure 2**).

78 Drug susceptibility results of study Ultras on FNABs

79 Of 74 study Ultra-positive patients, 70% (52/74) were rifampicin-susceptible, 4% (3/74)
80 resistant, and 26% (19/74) indeterminate (all trace). In patients who had actionable study Ultra
81 and culture results (n=84), 20% (17/84) had MTBDR*plus* done. Of these, 18% (3/17) were
82 MTBDR*plus* rifampicin-resistant and 82% (14/17) susceptible. 33% (1/3) of these
83 MTBDR*plus* rifampicin-resistant patients were study Ultra rifampicin-resistant (one study
84 Ultra trace-positive, rifampicin indeterminate and the other study Ultra negative), and 57%
85 (8/14) of MTBDR*plus* rifampicin-susceptible patients were study Ultra rifampicin-susceptible
86 (the remaining four were study Ultra trace-positive, rifampicin indeterminate and other
87 remaining two were study Ultra-negative).

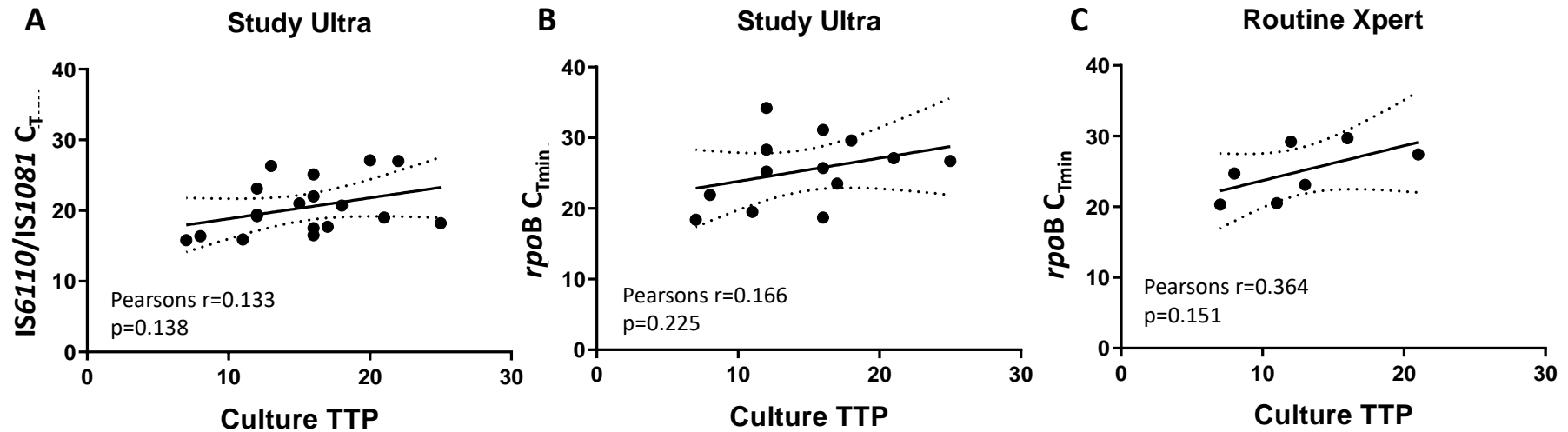
88 **Supplementary Figure 1:** Spaghetti and box and whiskers plots showing FNAB Ultra SPC
 89 C_T . (A) Study SPC C_T vs. routine SPC C_T . (B) SPC C_T from positive and negative study
 90 Ultras. More inhibition was observed in positives. (C) SPC C_T in true-positive vs. false-
 91 negative study Ultras, showing that greater inhibition is associated with Ultra missing TBL
 92 cases. Abbreviations: FNAB, fine needle aspirate biopsy; SPC C_T ; sample processing control
 93 cycle threshold value for the Xpert MTB/RIF Ultra (Ultra) internal positive control which
 94 measures PCR inhibition; Ultra, Xpert MTB/RIF Ultra.



95

96 **Supplementary Figure 2:** FNAB Quantitative information of Ultra (IS6110/IS1081, *rpoB*) and Xpert (*rpoB*) compared with bacillary load
97 (MGIT960 liquid culture TTP). (A) Study Ultra IS6110/IS1081 C_T vs. MGIT960 liquid culture TTP. (B) Study Ultra *rpoB* C_{Tmin} vs. MGIT960
98 liquid culture TTP. (C) Routine Xpert *rpoB* C_{Tmin} vs. MGIT960 liquid culture TTP. No correlations were observed. Only two culture-positive,
99 routine Ultra-positive FNABs were present and routine Ultra results are hence not graphed. Abbreviations: FNAB, fine needle aspirate biopsy;
100 TTP, culture time-to-positivity; Ultra, Xpert MTB/RIF Ultra; Xpert, Xpert MTB/RIF.

