# Appendix

## 1. Cost Calculations

**Table A: Cost of contact tracing, per contact traced ($C_0$), † indicated costs which were inflated to the base year 2016. HRG = healthcare resource group, IGRA = Interferon Gamma Release Assay, NHS = National Health Service, NICE = National Institute for Health & Care Excellence, TB = tuberculosis.**

| Item | Quantity | Unit costs (£) | Total costs, including uprating (£) | Reference |
|---|---|---|---|---|
| **TB specialist nurse - non face to face (HRG code N28AN)** | 1 | 21.10 | 21.10 | NHS Reference costs 2015-2016[31] |
| **TB specialist nurse - face to face (HRG code N28AF)** | 2 | 61.93 | 123.86 | NHS Reference costs 2015-2016[31] |
| **Mantoux skin test†** | 1 | 1.22 | 1.32 | NICE[32,33] |
| **IGRA blood test†** | 0.5 | 56 | 30.21 | Pareek et al.[33,34] |
| **Outpatient appointment for IGRA positive (HRG code WF02B)** | 0.25 | 239.83 | 59.96 | NHS Reference costs 2015-2016[31] |
| **Chest X-ray (to rule out active disease)†** | 0.25 | 28 | 8.04 | NICE[33,35] |
| **Per contact traced** | | | **244** | |

**Table B: Further tests if case is suspected to have active disease, per contact with suspected TB ($C_1$), † indicated costs which were inflate. HRG = healthcare resource group, NHS = National Health Service, NICE = National Institute for Health & Care Excellence, TB = tuberculosis.**

| Item | Quantity | Unit costs (£) | Total costs, including uprating (£) | Reference |
|---|---|---|---|---|
| **TB specialist nurse - face to face (HRG code N28AF)** | 3 | 61.93 | 185.78 | NHS Reference costs 2015-2016[31] |
| **Outpatient appointment for diagnosis (HRG code WF02B)** | 1 | 239.83 | 239.83 | NHS Reference costs 2015-2016[31] |
| **Chest X-ray†** | 1 | 28 | 32.17 | NICE[33,35] |
| **Sputum smear microscopy†** | 1 | 1.56 | 1.83 | Dowdy[33,36] |
| **Culture and MDR identification†** | 1 | 30 | 36.37 | Dinnes[33,37] |
| **Liver function test (HRG code DAPS04)** | 1 | 1.18 | 1.18 | NHS Reference costs 2015-2016[31] |
| **Per contact with suspected TB** | | | **497** | |

**Table C: Cost per full course PT (3 month rifampicin and isoniazid with pyridoxine) ($C_{PT}$) . BNF = British National Formulary, HRG = healthcare resource group, NHS = National Health Service, PT = preventive therapy.**

| Item | Quantity (pack-size if applicable) | Unit costs (£) | Total costs (£) | Reference |
|---|---|---|---|---|
| **Follow-up appointments nurse only (HRG code N28AF)** | 3 | 91.93 | 185.78 | NHS Reference costs 2015-2016[31] |
| **Follow-up appointments nurse & consultant (HRG code WF02A)** | 2 | 188.50 | 377 | NHS Reference costs 2015-2016[31] |
| **Isoniazid 300mg daily, 3 months** | 10 (28) | 19.24 | 192.40 | BNF 2017[11] |
| **Rifampicin 600mg daily, 3 months** | 4 (60) | 21.98 | 87.92 | BNF 2017[11] |
| **B6 pyridoxine 10mg tablets (per month)** | 1 (500) | 8.48 | 8.48 | BNF 2017[11] |
| **Per person completing treatment** | | | **852** | |

**Table D: Cost per full course of treatment for tuberculosis disease ($C_{FT}$), * assuming 15% do not complete treatment, after an average of 2 months. BNF = British National Formulary, HRG = healthcare resource group, IGRA = Interferon Gamma Release Assay, NHS = National Health Service, NICE = National Institute for Health & Care Excellence, TB = tuberculosis.**

