

## Additional file No. 2: Model parameters

| Parameter  | Symbol          | Value                     |                            |                            |                            | Source/Notes       |
|--|-----------------|---------------------------|----------------------------|----------------------------|----------------------------|--------------------|
|  |                 | South Africa              | Kenya                      | India                      | Brazil                     |                    |
| <b>TB natural history</b>  |                 |                           |                            |                            |                            |                    |
| Mean rate of transmission per DS-TB case   | $\beta_{as}$    | 5.1 (95% CrI 2.3 – 10.6)  | 8.8 (95% CrI 3.5 – 19)     | 11 (95% CrI 5 – 24)        | 11 (95% CrI 9.5 – 14)      | Model estimate     |
| Mean rate of transmission per DR-TB case   | $\beta_{dr}$    | 4.3 (95% CrI 2 – 7.7)     | 7.2 (95% CrI 3 – 16)       | 7.5 (95% CrI 3.6 – 16)     | 5.7 (95% CrI 5 – 6.9)      | Model estimate     |
| TB infectiousness in <b>HIV</b> <sup>+</sup> relative to <b>HIV</b> <sup>-</sup>           | $\alpha$        | 0.77(95% CrI 0.61 – 0.99) | 0.8 (95% CrI 0.6 – 0.98)   | 0.8 (95% CrI 0.61 – 0.98)  | 0.83 (95% CrI 0.6 – 0.99)  | Model estimate     |
| Breakdown to active disease in slow progressors  | $\gamma^{slow}$ | 0.000594                  |                            |                            |                            | Menzies et al [10] |
| Breakdown to active disease in fast progressors  | $\gamma^{fast}$ | 0.19 (95% CrI 0.07 – 0.6) | 0.09 (95% CrI 0.03 – 0.24) | 0.11 (95% CrI 0.05 – 0.24) | 0.13 (95% CrI 0.11 – 0.15) | Model estimate     |
| Rate of transition to the slow latent compartment  | $\delta$        | 0.87                      |                            |                            |                            | Menzies et al [10] |
| Increased progression to TB in <b>HIV</b> <sup>+</sup> relative to <b>HIV</b> <sup>-</sup> | $\varepsilon$   | 26                        |                            |                            |                            | Getahun et al [12] |

|   |                    |  |                            |                            |                             |   |  |
|---|--------------------|--|----------------------------|----------------------------|-----------------------------|---|--|
| Relapse, per-capita hazard rates                    | $\zeta_g$          | $g = 0$ ; relapse following treatment completion | 0.032                      |                            |                             |   | Driver et al [13], Thomas et al [14], Menzies et al [15] |
|   |                    | $g = 1$ ; relapse following treatment default    | 0.14                       |                            |                             |   |  |
|   |                    | $g = 2$ ; relapse >2 years after treatment       | 0.0015                     |                            |                             |   |  |
| 'Stabilisation' of relapse risk following treatment | $\eta$             | 0.5  |                            |                            |                             | Based on Thomas et al: most relapse occurs in first 2 yr after treatment.                         |  |
| TB mortality rate                                   | $\mu^{(tb)}$       | 0.16 (95% CrI 0.12 – 0.2)                        | 0.16 (95% CrI 0.12 – 0.19) | 0.16 (95% CrI 0.12 – 0.19) | 0.08 (95% CrI 0.08 – 0.099) | Specified together to yield ~50% cure, ~50% mortality in average of 3 years. Tiemersma et al [16] |  |
| Spontaneous cure                                    | $\theta$           | 0.15 [0.14 – 0.18]                               |                            |                            |                             |   |  |
| Relative Risk of TB mortality in HIV <sup>+</sup>   | RR <sup>(h+)</sup> | 3.3 (95% CrI 1.25-5.8)                           | 3.7 (95% CrI 1.2-5.8)      | 1.6 (95% CrI 1-3.4)        | 2.9 (95% CrI 1.4-5)         | Model estimate  |  |
| Reduced susceptibility from past infection          | $\iota$            | [0.25 – 0.75]                                    |                            |                            |                             | Assumed range (uniform distribution)  |  |
| <b>Health system</b>                                |                    |  |                            |                            |                             |   |  |
| Per-capita rate of initial presentation to care     | $\kappa$           | 2.8 (95% CrI 1 – 5.9)                            | 1.76 (95% CrI 0.71 – 6.2)  | 2.4 (95% CrI 1.2 – 4.2)    | 5 (95% CrI 3.9 – 7)         | Model estimate: corresponds to mean initial patient delay of 4.6 months (95% CrI 3.6 – 6)         |  |

