**WEB MATERIALS**

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**Web Figure 1.** Model structure. Flows and compartment descriptions listed in Web Table 1 below.

**Web Appendix 1.**

The system of ordinary differential equations governing the model is given by:

Where:

**Web Table 1. Pre-intervention intercompartment flow rates and their calculations.**

|  |  |  |
| --- | --- | --- |
| **Compartment** | |  |
| *SA* | Fully susceptible, unvaccinated persons, not previously exposed to TB | |
| *SB* | Partially immune persons, either recovered from past active TB or BCG-vaccinated | |
| *LA* | Recently acquired latent infection with DS-TB | |
| *LAm* | Recently acquired latent infection with MDR-TB | |
| *LB* | Latent infection with DS-TB, not recently acquired | |
| *LBm* | Latent infection with MDR-TB, not recently acquired | |
| *I* | Current active DS-TB, not commenced on treatment | |
| *Im* | Current active MDR-TB, not commenced on treatment | |
| *T* | Current active DS-TB, under treatment | |
| *Tm* | Current active MDR-TB, under treatment | |
| **Model parameters** | | **Parameter calculations** |
| *ι* a | BCG vaccination proportion | 0.65 |
| *π* | Birth rate | 29 ÷ 1000 = 0.029 |
| *μ* | Population death rate | 1 ÷ 61.5 = 0.0163 |
| *φ* | Treatment completion rate, DS-TB | 1 ÷ (6/12) = 2 |
| *φm* | Treatment completion rate, MDR-TB | 1 ÷ (24/12) = 0.5 |
| *ε* | Early progression rate | 0.129 ÷ (23/12) = 0.0673 |
| *κ* | Stabilisation rate | (1 – 0.129) ÷ (23/12) = 0.454 |
| *γ* b | Spontaneous recovery rate, smear-positive TB | (1 – 0.7) ÷ 3 = 0.1 |
| *γ* b | Spontaneous recovery rate, smear-negative and extrapulmonary TB | (1 – 0.2) ÷ 3 = 0.267 |
| *ν* | Late progression rate | 0.375 ÷ 100 = 0.00375 |
| *η* | Proportion amplifying to MDR-TB after default | 3.5 ÷ 100 = 0.035 |
| *ω* a | Default from treatment rate, both strains | (10, 15 or 20) ÷ 100 ÷ (6/12)  = 0.2, 0.3 or 0.4 |
| *δ* a | Treatment commencement rate, DS-TB | 0.7 ÷ 3 ÷ (1 – 0.7) = 0.778 |
| *δm* a | Treatment commencement rate, MDR-TB | 0 |
| *μi* b | Untreated mortality rate, smear-positive TB | 0.7 ÷ 3 = 0.233 |
| *μi* b | Untreated mortality rate, smear-negative and extrapulmonary TB | 0.2 ÷ 3 = 0.0667 |
| *μt­* b | Treated mortality rate, smear-positive TB | 0.7 ÷ 3 × 0.5 = 0.117 |
| *μt­* b | Treated mortality rate, smear-negative and extrapulmonary TB | 0.2 ÷ 3 × 0.5 = 0.0333 |
| *β*a | Effective contact rate | 25 |
| *ζ* | Relative fitness of MDR-TB | 0.7 |
| *ρ* a | Proportion smear-positive | 0.4 |
| *τ* | Proportion smear-negative, pulmonary | 0.378 |
| *θ* | Relative infectiousness of smear-negative TB | 0.24 |
| *ο* | Relative infectiousness under treatment, DS-TB | 0.02 |
| *οm* | Relative infectiousness under treatment, MDR-TB | 0.18 |
| *χ* | Protection from partial immunity | 0.49 |

TB, tuberculosis; BCG, Bacille Calmette-Guérin; MDR-TB, multidrug-resistant tuberculosis; DS-TB, drug-susceptible tuberculosis. aCalculation presented for median value, which is then varied throughout the uncertainty analysis and constrained by epidemiological outputs. Effective contact rate is effectively constrained by incidence in 2013, while relative fitness of MDR-TB is effectively constrained by year of MDR-TB emergence and proportion of incident cases MDR-TB in 2013.

bWeighted by smear status to obtain single parameter values for μi, μt and γ.

**Web Appendix 2.**

The following matrix describes the proportion of the force of infection for each district contributed by persons from each district incorporated in the model. Rows from top to bottom and columns from left to right are South Fly, Middle Fly, North Fly and the Indonesian Province of Papua.