| Item | Quantity (pack-size if applicable) | Unit costs (£) | Total costs (£) | Reference |
|---|---|---|---|---|
| **Admission (weighted average of HRG codes DZ14F, DZ14G, DZ14H, DZ14J, DZ51Z)** | 0.05 | 3904.16 | 195.21 | NHS Reference costs 2015-2016[31] |
| **Follow-up appointments nurse only (HRG code N28AF)** | 5 | 61.93 | 309.64 | NHS Reference costs 2015-2016[31] |
| **Follow-up appointments nurse & consultant (HRG code WF02A)** | 2 | 188.50 | 942.51 | NHS Reference costs 2015-2016[31] |
| **Rifater (R,I ,P) 120mg, 50mg, 300mg (Sanofi, 100 tabs) 6 tablets daily for 2 months** | 4 (100) | 26.34 | 105.36 | BNF 2017[11] |
| **Ethambutol hydrochloride (solo) 400mg (non-proprietary, 56 tabs) 3 tabs daily for 2 months** | 4 (56) | 42.74 | 170.96 | BNF 2017[11] |
| **Rifinah (R,I) 300/150 (Sanofi, 56 tabs) 2 tab daily for 4 months** | 5 (56) | 25.22 | 126.10 | BNF 2017[11] |
| **Pyridoxine B6 (solo) 10mg (non-proprietary, 500 tabs) 1 tab daily for 6 months** | 1 (500) | 8.48 | 8.48 | BNF 2017[11] |
| **Per person starting treatment*** | | | **1694** | |

**Comment on inflation of costs:** Cost values taken from past years were inflated to 2016 according to consumer price inflation[33].

**Comment on quantities:** Unless stated otherwise, estimated quantities for items other than drugs or NHS reference costs were taken from Mears et al.[12], who based the average estimates on standard treatment protocols, informed by expert judgement.

**Comment regarding tariff costs:** Using NHS tariff costs appeared to give higher costs for hospital admission than did the reference costs, and so the use of these costs was not further explored.

**Comment regarding sensitivity and uncertainty of costs:** We did not vary costs when calculating uncertainty, or in the sensitivity analyses, because the standard errors in the costs were very small relative to the standard errors in other parameters. We estimated the standard deviation of costs from the mean cost and quartile costs using the approach of Wan et al.[38]. We then calculated the standard error using the sample size in the NHS reference costs. For example, the unit cost for a TB specialist nurse (non-face to face) was £21.10 (see above), the lower and upper quartiles are £15.36 and £28.77, and the sample size is 53742. The approach referred to above calculates the standard deviation as £9.94, and hence the standard error is £0.04, or less than 0.5% of the cost.

## 2. Data tables

**Table E: Number of cases in each category and the respective mean symptomatic period (in days), with information on missing data. Note slightly different exclusion criteria used for each of the final three columns, hence the final two columns do not align exactly eih the first columns. See Cavany et al.[6] for details of exclusion criteria. CT = Contact tracing, s.e. = standard error**

| | All cases | Pulmonary or Laryngeal index | Non-pulmonary and non-laryngeal index |
|---|---|---|---|
| **Total number of cases in study period** | 11174 | 5084 | 6090 |
| **Total number included after applying exclusion criteria (% is of all cases in study period)** | 5509 (49%) | 2758 (54%) | 2897 (48%) |
| **With data on symptomatic period (% is of all those included)** | 4906 (89%) | 2465 (89%) | 2559 (88%) |
| **Found through CT (% is of all those included)** | 142 (2.6%) | 113 (4.1%) | 41 (1.4%) |
| **With data on symptomatic period (% is of all those included & found through CT)** | 102 (72%) | 82 (73%) | 26 (63%) |
| **Found through other routes (% is of all those included)** | 5367 (97%) | 2645 (96%) | 2856 (99%) |
| **With data on symptomatic period (% is of all those included & found through other routes)** | 4804 (90%) | 2383 (90%) | 2533 (89%) |
| **Mean symptomatic period , all cases (days)** | 147 [s.e. = 4.26] | 109 [s.e. = 3.55] | 180 [s.e. = 7.36] |
| **Mean symptomatic period if found through CT (days)** | 97.6 [s.e. = 19.3] | 76.6 [s.e. = 9.26] | 152 [s.e. = 69.9] |
| **Mean symptomatic period if found through other routes (days)** | 148 [s.e. = 4.33] | 110 [s.e. = 3.66] | 180 [s.e. = 7.41] |

