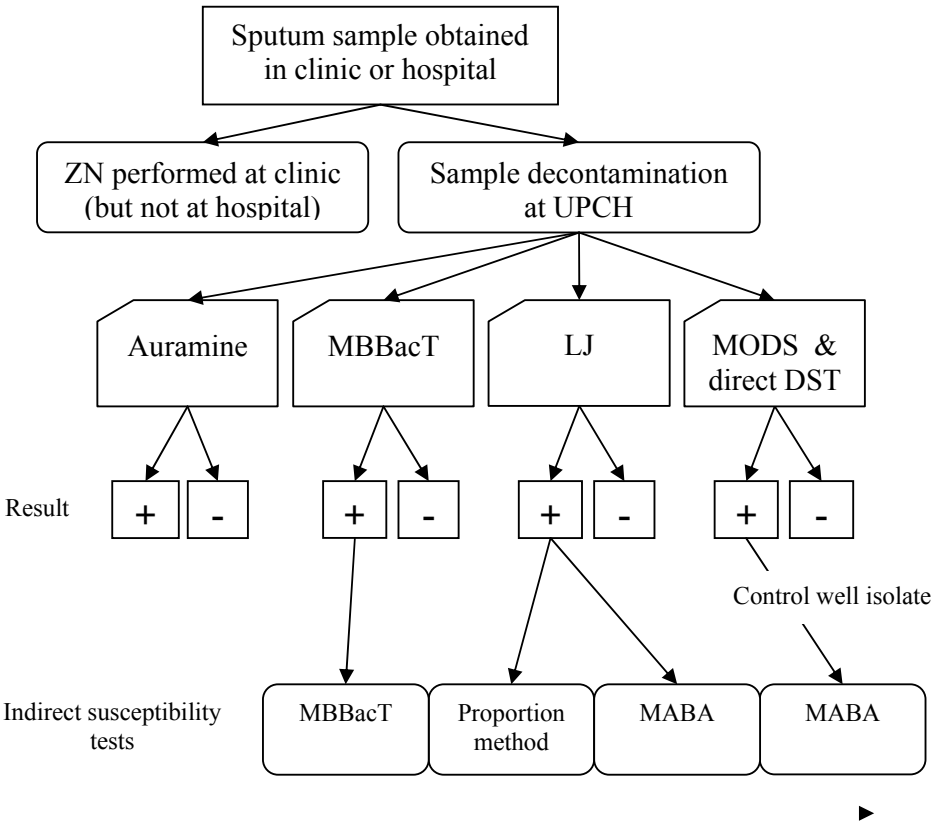
Supplementary Appendix

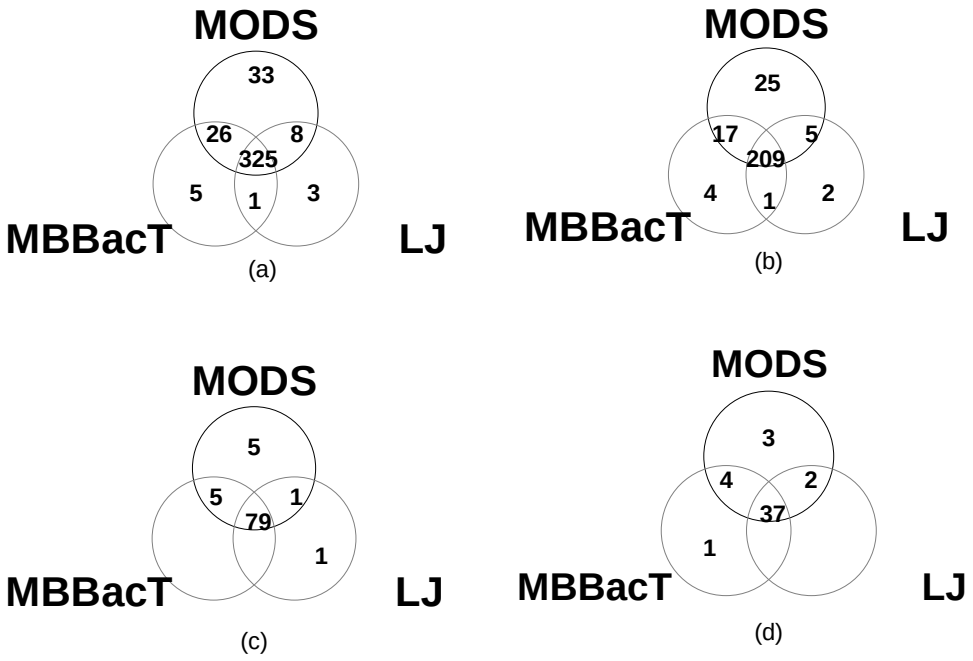
This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Moore DAJ, Evans CAW, Gilman RH, et al. Microscopic-observation drug-susceptibility assay for the diagnosis of TB. N Engl J Med 2006;355:1539-50.