101



102

103 **Supplementary Table 2:** Non-head-to-head and head-to-head diagnostic accuracy analyses of Xpert and Ultra using a MRS, eMRS and CRS for
 104 the detection of Mycobacterium tuberculosis complex DNA. Conclusions were like those for the MRS (**Table 2**). Data are %, 95% CI, and n/N

		Non-head-to-head											
		MRS				eMRS				CRS			
		n=96				n=97				n=97			
		Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
Xpert		73 (58, 85) 35/48	92 (80, 98) 44/48	90 (76, 97) 35/39	77 (64, 87) 44/57	69 (55, 81) 36/52 p=0.685*	91 (79, 98) 41/45 p=0.924*	90 (76, 97) 36/40 p=0.970*	72 (58, 83) 41/57 p=0.519*	65 (52, 77) 39/60 p=0.635 [±] p=0.379 [¥]	97 (86, 100) 36/37 p=0.244 [±] p=0.274 [¥]	98 (87, 100) 39/40 p=0.166 [±] p=0.157 [¥]	63 (49, 76) 36/57 p=0.317 [±] p=0.102 [¥]
		n=130				n=131				n=131			
Ultra		85 (73, 93) 51/60 p=0.121 [‡]	69 (56, 79) 48/70 p=0.003[‡]	70 (58, 80) 51/73 p=0.018[‡]	84 (76, 97) 48/57 p=0.343 [‡]	83 (71, 91) 53/64 p=0.085 [‡] p=0.741*	69 (56, 79) 46/67 p=0.005[‡] p=0.991*	72 (60, 81) 53/74 p=0.024[‡] p=0.815*	81 (68, 90) 46/57 p=0.271 [‡] p=0.622*	76 (65, 85) 58/76 p=0.147 [‡] p=0.345 [±] p=0.207 [¥]	71 (57, 82) 39/55 p=0.001[‡] p=0.788 [±] p=0.778 [¥]	78 (67, 87) 58/74 p=0.006[‡] p=0.343 [±] p=0.238 [¥]	68 (55, 80) 39/57 p=0.554 [‡] p=0.132 [±] p=0.047[¥]
		Head-to-head											
		n=92				n=92				n=92			
Xpert		72 (57, 84) 33/46	93 (82, 99) 43/46	92 (78, 98) 33/36	77 (64, 87) 43/56	67 (52, 80) 33/49 p=0.642*	93 (81, 99) 40/43 p=0.068*	92 (78, 98) 33/36 p>0.999*	71 (58, 83) 40/56 p=0.518*	64 (50, 76) 35/55 p=0.691 [±] p=0.387 [¥]	97 (86, 100) 36/37 p=0.382 [±] p=0.419 [¥]	97 (85, 100) 35/36 p=0.304 [±] p=0.304 [¥]	64 (50, 77) 36/56 p=0.418 [±] p=0.147 [¥]
	Ultra		91 (79, 98) 42/46 p=0.016[‡]	76 (61, 87) 35/46 p=0.020[‡]	79 (66, 89) 42/53 p=0.114 [‡]	90 (76, 97) 35/39 p=0.105 [‡]	88 (75, 95) 43/49 p=0.016[‡] p=0.573*	77 (61, 88) 33/43 p=0.035[‡] p=0.942*	81 (68, 91) 43/53 p=0.167 [‡] p=0.808*	85 (69, 94) 33/39 p=0.134 [‡] p=0.498*	84 (71, 92) 46/55 p=0.017[‡] p=0.551 [±] p=0.252 [¥]	81 (65, 92) 30/37 p=0.025[‡] p=0.636 [±] p=0.583 [¥]	87 (75, 95) 46/53 p=0.091 [‡] p=0.427 [±] p=0.301 [¥]

105 Within rows: *MRS vs. eMRS, eMRS vs. CRS[±], MRS vs. CRS[¥]; Within columns: Xpert vs. Ultra[‡]

106 Abbreviations: CI, confidence interval; CRS, composite reference standard; eMRS, extended microbiological reference standard; MRS, microbiological reference standard;

107 NPV, Negative predictive value; PPV, Positive predictable value; Ultra, Xpert MTB/RIF Ultra; Xpert, Xpert MTB/RIF.

108 **Supplementary Table 3:** Per patient information for study Ultra-positive patients that were
 109 MRS -negative (culture- and cytology-negative) with information on their Ultra semi-
 110 quantitation category, previous TB status, TB treatment initiation status and patient's status
 111 after at least 12-weeks of follow-up. Data are n/N (%).