**Table F: Break down of the number of LTBI cases starting and completing preventive therapy by disease type of the index. Note that different cases were included for the three categories (as the exclusion criteria were applied independently to each category), hence the lack of agreement. See Cavany et al.[6] for details of exclusion criteria. Cases found through contact tracing are excluded as their contact tracing results are not reported consistently. LTBI = latent *M.Tb* infection, PT = preventive therapy, s.e.=standard error.**

| | All cases found through routes other than contact tracing |
|---|---|
| **Number of index cases included and with data on PT** | 5367 (55%) |
| **Pulmonary/Laryngeal included** | 2645 (55%) |
| **Non-pulmonary & non-laryngeal included** | 2856 (56%) |
| **Mean number of contacts with LTBI per index** | 0.279 [s.e. = 0.0114] |
| **Pulmonary/Laryngeal** | 0.471 [s.e. = 0.0219] |
| **Non-pulmonary & non-laryngeal** | 0.119 [s.e. = 0.00395] |

| | |
|---|---|
| **Mean number of contacts starting PT per index** | 0.217 [s.e. = 0.00939] |
| **Pulmonary/Laryngeal** | 0.366 [s.e. = 0.0178] |
| **Non-pulmonary & non-laryngeal** | 0.0907 [s.e. = 0.00668] |
| **Mean number of contacts completing PT per index** | 0.171 [s.e. = 0.00819] |
| **Pulmonary/Laryngeal** | 0.289 [s.e. = 0.0157] |
| **Non-pulmonary & non-laryngeal** | 0.0683 [s.e. = 0.0219] |

**Table G: Break down of the proportion of contacts with LTBI starting and completing preventive therapy by disease type of the index and age of the contact. LTBI = latent *M.Tb* infection, PT = preventive therapy, s.e.=standard error. Child refers to ages 0-14 and adult to 15 and above.**

| | All contacts | Adult contacts | Child contacts |
|---|---|---|---|
| **Proportion of those with LTBI that start PT** | 0.778 [s.e. = 0.0147] | 0.655 [s.e. = 0.0279] | 0.962 [s.e. = 0.0231] |
| **Pulmonary/laryngeal** | 0.776 [s.e. = 0.0168] | 0.666 [s.e. = 0.0318] | 0.969 [s.e. = 0.0238] |
| **Non-pulmonary & non-laryngeal** | 0.762 [s.e. = 0.0274] | 0.611 [s.e. = 0.0515] | 0.931 [s.e. = 0.0477] |
| **Proportion of those who start PT that complete PT** | 0.786 [s.e. = 0.0164] | 0.822 [s.e. = 0.0266] | 0.917 [s.e. = 0.0245] |
| **Pulmonary/Laryngeal** | 0.790 [s.e. = 0.0186] | 0.803 [s.e. = 0.0310] | 0.906 [s.e. = 0.0311] |
| **Non-pulmonary & non-laryngeal** | 0.753 [s.e. = 0.0319] | 0.875 [s.e. = 0.0420] | 0.810 [s.e. = 0.0876] |

## 3. Equations

We use the following equations to quantify the ICER:

1. The prevention of subsequent generations of cases is calculated as follows. We say each prevented case would have generated

$$F = (1 - \epsilon_\sigma) S_{P,\text{overall}} r P$$

cases, and each of those prevented cases would have generated $F$ cases etc. Hence, taking the limit of this sum, we find that

$$N_{\text{later generations},\sigma} = \frac{\left(N_{\text{prevention},\,\sigma} + N_{\text{transmission},\,\sigma}\right) F}{1 - F}$$

2. The costs are calculated in the following ways:

The costs of screening contacts (note that contacts with TB are excluded from the second part of the equation, as we assume they will ultimately be diagnosed anyway):

$$\text{cost}_{\text{screening},\,\sigma} = N_\sigma \left( n_\sigma C_0 + Y_\sigma C_1 \left( \frac{1}{f_c} - 1 \right) \right)$$

The costs of administering preventive therapy to contacts, including those who begin but do not complete preventive therapy, and deducting costs of cases which do not occur. Costs are assumed to be incurred at a constant rate:

$$\text{cost}_{\text{preventive therapy},\,\sigma} = N_\sigma C_{\text{PT}} D \sum_{j=a,c} y_\sigma \phi_{\sigma,j} \theta_{j,\sigma,B} \left( \theta_{j,\sigma,C} + \left(1 - \theta_{j,\sigma,C}\right) f_i \right) - N_{\text{prevention},\,\sigma} (C_1 + C_{\text{FT}})$$