Web-only Appendix



Supplemental Figure (I) Flowchart of sample handling and procedures undertaken for each sample



Supplemental Figure (II) Absolute number of true positive cultures by each method performed in parallel on the same 3757 samples for (a) all subjects, (b) unselected community-based TB suspects alone (group I, n=3017), (c) pre-screened high-risk TB suspects alone (group II, n=446), and (d) unselected hospitalized HIV patients alone (group III, n=294).

MODS detected 98.8% and 98.3% of LJ and MBBacT culture-positive samples respectively and 99.7% of samples culture-positive by both LJ and MBBacT, as well as a further 21 additional positive cultures (and 12 cross-contamination positive cultures).

The following 17 positive cultures which were identified as false-positive due to cross-contamination are not shown. Group I – 13 cultures from 11 samples - 7 MODS, 1 MBBacT, 1 LJ and 2 both MODS & MBBacT; group II – 4 cultures from 3 samples – 2 MODS, 1 both MBBacT & MODS.

(a)

Rifampicin (n=349)			**1st round assignment**			**2nd round assignment based on MABA (LJ and MODS)**		
	Proportion method	MBBacT	Sensitive	Resistant	Inconclusive	Sensitive	Resistant	inconclusive
Susceptibility profile and allocation	Sensitive	Sensitive	305	-	-	-	-	-
	Resistant	Resistant	-	38	-	-	-	-
	Sensitive	Resistant	-	-	3	2[a]	1[b]	-
	Resistant	Sensitive	-	-	3	3[c]	-	-

[a] both MICs = 0.063 for each isolate; [b] both MICs ≥ 16; [c] both MICs = 0.25 for all 3 isolates

(b)

Isoniazid (n=349)			**1st round assignment**	**2nd round assignment based on MABA (LJ and MODS)**

	Proportion method	MBBacT	Sensitive	Resistant	Inconclusive	Sensitive	Resistant	inconclusive
Susceptibility profile and allocation	Sensitive	Sensitive	262	-	-	-	-	-
	Resistant	Resistant	-	64	-	-	-	-
	Sensitive	Resistant	-	-	21	13[d]	3[e]	5[f]
	Resistant	Sensitive	-	-	2	2[g]	-	-

[d] both MICs = 0.125 for 7, both MICs =0.25 for 5 and one MIC each of 0.25 and 0.125 for 1 sample; [e] both MICs = 0.5 for 2 and both MICs = 4 for 1; [f] MICs = 0.25 and 0.5 for 3 and MIC data unavailable for one of each MABA for 2 samples; [g] both MICs = 0.125 for both isolates.

(c)

Ethambutol (n=349)			**1st round assignment**			**2nd round assignment based on MABA (LJ and MODS)**		
	Proportion method	MBBacT	Sensitive	Resistant	Inconclusive	Sensitive	Resistant	inconclusive
Susceptibility profile and allocation	Sensitive	Sensitive	286	-	-	-	-	-
	Resistant	Resistant	-	12	-	-	-	-
	Sensitive	Resistant	-	-	50	15[h]	23[i]	12[j]
	Resistant	Sensitive	-	-	1	-	1[k]	-

[h] both MICs 1 or 2; [i] both MICs ≥ 4; [j] MICs discordant around cutpoint for 9 pairs and MIC data unavailable for one each of 3 pairs; [k] MICs of 8 & 32;

(d)

Streptomycin (n=349)			**1st round assignment**			**2nd round assignment based on MABA (LJ and MODS)**		
	Proportion method	MBBacT	Sensitive	Resistant	Inconclusive	Sensitive	Resistant	inconclusive
Susceptibility profile and allocation	Sensitive	Sensitive	192	-	-	-	-	-
	Resistant	Resistant	-	74	-	-	-	-
	Sensitive	Resistant	-	-	7	7 [l]	-	-
	Resistant	Sensitive	-	-	76	64 [m]	-	12 [n]

[l] both MICs < 1 for all 7; [m] both MICs ≤ 1; [n] MICs discordant around cutpoint for 6 pairs and MIC data unavailable for one each of 6 pairs

Supplemental Table I (a-d).

Assignment of susceptibility status by discrepant analysis (a) rifampicin, (b) isoniazid, (c) ethambutol, (d) streptomycin. Concordant results in the two gold-standard reference tests were accepted; discrepant results were resolved in the second round by consideration of the results from two colorimetric MICs (MABA) concurrently; samples with inconclusive gold-standard reference test assignments after 2nd round were excluded from analysis.