|  |               |  |                                 |                                |                                |  |
|--|---------------|--|---------------------------------|--------------------------------|--------------------------------|--|
| Rate of Interval between care-seeking episodes (factor increase relative to initial careseeking) | $\nu$         | 2  |                                 |                                |                                | Model assumption corresponds to delay decrease of 50% between careseeking episodes |
| Treatment initiation delay   | $\xi$         | 52   |                                 |                                |                                | Sreeramareddy et al [17]; corresponds a mean treatment delay of 1 week             |
| Probability of diagnosis per patient-provider interaction  | $\theta_h$    | h=0; 0.7 (95% CrI 0.51 – 0.94)   | h=0; 0.71 (95% CrI 0.5 – 0.97)  | h=0; 0.71 (95% CrI 0.5 – 0.95) | h=0; 0.9 (95% CrI 0.79 – 0.97) | Model estimate   |
|  |               | h=1; 0.73 (95% CrI 0.52 – 0.97)  | h=1; 0.72 (95% CrI 0.51 – 0.96) | h=1; 0.81 (95% CrI 0.5 – 0.97) | h=1; 0.7 (95% CrI 0.51 – 0.96) |  |
| Probability of rapid DST during diagnostic attempt   | $\omega$      | 71%  | 47%                             | 15%                            | 33%                            | WHO Country profiles   |
| Rapid DST sensitivity  | $\rho^{(xp)}$ | 90%  |                                 |                                |                                | Steingart et al [18]   |
| Smear test sensitivity   | $\rho^{(sm)}$ | 80%  |                                 |                                |                                | Steingart et al [18]   |
| Treatment initiation probability   | $\varrho$     | 0.72 (95% CrI 0.51 – 0.96)   | 0.67 (95% CrI 0.5 – 0.94)       | 0.74 (95% CrI 0.51 – 0.95)     | 0.89 (95% CrI 0.69 – 0.97)     | Model estimate   |
| Overall diagnostic probability   | $\epsilon_s$  | $\epsilon_s = \theta_h(\omega\rho^{(xp)} + (1 - \omega)\rho^{(sm)}), \text{ for } s = 0$ |                                 |                                |                                | Reflects the probability of diagnosis given is a DS strain                         |

|   |                 | $\epsilon_s = \sigma_h \omega \rho^{(xp)}$ , for $s = 1$ |        |        |        | Reflects the probability of diagnosis given is a DR strain                           |
|---|-----------------|--|--------|--------|--------|--|
| Proportion completing first line treatment            | $\sigma^{(fl)}$ | 84.19%   | 87.58% | 90.79% | 71.02% | WHO TB programme data [19]   |
| Proportion completing second line treatment           | $\sigma^{(sl)}$ | 55.2%  | 72.0%  | 50.9%  | 61.2%  | WHO TB programme data [19]   |
| Proportion failing first line treatment               | $x^{(fl)}$      | 0.38%  | 0.39%  | 0.93%  | 0.05%  | WHO TB programme data [19]   |
| Proportion failing second line treatment              | $x^{(sl)}$      | 3.27%  | 1.04%  | 9.11%  | 5.31%  | WHO TB programme data [19]   |
| Proportion lost to follow-up in first line treatment  | $y^{(fl)}$      | 8.3%   | 5.4%   | 4.5%   | 10.7%  | WHO TB programme data [19]   |
| Proportion lost to follow-up in second line treatment | $y^{(sl)}$      | 20.1%  | 8.3%   | 20.3%  | 20.9%  | WHO TB programme data [19]   |
| Proportion dying in first line treatment              | $j^{(fl)}$      | 7.1%   | 6.6%   | 3.8%   | 7.8%   | WHO TB programme data [19]   |
| Proportion dying in second line treatment             | $j^{(sl)}$      | 21.4%  | 18.7%  | 19.7%  | 11.2%  | WHO TB programme data [19]   |
| First line treatment duration                         | $\tau^{(fl)}$   | $2 \text{ y}^{-1}$                                       |        |        |        | Corresponds to 6 month duration for standard first-line regimen. WHO guidelines [20] |