The costs saved by preventing transmission from contacts and stopping transmission from prevented cases:

$$\text{cost}_{\text{transmission},\,\sigma} = -(C_1 + C_{\text{FT}}) \left( N_{\text{transmission},\,\sigma} + N_{\text{later generations},\,\sigma} \right)$$

3. The effectiveness measured in QALYs is calculated as follows:

The QALYs gained by finding cases sooner:

$$\text{QALY}_{\text{morbidity},\,\sigma} = (U_H - U| \quad |0) t_{\text{morbidity},\,\sigma}$$

The QALYs gained for each case prevented is:

$$\text{QALY}_{\text{extra case}} = (U_H - U| \quad |0)\frac{S_{\text{overall}}}{365.25} + \frac{6(U_H - U_1)}{12}$$

The QALYs gained by administering preventive therapy to contacts with latent infection (the number of QALYs gained by preventing cases by preventive therapy), and subtracting QALYs lost from three months of preventive therapy:

$$\begin{aligned}\text{QALY}_{\text{prevention, }\sigma} &= N_{\text{prevention, }\sigma}\text{QALY}_{\text{extra case}} \\ &- \frac{3N_\sigma(U_{\text{H}} - U| \quad |\text{PT})}{12}\sum_{j=a,c} y_{j,\sigma}\theta_{j,\sigma,B}\left(\theta_{j,\sigma,C} + \left(1 - \theta_{j,\sigma,C}\right)f_i\right)\end{aligned}$$

The QALYs gained by reducing transmission from contacts with TB:

$$\text{QALY}_{\text{transmission, }\sigma} = \left(N_{\text{transmission, }\sigma} + N_{later_{generations},\sigma}\right)\text{QALY}_{\text{extra case}}$$

The QALYs gained by reducing the number of deaths:

$$\text{QALY}_{\text{mortality, }\sigma} = \left(N_{\text{mortality, }\sigma} - N_{\text{later generations, }\sigma}\right)\mu(A_H - A_{TB})$$

4. Putting all this together we get an incremental cost effectiveness ratio (ICER) per QALY gained, using no screening as the baseline, of

$$\text{ICER}_\sigma = \frac{\text{cost}_{\text{screening, }\sigma} + \text{cost}_{\text{preventive therapy, }\sigma} + \text{cost}_{\text{transmission, }\sigma}}{\text{QALY}_{\text{morbidity, }\sigma} + \text{QALY}_{\text{prevention, }\sigma} + \text{QALY}_{\text{transmission, }\sigma} + \text{QALY}_{\text{mortality, }\sigma}}$$

Note that the ICER is independent of the number of index cases ($N$) as this appears once in each term on the numerator and denominator

## 4. Styblo Rule

Given that in London 45% of PTB cases are smear positive(21), and assuming that smear negative PTB cases are 0.22 times as infectious as smear positive PTB cases(22), if each PTB case is symptomatic for 0.3 years , then a value of $r = 1$ (or each PTB case generates 12 infections per year) means that each smear positive case equates to about 6.3 new infections.

Let $r_+$ be the number of new infections per PTB smear positive case per month infectious (and recall that $r$ is the number of new infections per PTB case per month infectious), $p_+$ the proportion of PTB cases that are smear positive, and $\rho_-$ be the relative infectiousness of smear negative cases (estimated as 0.22[19]). Then $r = r_{+p_{++r_{+\rho_-}}}$, or rearranging, $r_{+=\frac{r}{p_{++\rho_-}}}$.

Then, with $p_{+=0.45}$ and $\rho_{-=0.22}$, with $S_{P,\text{overall}} = 0.3$ years, we find that $r = 1$ corresponds to each smear positive case generating $r_{+S_{P,\text{overall}}=6.3}$ infections. This is broadly in line with the two re-estimations of the Styblo rule[16,17], although it is at the upper end of the ranges found in those studies.

