

Web Appendix 1: Full specification of latent class models

Let T_{iCu}, \dots, T_{iTS} denote the observed outcomes on the 5 binary tests (Cu = Culture, Xp = Xpert, Mi = Microscopy, Ra = Radiography, TS = TST) for subject i , $i = 1, \dots, 749$. It is assumed that the true CPTB status of each subject is a Bernoulli latent variable, d_i , where $d_i = 0$ (1) denotes absence (presence) of CPTB. The joint distribution of test observations is modeled by a two-class latent class model,

$$\Pr(T_{iCu}, \dots, T_{iTS}) = \sum_{d_i=0}^1 \Pr(d_i) \Pr(T_{iCu}, \dots, T_{iTS} | d_i).$$

Conditional dependence latent class models

To relax the conditional independence assumption (M1) we evaluated three conditional dependence latent class models (M2 to M4). We let r denote the random effect representing bacillary load, $r \sim N(0,1)$. Further, we let Z_{iHhTB} , Z_{iHIV} , Z_{iAge} and Z_{iMal} denote subject i 's observed values on the binary covariates: Household contact with a TB patient, HIV infection status, Age (dichotomized at 24 months) and Malnutrition, respectively.

For M4, the most elaborate latent class model considered here, the latent disease status d_i is regressed on the binary covariates via the logistic function, $\log\left(\frac{\Pr(d_i=1)}{\Pr(d_i=0)}\right) = \alpha_0 + \alpha_1 Z_{iHhTB} + \alpha_2 Z_{iHIV} + \alpha_3 Z_{iAge} + \alpha_4 Z_{iMal}$. For each test j , the marginal conditional probability distribution $\Pr(T_{ij} | d_i)$ is assumed independent Bernoulli with probability $\Phi(\eta_{j|d_i})$, where Φ denotes the cumulative distribution function (c.d.f) of a standard normal distribution ($N(0,1)$). The specific forms of $\Phi(\eta_{j|d_i})$ for M4 are detailed in Web Table 1.

M1, M2 and M3 are nested within model M4. M1 (conditional independence model) is the special case of M4, where all covariate (including the covariate effects on d_i) and random effects are assumed to be null. In M2, all the covariate effects are assumed to be null and TST outcomes do not depend on the random effect (i.e., $\sigma_4 = \sigma_5 = 0$). In M3, the covariate effects for culture, Xpert, microscopy and radiography are assumed to be null.

Prior distributions

For M1 the prior distributions were as follows,

$$\alpha_0, \beta_{10}, \dots, \beta_{50}, \gamma_{30}, \dots, \gamma_{50} \sim N(0,1),$$

$$\gamma_{10} \sim N(3.023, 0.126), \gamma_{20} \sim N(2.886, 0.126).$$

For M2 the same prior distributions as M1 are used, and we add random effect parameters with corresponding prior distributions,

$$\sigma_1 \sim \text{Uniform}(0,5), \sigma_1 = \sigma_2 = \sigma_3.$$

For M3 we additionally define,

$$\sigma_4 \sim \text{Uniform}(-5,5), \sigma_5 \sim \text{Uniform}(0,5),$$

$$\alpha_1, \dots, \alpha_4, \beta_{41}, \beta_{42} \sim N(0,10).$$

Finally, for M4 we add,

$$\gamma_{41}, \beta_{11}, \dots, \beta_{42} \sim \text{DoubleExponential}(0, \lambda), \lambda \sim U(0, 10).$$

Posterior distribution

The joint posterior distribution is proportional to the product of the likelihood function and all prior distributions. The analytical form of the joint posterior distribution or the marginal posterior distributions of individual parameters cannot be obtained for any of the four models considered. Therefore, an MCMC approach was used to sample from these distributions. This approach was implemented using JAGS software (for details see Web Appendix 1).

Overtreatment and undertreatment

We used M3 to gain insight in potential overtreatment and undertreatment in the cohort. Let anti-TB treatment received by subject i be denoted by δ_i , taking on the values 0 for no treatment received and 1 for treatment received. We estimate the probability of being a CPTB positive case for each individual, $\widehat{Pr}(d_i = 1)$, by averaging d_i over MCMC samples. The proportion of CPTB positives within the strata of treatment status ($\widehat{Pr}(d = 1 | \delta = 0)$) and ($\widehat{Pr}(d = 1 | \delta = 1)$) are estimated by the average $\widehat{Pr}(d_i = 1)$ within each of the strata. By applying Bayes theorem,

we can then estimate the probability of receiving treatment for CPTB positive children $\widehat{Pr}(\delta = 1 | d_i = 0)$ and probability of not receiving treatment for CPTB positive children $\widehat{Pr}(\delta = 0 | d_i = 1)$.