Patient ID	Previous TB	Study Ultra semi-quantitation category	Routine PCR result	Treatment initiated after 12-week follow up	Did the patient get better? (asked telephonically if patient started treatment)
FNAB038	No	Trace	Xpert-negative	No	N/A
FNAB060	No	Very Low	Xpert-negative	Yes	Yes
FNAB072	No	Very Low	Xpert-negative	No	N/A
FNAB076	No	Medium	Xpert-positive (Low)	Yes	Yes
FNAB110	No	Trace	Xpert-negative	No	N/A
FNAB114	No	Medium	Xpert-positive (Medium)	No	N/A
FNAB128	No	Trace	Xpert-negative	No	N/A
FNAB132	No	Trace	Xpert-negative	No	N/A
FNAB172	No	Low	Xpert-negative	Yes	Yes
FNAB180	Yes	Low	Xpert-negative	No	N/A
FNAB200	No	Low	Xpert-positive (Low)	Yes	Yes
FNAB206	Yes	Trace	Not done	No	N/A
FNAB210	Yes	Trace	Ultra-negative	No	N/A
FNAB214	No	Trace	Ultra-negative	No	N/A
FNAB218	Yes	Trace	Ultra-negative	No	N/A
FNAB220	No	Trace	Ultra-positive (Very low)	Yes	Yes
FNAB230	No	Trace	Ultra-negative	No	N/A
FNAB232	Yes	Medium	Ultra-positive (Medium)	Yes	Yes
FNAB245	No	Trace	Ultra-negative	No	N/A
FNAB251	Yes	Trace	Ultra-negative	No	N/A
FNAB273	No	Trace	Ultra-negative	No	N/A
FNAB403	No	Medium	Ultra-positive (Medium)	No	N/A
Overall	6/22 (27)	Trace: 13/22 (59) Very low: 2/22 (9) Low: 3/22 (14) Medium: 4/22 (18)	Xpert: 11/21 (52) positive, 3/11 (27) negative, 8/11 (73) Ultra: 10/21 (48) positive, 3/10 (30) negative, 7/10 (70)	6/22 (27)	6/6 (100)

112 Missing data: Routine PCR not done, n=1.

- 113 Abbreviations: FNAB, fine needle aspirate biopsy; PCR, polymerase chain reaction; Ultra, Xpert MTB/RIF
114 Ultra.
115 If the patient was not initiated on TB treatment, N/A was recorded in the last column.

116 **Supplementary Table 4:** Diagnostic accuracy of Ultra on urine or FNABs measured using the MRS in a head-to-head analysis stratified by HIV
 117 status. Urine Ultra had lower sensitivity than FNAB Ultra but increased specificity (**Table 2**). Data are %, 95% CI, and n/N

	All patients				HIV-negative				HIV-positive			
	n=76				n=18/75 (24)				n=57/75 (76)			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
Urine-Ultra	18 (7, 35) 6/33	98 (88, 100) 42/43	86 (42, 100) 6/7	61 (48, 72) 42/69	0 (0, 52) 0/5	100 (75, 100) 13/13	0/0	72 (47, 90) 13/18	21 (8, 41) 6/28 p=0.252*	97 (82, 100) 28/29 p=498*	86 (42, 100) 6/7	56 (41, 70) 28/50 p=0.228*
Study FNAB-Ultra	91 (76, 98) 30/33 p<0.001‡	60 (44, 75) 26/43 p<0.001‡	64 (49, 77) 30/47 p=0.252‡	90 (73, 98) 26/29 p=0.005‡	80 (28, 99) 4/5 p=0.010‡	38 (14, 68) 5/13 p=0.001‡	33 (10, 65) 4/12	83 (36, 100) 5/6 p=0.586‡	93 (76, 99) 26/28 p<0.001‡ p=0.357*	69 (49, 85) 20/29 p=0.005‡ p=0.063*	74 (57, 88) 26/35 p=0.517‡ p=0.011*	91 (71, 99) 20/22 p=0.004‡ p=0.595*