## 5. Discounting

Whilst discounting was not included in the main analysis, we explored the potential impact of including discounting in a rudimentary fashion, using the following approach. First, we calculate a discounting factor, $D$, by assuming new cases occur after infection according to the distribution given in Sloot et al.[13] , and assume all those with infection have been recently infected. We then discount cases which occur after the first year at a rate of 3.5% per year and 1.5% per year (as recommended by NICE[21]). Finally we multiply those costs and QALYs which occur in the future by this factor $D$ (i.e. costs and QALYs associated with mortality and cases prevented through reduced transmission and preventive therapy). As most cases develop disease in the first year using this approach, this equated to multiplying the total number of QALYs and costs gained/incurred from these cases by $D = 0.987$ for a rate of 3.5%/year and $D = 0.994$ for a rate of 1.5%/year.

For example, we calculate the discounting factor for a 3.5% per year rate of discounting according to Table H. Column 2 is taken from Sloot et al. and shows the cumulative risk of developing disease by year, and column 3 the yearly risk. The fourth column indicates the factor by which we should discount costs and QALYs occurring this year, calculated as $\frac{1}{(1+0.035)^{\text{year}-1}}$, so that cases in the first year are undiscounted. The final column is then the discounted risk in the given year, i.e. the product of columns three and four. The discounting factor is then the cumulate discounted risk (sum of last column) divided by the cumulative undiscounted risk (sum of third column).

**Table H: Calculating the discounting factor, see text for explanation. The discounting factor is the ratio of the sum of the final column to the sum of the third column**

| Year | Cumulative risk of developing disease | Risk of developing disease this year | Discount cases in this year by a factor of… | Discounted risk this year |
|---|---|---|---|---|
| **1** | 0.083005 | 0.083005 | 1 | 0.083005 |
| **2** | 0.094874 | 0.011869 | 0.985222 | 0.011694 |
| **3** | 0.096503 | 0.001629 | 0.970662 | 0.001581 |
| **4** | 0.096503 | 0 | 0.956317 | 0 |
| **5** | 0.096503 | 0 | 0.942184 | 0 |
| **6** | 0.096503 | 0 | 0.92826 | 0 |
| **7** | 0.099067 | 0.002564 | 0.914542 | 0.002345 |
| **8** | 0.099067 | 0 | 0.901027 | 0 |
| **9** | 0.099067 | 0 | 0.887711 | 0 |
| **10** | 0.099067 | 0 | 0.874592 | 0 |
| **11** | 0.099067 | 0 | 0.861667 | 0 |
| **12+** | 0.1 | 0.000933 | 0.848933 | 0.000792 |

The following two tables show results when discounting is set to 3.5%/year, and 1.5%/year. As most cases occur in the first year, which is undiscounted, discounting has little impact on results.

**Table 1: Summary of the effectiveness measures included, costs incurred, quality adjusted life years(QALYs) gained and resulting incremental cost effectiveness ratio (ICER) for screening contacts of the indicated index cases compared to a baseline of not screening those contacts, with a discounting rate of 3.5%/year. Numbers are given for a year with a case-load that is the average caseload of the years 2012-15 (i.e. 2790 cases); note that the case-load does not affect the ICER. Case-equivalents averted refers to both cases averted, and the reduction in the time contacts are symptomatic divided by the mean symptomatic period of TB cases. ETB = non-pulmonary, non-laryngeal; PTB = pulmonary or laryngeal; $r$ = the number of infections generated by a pulmonary contact per month infectious; ICER = incremental cost-effectiveness ratio; PT = preventive therapy (3 months of isoniazid and rifampicin). Numbers in brackets indicate the 95% confidence intervals. Discounting makes little difference to the ICER in this analysis.**