|  |                  |  |                       |                         |                         |   |
|--|------------------|--|-----------------------|-------------------------|-------------------------|---|
| Second line treatment duration   | $\tau^{(sl)}$    | 0.5 y <sup>-1</sup>  |                       |                         |                         | Corresponds to 24 month duration for standard second-line regimen. WHO [20] |
| Probability of cure after first line completion  | $\zeta^{(fl)}$   | $\zeta^{(fl)} = \frac{\sigma^{(fl)}}{(\sigma^{(fl)} + x^{(fl)})}$          |                       |                         |                         |   |
| Probability of cure after second line completion                                       | $\zeta^{(sl)}$   | $\zeta^{(sl)} = \frac{\sigma^{(sl)}}{(\sigma^{(sl)} + x^{(sl)})}$          |                       |                         |                         |   |
| First line default hazard  | $\varphi^{(fl)}$ | $\varphi^{(fl)} = y^{(fl)} \frac{\tau^{(fl)}}{(\sigma^{(fl)} + x^{(fl)})}$ |                       |                         |                         |   |
| Second line default hazard   | $\varphi^{(sl)}$ | $\varphi^{(sl)} = y^{(sl)} \frac{\tau^{(sl)}}{(\sigma^{(sl)} + x^{(sl)})}$ |                       |                         |                         |   |
| Mortality hazard during first line treatment   | $\mu^{(fl)}$     | $\mu^{(fl)} = j^{(fl)} \frac{\tau^{(fl)}}{(\sigma^{(fl)} + x^{(fl)})}$     |                       |                         |                         |   |
| Mortality hazard during first line treatment   | $\mu^{(sl)}$     | $\mu^{(sl)} = j^{(sl)} \frac{\tau^{(sl)}}{(\sigma^{(sl)} + x^{(sl)})}$     |                       |                         |                         |   |
| Rate of recruitment into ART   | $\Pi$            | 4.4 (95% CrI 3.3 – 6.8)  | 8 (95% CrI 5.5 – 9.8) | 5.5 (95% CrI 3.3 – 9.5) | 4.9 (95% CrI 3.5 – 9.1) | Model estimate  |
| Fraction of new ART starters enrolled in PT  | A                | 0.7 (95% CrI 0.54 – 0.82)  |                       |                         |                         | Model estimate  |
| <b>Preventive therapy (parameters for a baseline 6 months course of isoniazid -6H)</b> |                  |  |                       |                         |                         |   |
| PT regimen duration (months)   | $\Gamma$         | 6  |                       |                         |                         | WHO LTBI treatment guidelines [4]   |
| Rate of transition over half-course of PT  | m                | $m = \frac{\Gamma}{2}$   |                       |                         |                         | Assumption  |
| Ease of adherence (completion)   | $\theta$         | 70%  |                       |                         |                         | Alsdurf et al [6]   |
| PT default hazard  | d                | $d = \frac{12(1 - \theta)}{\Gamma\theta}$                                  |                       |                         |                         |   |

|                                    |       |                     |       |       |       |   |
|------------------------------------|-------|---------------------|-------|-------|-------|---|
| Forgiveness of non-completion      | f     | 25%                 |       |       |       | Assumption  |
| Waning of PT effect                | g     | $g = \frac{12}{60}$ |       |       |       | To reflect an annualised rate of 60 months average protection       |
| Suppression of reactivation effect | e     | 70%                 |       |       |       | Whalen et al [21]   |
| Curative effect of PT              | c     | 0%                  |       |       |       | Assumption  |
| PT <i>Rif</i> resistance barrier   | b     | 100%                |       |       |       | Assumption: 6H regimen cannot induce Rif resistance                 |
| <b>Demographics</b>                |       |                     |       |       |       |   |
| Birth rate                         | B     | 0.013               | 0.023 | 0.01  | 0.008 | WHO (GHO) [21]–adjusted to yield annual population growth from 1970 |
| Background mortality rate          | $\mu$ | 0.016               | 0.015 | 0.016 | 0.013 | WHO (GHO)[21], corresponds to mean life expectancy                  |

Table S1 **List of model parameters.** Symbols are as used in the model equations, listed above. Numbers in brackets show 95% uncertainty intervals.