Sensitivity analyses

To evaluate the robustness of the random effects structure a 3-class condition independence latent class model (M2b) is developed that is defined by,

$$\Pr(T_{iCu}, \dots, T_{iTS}) = \sum_{l_i=0}^2 \Pr(l_i) \prod_{j=1}^J \Pr(T_j | l_i), \text{ where } \Pr(T_j | l_i) = \pi_{jl}.$$

Class $l_i = 0$ represents truly CPTB negative children; $l_i = 1$ CPTB disease with TB detectable in respiratory secretions and $l_i = 2$ CPTB disease with TB not detectable in respiratory secretions. The assumptions are reflected in informative prior distributions for culture, Xpert and microscopy,

$$\pi_{Cu1} \sim \text{Beta}(1, 400), \pi_{Xp1} \sim \text{Beta}(1, 198), \pi_{Mi1} \sim \text{Beta}(1, 1),$$

$$\pi_{Cu2} = 0, \pi_{Xp2} = 0, \pi_{Mi2} = 0.$$

It is also assumed that for TST, $\pi_{Ts1} = \pi_{Ts2}$. The remaining π -parameters have Beta(1,1) prior distributions. The prior distribution for $\Pr(l_i)$ is Dirichlet(1,1,1).

Finally, we perform sensitivity analysis for M3 by adjusting its prior distributions. M3b, $\sigma_2, \sigma_3, \sim \text{Uniform}(0,5)$, M3c, $\gamma_{10} \sim N(0,1)$, M3d, $\gamma_{20} \sim N(0,1)$.

Web Table 1. Specification of marginal conditional probability distributions of M4

Test	$\eta_{j d_i=0}$	$\eta_{j d_i=1}$
Culture	$\eta_{Cu d_i=0} = \gamma_{10}$	$\eta_{Cu d_i=1} = \beta_{10} + \beta_{11} Z_{iHIV} + \beta_{12} Z_{iAge} + \sigma_1 r_i$
Xpert	$\eta_{Xp d_i=0} = \gamma_{20}$	$\eta_{Xp d_i=1} = \beta_{20} + \beta_{21} Z_{iHIV} + \beta_{22} Z_{iAge} + \sigma_2 r_i$
Microscopy	$\eta_{Mi d_i=0} = \gamma_{30}$	$\eta_{Mi d_i=1} = \beta_{30} + \beta_{31} Z_{iHIV} + \beta_{32} Z_{iAge} + \sigma_3 r_i$
Radiography	$\eta_{Ra d_i=0} = \gamma_{40} + \gamma_{41} Z_{iHIV}$	$\eta_{Ra d_i=1} = \beta_{40} + \beta_{41} Z_{iHIV} + \beta_{42} Z_{iMal}$
TST	$\eta_{Ts d_i=0} = \gamma_{50}$	$\eta_{Ts d_i=1} = \beta_{50} + \beta_{51} Z_{iHIV} + \beta_{52} Z_{iMal} + \sigma_4 r_i - \sigma_5 r_i^2$

Web Appendix 2: Code for running model M3 using JAGS in R

```
model <- function(){

# order variables (in dataset y):
# 1. "culture"
# 2. "xpert"
# 3. "smear"
# 4. "radiography"
# 5. "TST"
# 6. "household contact TB"
# 7. "HIV"
# 8. "malnutrition"
# 9. "age"

## priors -----
for(j in 1:5){a[j, 1] ~ dnorm(0,1)}
a[1, 2] ~ dnorm(3.023, 7.923)
a[2, 2] ~ dnorm(2.886, 7.923)
a[3, 2] ~ dnorm(0, 1)
a[4, 2] ~ dnorm(0, 1)
a[5, 2] ~ dnorm(0, 1)

b.RE[1] ~ dunif(0,5)
b.RE[2] <- b.RE[1]
b.RE[3] <- b.RE[1]
b.RE[4] ~ dunif(-5,5)
b.RE[5] ~ dunif(0,5)

a_prev ~ dnorm(0, 1)

b.hhtb ~ dnorm(0, 0.1)
for(j in 1:2){ b.hiv[j] ~ dnorm(0, 0.1)}
b.age ~ dnorm(0, 0.1)
for(j in 1:2){ b.mal[j] ~ dnorm(0, 0.1)}

## likelihood -----
for (i in 1:N) {
  r[i] ~ dnorm(0, 1)
  for (j in 1:5) {
    y[i, j] ~ dbin(p[i, j], 1)
    p[i, j] <- (s[i, j]^d[i]) * (1 - c[i, j])^(1 - d[i])
  }
  d[i] ~ dbern(pd[i])
  logit(pd[i]) <- a_prev + b.hhtb * y[i, 6] + b.hiv[1] * y[i, 7] + b.mal[1] * y[i,8] + b.age * y[i, 9]

  s[i, 1] <- phi(a[1, 1] + b.RE[1] * r[i])
  c[i, 1] <- phi(a[1, 2])
  s[i, 2] <- phi(a[2, 1] + b.RE[2] * r[i])
  c[i, 2] <- phi(a[2, 2])
  s[i, 3] <- phi(a[3, 1] + b.RE[3] * r[i])
  c[i, 3] <- phi(a[3, 2])
  s[i, 4] <- phi(a[4, 1])
  c[i, 4] <- phi(a[4, 2])
  s[i, 5] <- phi(a[5, 1] + b.hiv[2] * y[i, 7] + b.mal[2] * y[i, 8] + b.RE[4] * r[i] - b.RE[5] * r[i] * r[i])
  c[i, 5] <- phi(a[5, 2]) }
}
```

Web Table 2: Sensitivity analyses

Sensitivity analysis for model M2 and M3. Posterior median estimates (95% Credible Interval) of marginalized sensitivity, specificity and PTB prevalence for M2b: 3-class latent class model (defined in appendix A), M3a (Random effect Culture, XPERT, Microscopy freely estimated), M3b (non-informative priors for Culture) and M3c (non-informative priors for Xpert).