**Web Table 2. Description and parameterisation of scenarios.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Scenario 1** | **Scenario 2** | **Scenario 3** | **Scenario 4** | **Scenario 5** |
| Pictorial represent-ation | C:\Users\JTrauer\Dropbox\AusAID PNG report\Lancet PNG article\Graphs\wpmapslowres.tif | | | | | |
| PMDT North and Middle Fly | Unchanged, nil | Pilot program,  40 patients on treatmenta | Comprehensive PMDT,  as for South Fly below | | Unchanged, nil |
| Average treatment duration MDR-TB | 24 months | 24 months | 24 months | 10 months | Not applicable |
|  | **Scenario 1** | **Interventions common to Scenarios 2 to 4** | | | **Scenario 5** |
| PMDT  South Fly | Pilot program, 80 patients on treatmenta | Comprehensive PMDT  Case detection rate as for DS-TB   * GeneXpert allows for immediate identification of detected cases as MDR-TB | | | Unchanged, nil |
| Programm-atic response (other than PMDT) | Passive case finding with single added GeneXpert in Daru (capital of Western Province) | Expanded support for TB program across Province  via improvements in BMU capacity  Support for MCH activities  to improve BCG vaccination proportion  Support for patients on treatment  through improved human resources, drug supply chain and record keeping  Intensified case finding at health facilities and through contacts of TB patients | | | Unchanged |
| BCG coverage | Unchanged | Coverage increases by 10% from baseline proportionb | | | Unchanged |
| Case detection rate South Fly | Small increase (~3%), due to detection of smear-negative TBc | Case detection rate increases, so that proportion of cases missed decreases by 60% from baseline (i.e. case detection rate increases from *x* to *x*+(1-*x*)×0.6) | | | Unchanged |
| Case detection rate Middle and North Fly | Unchanged | As for South Fly case detection rate above | | | Unchanged |
| Average default rated | 15% | 7.5% | | | 15% |
| PMDT, programmatic management of drug-resistant tuberculosis; BMU, basic management unit; MCH, maternal and child health; BCG, bacille Calmette-Guérin; DS-TB, drug-susceptible tuberculosis; MDR-TB, multidrug resistant tuberculosis; unchanged, pre-2013 values carried forward.  aCase detection rate falls from target value to zero as total number of patients on treatment approaches target value.  bAs BCG coverage is a variable parameter in the uncertainty analysis, if this value exceeds 90% at 2013, a ceiling value is placed at 100%.  cCase detection rate increases according to the proportion of smear-negative patients at 2013 multiplied by the 68% estimated sensitivity of GeneXpert for smear-negative TB.(61)  dAverage default rate over six months of treatment. Varies by district, with rates remaining fixed to a constant ratio between districts. | | | | | | |

**Web Table 3. Treatment regimens used for economic analysis.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Regimen** | **Medication** | **Strength** | **Doses per day** |
| Drug-susceptible TB, continuation phase | RH FDC | 150/75mg | 4 adult,  3 paediatric |
| Drug-susceptible TB, intensive phase | RHZE FDC | 150/75/400/275mg | 4 adult,  3 paediatric |
| Standard MDR-TB regimen,  continuation phase | Pyrazinamide | 400mg | 4 adult,  3 paediatric |
| Levofloxacin | 250mg | 3 all patients |
| Ethionamide | 250mg | 3 adult,  2 paediatric |
| Cycloserine | 250mg | 3 adult,  2 paediatric |
| Standard MDR-TB regimen,  additional medication for intensive phasea | Kanamycin | 1000mg | 1 adult,  ½ paediatric |
| Short MDR-TB regimen,  continuation phase | Pyrazinamide | 400mg | 4 adult,  3 paediatric |
| Gatifloxacin | 400mg | 2 all patients |
| Ethambutol | 800mg | 2 adult,  1 paediatric |
| Clofazamine | 100mg | 1 all patients |
| Short MDR-TB regimen,  additional medications for intensive phasea | Kanamycin | 1000mg | 1 adult,  ½ paediatric |
| Ethionamide | 250mg | 3 adult,  2 paediatric |
| Isoniazidb | 300mg | 2 adult,  1½ paediatric |

The frequency of administration of all medications is daily. FDC, fixed dose combination; RH, rifampicin/isoniazid; RHZE, rifampicin/isoniazid/pyrazinamide/ethambutol.

aAll medications in continuation phase of both MDR-TB regimens are also used throughout the intensive phase.

bNote higher isoniazid dosage than that standardly used for treatment of drug-susceptible TB.