| Quantity (units, if applicable) | ETB indexes | | | PTB indexes | | |
|---|---|---|---|---|---|---|
| | $r = 0$ | $r = 1$ | $r = 2$ | $r = 0$ | $r = 1$ | $r = 2$ |
| **Reduction in time contacts are symptomatic (years)** | | 2.58 [0.665, 8.78] | | | 10.5 [4.0, 27.0] | |
| **Cases prevented by administering PT (cases)** | | 5.45 [3.72, 7.59] | | | 18.9 [13.2, 25.5] | |
| **Transmission reduced by finding contacts sooner (cases)** | 0.0 [0.0, 0.0] | 1.71 [0.591, 3.31] | 3.41 [1.16, 6.62] | 0.0 [0.0, 0.0] | 8.76 [3.54, 14.9] | 17.5 [7.08, 29.7] |
| **Transmission reduced from prevented cases (cases)** | 0.0 [0.0, 0.0] | 1.62 [0.754, 3.13] | 5.19 [2.11, 12.2] | 0.0 [0.0, 0.0] | 8.63 [4.73, 14.8] | 33.1 [16.0, 66.7] |
| **Reduction in mortality (deaths)** | 0.431 [0.239, 1.0] | 0.551 [0.307, 1.15] | 0.743 [0.399, 1.44] | 1.64 [0.999, 3.15] | 2.27 [1.38, 3.89] | 3.47 [2.02, 5.89] |
| **Total case-equivalents averted** | 11.9 [6.58, 27.6] | 15.2 [8.44, 31.7] | 20.5 [11.0, 39.8] | 45.0 [27.5, 86.9] | 62.4 [37.9, 107.0] | 95.6 [55.6, 162.0] |
| **Total QALYs gained** | 10.4 [5.93, 23.7] | 13.5 [7.65, 27.3] | 18.4 [9.96, 35.2] | 39.4 [24.5, 74.6] | 55.5 [34.0, 94.0] | 86.0 [50.2, 146.0] |
| **Total costs incurred (£ 000 000s)** | 1.07 [1.03, 1.12] | 1.06 [1.02, 1.11] | 1.05 [1.01, 1.1] | 1.75 [1.67, 1.82] | 1.71 [1.63, 1.78] | 1.64 [1.53, 1.73] |
| **Incremental cost-effectiveness ratio (£ 000s/QALY)** | 103.0 [45.6, 179.0] | 78.8 [39.2, 138.0] | 57.4 [29.9, 107.0] | 44.2 [23.5, 71.1] | 30.8 [18.1, 50.7] | 19.0 [10.7, 33.4] |

**Table J: Summary of the effectiveness measures included, costs incurred, quality adjusted life years(QALYs) gained and resulting incremental cost effectiveness ratio (ICER) for screening contacts of the indicated index cases compared to a baseline of not screening those contacts, with a discounting rate of 1.5%/year. Numbers are given for a year with a case-load that is the average caseload of the years 2012-15 (i.e. 2790 cases); note that the case-load does not affect the ICER. Case-equivalents averted refers to both cases averted, and the reduction in the time contacts are symptomatic divided by the mean symptomatic period of TB cases. ETB = non-pulmonary, non-laryngeal; PTB = pulmonary or laryngeal; $r$ = the number of infections generated by a pulmonary contact per month infectious; ICER = incremental cost-effectiveness ratio; PT = preventive therapy (3 months of isoniazid and rifampicin). Numbers in brackets indicate the 95% confidence intervals. Discounting makes little difference to the ICER in this analysis.**

| Quantity (units, if applicable) | ETB indexes | | | PTB indexes | | |
|---|---|---|---|---|---|---|
| | $r = 0$ | $r = 1$ | $r = 2$ | $r = 0$ | $r = 1$ | $r = 2$ |
| **Reduction in time contacts are symptomatic (years)** | | 2.58 [0.683, 8.93] | | | 10.5 [4.02, 26.8] | |
| **Cases prevented by administering PT (cases)** | | 5.45 [3.73, 7.61] | | | 18.9 [13.3, 25.8] | |
| **Transmission reduced by finding contacts sooner (cases)** | 0.0 [0.0, 0.0] | 1.71 [0.569, 3.29] | 3.41 [1.16, 6.68] | 0.0 [0.0, 0.0] | 8.76 [3.4, 14.8] | 17.5 [7.02, 29.7] |
| **Transmission reduced from prevented cases (cases)** | 0.0 [0.0, 0.0] | 1.62 [0.765, 3.11] | 5.19 [2.12, 12.3] | 0.0 [0.0, 0.0] | 8.63 [4.81, 14.6] | 33.1 [15.8, 66.7] |
| **Reduction in mortality (deaths)** | 0.431 [0.24, 1.0] | 0.551 [0.307, 1.14] | 0.743 [0.399, 1.43] | 1.64 [1.01, 3.13] | 2.27 [1.38, 3.88] | 3.47 [2.02, 5.82] |
| **Total case-equivalents averted** | 11.9 [6.61, 27.7] | 15.2 [8.46, 31.5] | 20.5 [11.0, 39.3] | 45.0 [27.9, 86.3] | 62.4 [38.1, 107.0] | 95.6 [55.7, 160.0] |
| **Total QALYs gained** | 10.5 [5.98, 23.9] | 13.6 [7.68, 27.4] | 18.5 [10.1, 35.1] | 39.7 [24.9, 74.6] | 55.9 [34.5, 94.1] | 86.8 [50.9, 145.0] |
| **Total costs incurred (£ 000 000s)** | 1.07 [1.03, 1.12] | 1.06 [1.02, 1.11] | 1.05 [1.01, 1.1] | 1.75 [1.68, 1.82] | 1.71 [1.64, 1.78] | 1.64 [1.52, 1.73] |
| **Incremental cost-effectiveness ratio (£ 000s/QALY)** | 102.0 [45.3, 177.0] | 78.2 [39.1, 138.0] | 56.9 [29.8, 105.0] | 43.9 [23.4, 69.9] | 30.5 [18.1, 49.7] | 18.8 [10.7, 33.1] |