Test	Parameters	M2	M2b	M3	M3a	M3b	M3c
Culture	Prevalence	28.7 (22.2; 36.3)	29.7 (20.2; 49.7)	26.7 (20.8; 35.2)	26.6 (20.2; 35.0)	25.6 (20.0; 33.8)	25.9 (20.6; 33.4)
	Sensitivity	57.2 (44.8; 73.5)	54.0 (32.0; 77.8)	60.0 (45.7; 75.5)	60.2 (46.1; 78.0)	61.6 (46.9; 77.5)	61.7 (48.4; 76.4)
	Specificity	99.9 (99.3; 100.0)	99.8 (99.1; 100.0)	99.6 (98.7; 100.0)	99.6 (98.6; 100.0)	98.9 (97.6; 99.7)	99.6 (98.7; 100.0)
Xpert	Sensitivity	46.7 (37.1; 59.1)	42.2 (25.6; 61.1)	49.4 (37.7; 62.2)	49.5 (37.9; 64.0)	51.2 (39.1; 64.8)	50.0 (39.1; 62.4)
	Specificity	98.9 (97.3; 99.9)	98.3 (96.9; 99.4)	98.6 (97.3; 99.5)	98.6 (97.2; 99.5)	98.6 (97.2; 99.5)	97.8 (96.2; 99.0)
Microscopy	Sensitivity	20.4 (14.6; 27.9)	18.5 (10.5; 29.0)	22.3 (15.6; 30.3)	22.3 (15.5; 31.4)	23.2 (16.3; 31.6)	23.1 (16.5; 30.8)
	Specificity	99.7 (99.0; 100.0)					
Radiography	Sensitivity	64.7 (56.0; 73.0)	66.9 (47.3; 79.5)	64.2 (54.9; 72.8)	64.3 (55.2; 73.0)	64.9 (55.6; 73.5)	65.0 (56.0; 73.6)
	Specificity	79.4 (74.2; 84.9)	80.8 (74.1; 88.3)	78.0 (73.4; 83.4)	78.0 (73.3; 83.5)	77.7 (73.1; 82.8)	77.9 (73.4; 82.9)
TST	Sensitivity	69.3 (61.1; 76.8)	68.6 (59.9; 76.4)	75.2 (61.2; 83.8)	75.3 (61.7; 83.8)	75.8 (62.9; 83.8)	75.2 (61.2; 83.5)
	Specificity	67.8 (62.6; 73.4)	68.1 (62.2; 81.6)	69.3 (63.2; 75.9)	69.2 (63.1; 75.8)	68.8 (63.1; 75.3)	68.8 (62.8; 75.1)

Web Table 3: Covariate effects

Sensitivity and specificity estimates within sub-groups defined by covariates estimated by M4

Test	Parameter	Sub-group	Posterior Median (95% Credible Interval)	Sub-group	Posterior Median (95% Credible Interval)
Culture	Sensitivity	HIV positive	64.0 (46.9,96.3)	HIV negative	57.9 (44.1,72.5)
	Sensitivity	Age > 24 months	56.2 (40.0,72.4)	Age ≤ 24 months	61.3 (46.5,76.0)
Xpert	Sensitivity	HIV positive	49.9 (36.1,75.9)	HIV negative	48.4 (36.8,60.9)
	Sensitivity	Age > 24 months	47.3 (33.6,60.8)	Age ≤ 24 months	49.9 (37.8,62.7)
Microscopy	Sensitivity	HIV positive	24.8 (16.1,47.9)	HIV negative	21.2 (14.1,29.6)
	Sensitivity	Age > 24 months	21.4 (13.7,30.3)	Age ≤ 24 months	22.3 (15.1,31.0)
Radiography	Sensitivity	HIV positive	73.4 (59.0,87.7)	HIV negative	63.6 (54.6,72.0)
	Sensitivity	Age > 24 months	52.5 (39.4,66.0)	Age ≤ 24 months	75.0 (62.6,85.8)
	Sensitivity	Malnourished	64.6 (53.4,75.9)	Not malnourished	65.4 (55.5,74.1)
	Specificity	HIV positive	77.7 (70.1,85.0)	HIV negative	78.3 (73.3,84.3)
TST	Sensitivity	HIV positive	66.9 (39.2,84.0)	HIV negative	78.5 (65.8,86.6)
	Sensitivity	Malnourished	71.8 (53.2,83.7)	Not malnourished	78.9 (65.1,87.1)

Estimates of sensitivity and specificity in a given sub-group are obtained by averaging across any other covariates involved