**Web Table 4. Medication costs per dosage used in economic analysis.**

|  |  |  |
| --- | --- | --- |
| **Drug** | **Strength** | **Cost per dose** |
| RH FDC | 150/75mg | 0.068 K |
| RHZE FDC | 150/75/400/275mg | 0.136 K |
| Pyrazinamide | 400mg | 0.038 K |
| Levofloxacin | 250mg | 0.118 K |
| Ethionamide | 250mg | 0.156 K |
| Cycloserine | 250mg | 1.269 K |
| Kanamycina | 1000mg | 5.547 K |
| Pyrazinamide | 400mg | 0.038 K |
| Gatifloxacin | 400mg | 0.280 K |
| Ethambutol | 800mg | 0.072 K |
| Clofazamine | 100mg | 3.074 K |
| Prothionamide | 250mg | 0.251 K |
| Isoniazid | 300mg | 0.016 K |

FDC, fixed dose combination; RH, rifampicin/isoniazid; RHZE, rifampicin/isoniazid/pyrazinamide/ethambutol.

aKanamycin is cost per ampoule, all other medications are costs per tablet.

**Web Table 5. Daily medication cost of treatment (derived from Web Tables 3 and 4).**

|  |  |
| --- | --- |
| **Treatment phase** | **Cost per day of treatment** |
| Drug-susceptible TB, intensive phase | 0.544 K |
| Drug-susceptible TB, continuation phase | 0.271 K |
| Standard MDR-TB, intensive phase | 10.325 K |
| Standard MDR-TB, continuation phase | 4.778 K |
| Short course MDR-TB, intensive phase | 10.260 K |
| Short course MDR-TB, continuation phase | 3.928 K |

**Web Table 6. Other unit and Scenario costs.**

|  |  |
| --- | --- |
| **Unit** | **2011 unit cost** |
| BCG vaccination | 0.22K |
| Overnight hospital stay | 189.9K (inflated from 85K in 1995) |
| Incentive payments | 100K |
| GeneXpert module (4-cartridge device) | 41,280K |
| GeneXpert cartridge | 36.12K |
| **Additional costs common to Scenarios 2 to 4** | **Total cost** |
| Furnishing BMUs with all equipment required for comprehensive DOTS-based care | 100,000K |
| Building works and physical infrastructure improvements | 500,000K |
| Communications and reporting infrastructure improvements | 65,000K |
| Employment for BMU-based TB Community Workers  (to provide intensified case finding activities, etc.) | 400,000K |
| Additional monthly incentive payments to TB Community Workers | 300,000K |
| Employment costs for hospital TB/HIV Medical Officer | 250,000K |
| Employment costs for three district TB Coordinators | 300,000K |
| **Additional costs common to Scenarios 3 and 4** | **Total cost** |
| Staff training | 150,000K |
| Infection control equipment | 50,000K |
| Logistic support for transfer of sputum specimens | 150,000K |