118 Missing data: Non-actionable Ultras (n=1), no HIV (n=1) in the head-to-head table.

119 Within column p-values: ‡ Urine-Ultra vs. FNAB-Ultra

120 Within row p-values: *HIV-negative vs. HIV-positive

121 Abbreviations: CI, confidence interval; CRS, composite reference standard; eMRS, extended microbiological reference standard; MRS, microbiological reference standard;

122 NPV, negative predictive value; PPV, positive predictive value; Xpert, Xpert MTB/RIF; Ultra, Xpert MTB/RIF Ultra

123 **Supplementary Table 5:** Non-head-to-head and head-to-head diagnostic accuracy analyses of Xpert and Ultra using a MRS, eMRS and CRS for
 124 the detection of *Mycobacterium tuberculosis complex* DNA with and without exclusion of Ultra trace results. Routine Xpert results were compared
 125 to study Ultra results. Ultra has similar diagnostic accuracy compared to Xpert after trace positive exclusion. Study Ultra results with trace excluded
 126 were like study Ultra results. Similar trends are seen across reference standards. Data are %, 95% CI, and n/N.

Non-head-to-head												
MRS				eMRS				CRS				
n=96				n=97				n=97				
Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV	
Xpert ^o	73 (58, 85) 35/48	92 (80, 98) 44/48	90 (76, 97) 35/39	77 (64, 87) 44/57	69 (55, 81) 36/52 p=0.685*	91 (79, 98) 41/45 p=0.924*	90 (76, 97) 36/40 p=0.510*	72 (58, 83) 41/57 p=0.519*	65 (52, 77) 39/60 p=0.635± p=0.379 [¥]	97 (86, 100) 36/37 p=0.244± p=0.274 [¥]	98 (87, 100) 39/40 p=0.166± p=0.157 [¥]	63 (49, 76) 36/57 p=0.317± p=0.102 [¥]
	n=111			n=112				n=112				
Ultra excluding trace	83 (71, 92) 45/54 p=0.201 [‡]	84 (72, 93) 48/57 p=0.248 [‡]	83 (71, 92) 45/54 p=0.379 [‡]	84 (72, 93) 48/57 p=0.343 [‡]	81 (69, 90) 47/58 p=0.151 [‡] p=0.751*	85 (73, 93) 46/54 p=0.368 [‡] p=0.887*	85 (73, 94) 47/55 p=0.510 [‡] p=0.760*	81 (68, 90) 46/57 p=0.271 [‡] p=0.622*	74 (62, 84) 51/69 p=0.272 [‡] p=0.341± p=0.210 [¥]	91 (78, 97) 39/43 p=0.224 [‡] p=0.413± p=0.340 [¥]	93 (82, 98) 51/55 p=0.304 [‡] p=0.221± p=0.120 [¥]	68 (55, 80) 39/57 p=0.554 [‡] p=0.132± p=0.047 [¥]
Δ Trace excluded ^Φ	-2 (-15, 12) p=0.808 [§]	+15 (1, 30) p=0.041 [§]	+13 (-1, 28) p=0.081 [§]	0 (-13, 13) p>0.999 [§]	-2 (-15, 12) p=0.799 [§]	+16 (2, 31) p=0.034 [§]	+13 (-0.03, 28) p=0.063 [§]	0 (-14, 14) p>0.999 [§]	-2 (-16, 12) p=0.738 [§]	+20 (5, 35) p=0.016 [§]	+15 (3, 26) p=0.026 [§]	0 (-17, 17) p>0.999 [§]
Head-to-head												
n=82				n=82				n=82				
Xpert ^o	80 (64, 91) 32/40	93 (81, 99) 39/42	91 (77, 98) 32/35	83 (69, 92) 39/47	74 (59, 86) 32/43 p=0.545*	92 (79, 98) 36/39 p=0.925*	91 (77, 98) 32/35 p>0.999*	77 (62, 88) 36/47 p=0.441*	69 (55, 82) 34/49 p=0.593± p=0.255 [¥]	97 (84, 100) 32/33 p=0.390± p=0.431 [¥]	97 (85, 100) 34/35 p=0.303± p=0.303 [¥]	68 (53, 81) 32/47 p=0.356± p=0.093 [¥]
Ultra excluding trace	90 (76, 97) 36/40 p=0.210 [‡]	83 (69, 93) 35/42 p=0.178 [‡]	84 (69, 93) 36/43 p=0.311 [‡]	90 (76, 97) 35/39 p=0.367 [‡]	86 (72, 95) 37/43 p=0.176 [‡] p=0.580*	85 (69, 94) 33/39 p=0.288 [‡] p=0.875*	86 (72, 95) 37/43 p=0.459 [‡] p=0.763*	85 (69, 94) 33/39 p=0.353 [‡] p=0.498*	82 (68, 91) 40/49 p=0.159 [‡] p=0.567± p=0.266 [¥]	91 (76, 98) 30/33 p=0.302 [‡] p=0.421± p=0.338 [¥]	93 (81, 99) 40/43 p=0.412 [‡] p=0.291 p=0.178 [¥]	77 (61, 89) 30/39 p=0.363 [‡] p=0.389± p=0.129 [¥]
Δ Trace excluded ^Φ	-1 (-14, 11) p=0.836 [§]	+7 (-9, 24) p=0.400 [§]	+5 (-11, 20) p=0.576 [§]	0 (-13, 13) p>0.999 [§]	-2 (-16, 12) p=0.808 [§]	+8 (-9, 25) p=0.369 [§]	+5 (-10, 20) p=0.521 [§]	0 (-16, 16) p=0.484 [§]	-2 (-17, 13) p=0.788 [§]	+10 (-6, 26) p=0.241 [§]	+6 (-6, 18) p=0.320 [§]	0 (-18, 18) p>0.999 [§]