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**Web Table 7. Economic results under alternative economic assumptions (using same epidemiological outputs)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cost** | **Scenario 1** | **Scenario 2** | **Scenario 3** | **Scenario 4** | **Scenario 5** |
| **Revised costs under 3% per annum discounting rate (of both costs and health outcomes)** | | | | | |
| Cumulative cases | 10.0 | 8.0 | 6.8 | 6.7 | 10.6 |
| Thousands | (8.2-12.9) | (6.5-10.3) | (5.9-8.1) | (5.9-8.0) | (8.8-13.6) |
| Cumulative deaths | 2.1 | 1.5 | 0.9 | 0.9 | 2.4 |
| Thousands | (1.4-2.8) | (0.8-1.9) | (0.6-1.2) | (0.5-1.1) | (1.6-3.1) |
| DS-TB drug regimen costs  Million Kina | 0.45 | 0.46 | 0.47 | 0.47 | 0.44 |
| (0.35-0.56) | (0.35-0.57) | (0.36-0.58) | (0.36-0.58) | (0.34-0.56) |
| MDR-TB drug regimen costs  Million Kina | 1.1 | 2.0 | 6.4 | 3.3 | 0 |
| (0.9-1.3) | (0.4-4.3) | (1.3-13.2) | (0.7-6.8) | (0-0) |
| Hospitalisation costs  Million Kina | 28.5 | 30.5 | 46.9 | 70.4 | 23.5 |
| (22.1-35.3) | (19.2-44.6) | (23.1-77.7) | (27.9-126.3) | (18.0-29.6) |
| Program costs  Thousand Kina | 0 | 1915 | 2065 | 2065 | 0 |
|  |  |  |  |  |
| Total costs  Million Kina | 30.0 | 34.8 | 55.8 | 76.2 | 23.9 |
| (23.3-37.3) | (21.9-51.3) | (26.9-93.6) | (31.0-136.7) | (18.3-30.1) |
| **Revised costs under the assumption of 100K per night hospitalisation cost (0% discounting)** | | | | | |
| Cumulative cases | 11.7 | 9.1 | 7.9 | 7.9 | 12.6 |
| Thousands | (9.5-15.0) | (7.4-11.8) | (6.7-9.2) | (6.7-9.1) | (10.3-15.9) |
| Cumulative deaths | 2.3 | 1.5 | 1.0 | 0.9 | 2.6 |
| Thousands | (1.6-3.3) | (0.9-2.2) | (0.7-1.3) | (0.6-1.2) | (1.9-3.6) |
| DS-TB drug regimen costs  Million Kina | 0.55 | 0.55 | 0.56 | 0.56 | 0.54 |
| (0.42-0.68) | (0.42-0.68) | (0.43-0.69) | (0.43-0.70) | (0.41-0.68) |
| MDR-TB drug regimen costs  Million Kina | 1.4 | 2.5 | 7.8 | 3.9 | 0 |
| (1.1-1.6) | (0.5-5.2) | (1.6-16.2) | (0.8-8.2) | (0-0) |
| Hospitalisation costs  Million Kina | 18.2 | 19.3 | 29.9 | 44.4 | 15.0 |
| (14.1-22.7) | (12.1-28.3) | (14.6-49.7) | (17.4-79.8) | (11.5-18.9) |
| Program costs  Thousand Kina | 0 | 1915 | 2065 | 2065 | 0 |
|  |  |  |  |  |
| Total costs  Million Kina | 20.1 | 24.2 | 40.3 | 51.0 | 15.6 |
| (15.6-25.0) | (14.9-36.1) | (18.6-68.6) | (20.7-90.8) | (11.9-19.6) |
| **Revised costs under two month hospitalisation period for short course regimen** | | | | | |
| Cumulative cases | 11.7 | 9.1 | 7.9 | 7.9 | 12.6 |
| Thousands | (9.5-15.0) | (7.4-11.8) | (6.7-9.2) | (6.7-9.1) | (10.3-15.9) |
| Cumulative deaths | 2.3 | 1.5 | 1.0 | 0.9 | 2.6 |
| Thousands | (1.6-3.3) | (0.9-2.2) | (0.7-1.3) | (0.6-1.2) | (1.9-3.6) |
| DS-TB drug regimen costs  Million Kina | 0.55 | 0.55 | 0.56 | 0.56 | 0.54 |
| (0.42-0.68) | (0.42-0.68) | (0.43-0.69) | (0.43-0.70) | (0.41-0.68) |
| MDR-TB drug regimen costs  Million Kina | 1.4 | 2.5 | 7.8 | 3.9 | 0 |
| (1.1-1.6) | (0.5-5.2) | (1.6-16.2) | (0.8-8.2) | (0-0) |
| Hospitalisation costs  Million Kina | 34.1 | 36.6 | 56.5 | 52.5 | 27.8 |
| (26.1-43.0) | (22.6-55.0) | (27.3-96.4) | (26.7-85.3) | (21.0-36.9) |
| Program costs  Thousand Kina | 0 | 1915 | 2065 | 2065 | 0 |
|  |  |  |  |  |
| Total costs  Million Kina | 36.5 | 41.5 | 67.1 | 59.6 | 29.1 |
| (28.3-45.3) | (25.8-61.6) | (31.7-113.3) | (30.0-96.3) | (22.2-36.6) |

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**Web Figure 2.** Accepted parameter sets by model run.

β, per capita effective contact rate; MDR, proportion of incident cases attributable to multidrug-resistant tuberculosis; relative fitness MDR, relative infectiousness of multidrug resistant TB by comparison to drug-susceptible TB; MDR introduction, calendar year that multidrug-resistant TB first emerges; BCG coverage, proportion of births vaccinated with bacille Calmette-Guérin. Horizontal axis, model run iteration. Vertical axis runs from lower limit to upper limit of prior distribution (or lower limit of confidence interval for incidence and MDR proportion in first two upper panels). Horizontal grey bar, starting parameter value. Horizontal red bar, mean parameter value from all accepted parameter sets.

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**Web Figure 3.** Histograms of accepted parameter values.

β, per capita effective contact rate; MDR, proportion of incident cases attributable to multidrug-resistant tuberculosis; relative fitness MDR, relative infectiousness of multidrug resistant TB by comparison to drug-susceptible TB; MDR introduction, calendar year that multidrug-resistant TB first emerges; BCG coverage, proportion of births vaccinated with Bacille Calmette-Guérin. Grey lines show shape of prior distributions (not to scale).

61. **Steingart KR, Sohn H, Schiller I, Kloda LA, Boehme CC, Pai M, et al.** Xpert(R) MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane Database Syst Rev. 2013;1:CD009593.