127 Within column p-values: [‡]Xpert vs. Ultra within an analysis (non-head-to-head or head-to-head) in patients of the same HIV status (overall, negative, or positive), [§]Study
128 Ultra results (Supplementary Table 2) vs. study Ultra results excluding trace results within an analysis (non-head-to-head or head-to-head) in patients using different
129 reference standards (MRS, eMRS, or CRS).
130 Within row p-values: ^{*}MRS vs. eMRS, [‡]eMRS vs. CRS, [¥]MRS vs. CRS within an analysis (non-head-to-head or head-to-head).
131 [°]Although Xpert data are already shown in Supplementary Table 2, small differences in the number of samples included occur in the head-to-head comparison. For the non-
132 head-to-head comparison the Xpert data are identical to that in Supplementary Table 2 but are included here for readability.
133 ^ϕThis comparison is Ultra with traces excluded vs. Ultra with traces included and considered positive.
134 Abbreviations: CRS, composite reference standard; eMRS, extended microbiological reference standard; MRS, microbiological reference standard; Ultra, Xpert MTB/RIF
135 Ultra; Xpert, Xpert MTB/RIF.

136

137 **Supplementary Table 6:** Non-head-to-head and head-to-head diagnostic accuracy analyses of Xpert and Ultra using a MRS, eMRS and CRS for
 138 the detection of Mycobacterium tuberculosis complex DNA, reclassifying trace positive Ultra results as negative. Routine Xpert results were
 139 compared to study Ultra results. Ultra has similar diagnostic accuracy compared to Xpert when trace positive results are reclassified as negative.
 140 Study Ultra results with trace reclassified had increased sensitivity and decreased specificity compared to normal study Ultra results. Similar trends
 141 are seen across reference standards. Data are %, 95% CI, and n/N.

	Non-head-to-head											
	MRS				eMRS				CRS			
	n=96				n=97				n=97			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
Xpert^o	73 (58, 85) 35/48	92 (80, 98) 44/48	90 (76, 97) 35/39	77 (64, 87) 44/57	69 (55, 81) 36/52 p=0.685*	91 (79, 98) 41/45 p=0.924*	90 (76, 97) 36/40 p=0.510*	72 (58, 83) 41/57 p=0.519*	65 (52, 77) 39/60 p=0.635± p=0.379 [‡]	97 (86, 100) 36/37 p=0.244± p=0.274 [‡]	98 (87, 100) 39/40 p=0.166± p=0.157 [‡]	63 (49, 76) 36/57 p=0.317± p=0.102 [‡]
	n=130				n=131				n=131			
Ultra with trace reclassified	75 (62, 85) 45/60 p=0.806 [‡]	87 (77, 94) 61/70 p=0.441 [‡]	83 (71, 92) 45/54 p=0.379 [‡]	80 (70, 89) 61/76 p=0.667 [‡]	73 (61, 84) 47/64 p=0.618 [‡] p=0.843*	88 (78, 95) 59/67 p=0.609 [‡] p=0.871*	85 (73, 94) 47/55 p=0.510 [‡] p=0.760*	78 (67, 86) 59/76 p=0.451 [‡] p=0.691*	67 (55, 77) 51/76 p=0.797 [‡] p=0.415± p=0.316 [‡]	93 (82, 98) 51/55 p=0.343 [‡] p=0.389± p=0.310 [‡]	93 (82, 98) 51/55 p=0.304 [‡] p=0.221± p=0.130 [‡]	67 (55, 77) 51/76 p=0.636 [‡] p=0.147± p=0.066 [‡]
Δ Trace reclassified^φ	-10 (-19, -1) p=0.014[§]	+18 (8, 29) p<0.001[§]	+13 (-1, 28) p=0.081 [§]	-4 (-17, 9) p=0.558 [§]	+10 (-18, 1) p=0.014[§]	+19 (8, 30) p<0.001[§]	+13 (-0.03, 28) p=0.063 [§]	-3 (-17, 11) p=0.667 [§]	-9 (-17, 1) p=0.008[§]	+22 (9, 35) p=0.001[§]	+15 (3, 26) p=0.026[§]	+1 (-17, 14) p=0.873 [§]
	Head-to-head											
	n=92				n=92				n=92			
Xpert^o	72 (57, 84) 33/46	93 (82, 99) 43/46	92 (78, 98) 33/36	77 (64, 87) 43/56	67 (52, 80) 33/49 p=0.642*	93 (81, 99) 40/43 p=0.932*	92 (78, 98) 33/36 p>0.999*	71 (58, 83) 40/56 p=0.518*	64 (50, 76) 35/55 p=0.691± p=0.387 [‡]	97 (86, 100) 36/37 p=0.382± p=0.419 [‡]	97 (85, 100) 35/36 p=0.304± p=0.303 [‡]	64 (50, 77) 36/56 p=0.418± p=0.147 [‡]
Ultra with trace reclassified	78 (64, 89) 36/46 p=0.470 [‡]	85 (71, 94) 39/46 p=0.180 [‡]	84 (69, 93) 36/43 p=0.290 [‡]	80 (66, 90) 39/49 p=0.729 [‡]	76 (61, 87) 37/49 p=0.371 [‡] p=0.751*	86 (72, 95) 37/43 p=0.291 [‡] p=0.763*	86 (72, 95) 37/43 p=0.434 [‡] p=0.763*	76 (61, 87) 37/49 p=0.637 [‡] p=0.498*	73 (59, 84) 40/55 p=0.306 [‡] p=0.747± p=0.521 [‡]	92 (78, 98) 34/37 p=0.304 [‡] p=0.409± p=0.323 [‡]	93 (81, 99) 40/43 p=0.397 [‡] p=0.291± p=0.178 [‡]	69 (55, 82) 34/49 p=0.580 [‡] p=0.489± p=0.247 [‡]
Δ Trace reclassified^φ	-13 (-25, 1) p=0.014[§]	+9 (-2, 19) p=0.046[§]	+5 (-11, 20) p=0.576 [§]	-10 (-25, 5) p=0.196 [§]	-12 (-23, -1) p=0.014[§]	+9 (-2, 20) p=0.046[§]	+5 (-10, 20) p=0.521 [§]	-9 (-26, 7) p=0.293 [§]	-11 (-21, -1) p=0.014[§]	+11 (-2, 24) p=0.046[§]	+6 (-6, 18) p=0.320 [§]	-8 (-26, 11) p=0.430 [§]

142 Within column p-values: [‡]Xpert vs. Ultra within an analysis (non-head-to-head or head-to-head) in patients of the same HIV status (overall, negative, or positive), [§]Study
143 Ultra results (Supplementary Table 2) vs. study Ultra results excluding trace results within an analysis (non-head-to-head or head-to-head) in patients using different
144 reference standards (MRS, eMRS, or CRS).
145 Within row p-values: ^{*}MRS vs. eMRS, [‡]eMRS vs. CRS, [¥]MRS vs. CRS within an analysis (non-head-to-head or head-to-head).
146 [°]Although Xpert data are already shown in Supplementary Table 2, small differences in the number of samples included occur in the head-to-head comparison. For the non-
147 head-to-head comparison the Xpert data are identical to that in Supplementary Table 2 but are included here for readability.
148 [‡]This comparison is Ultra with traces reclassified as negative vs. Ultra with traces considered positive.
149 Abbreviations: CRS, composite reference standard; eMRS, extended microbiological reference standard; MRS, microbiological reference standard; Ultra, Xpert MTB/RIF
150 Ultra; Xpert, Xpert MTB/RIF.