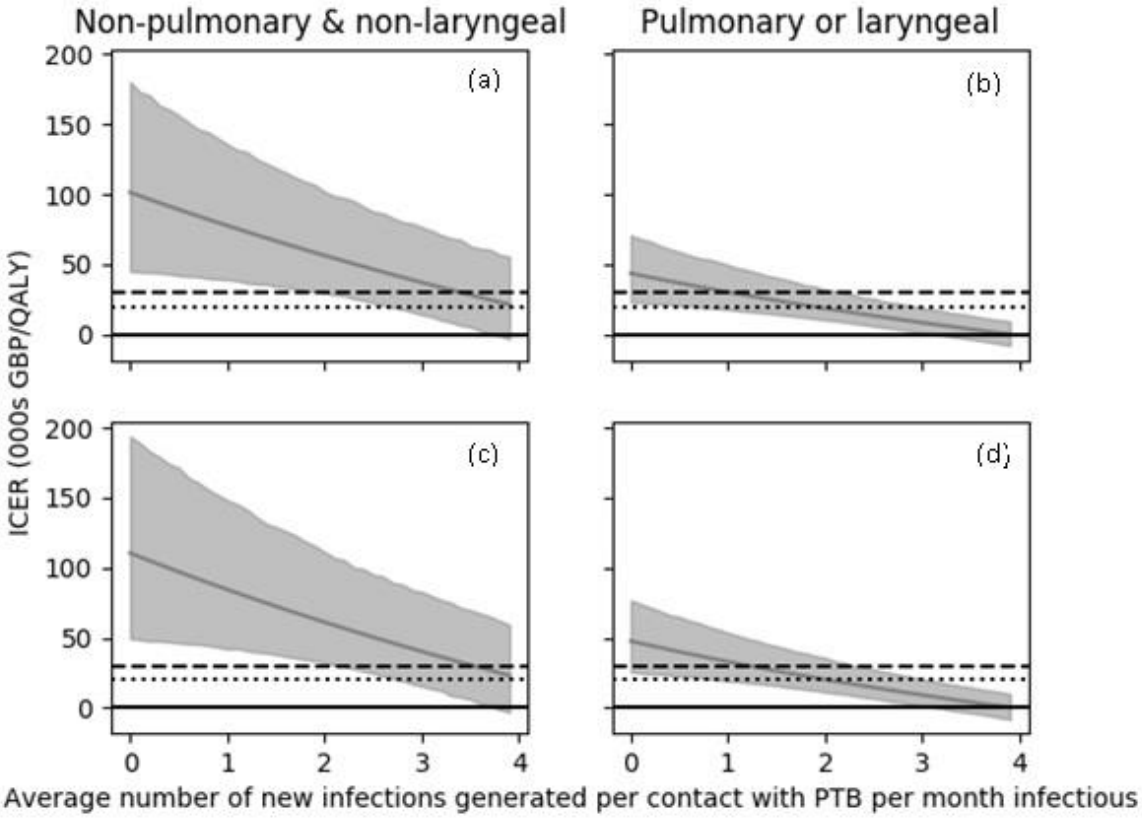
## 6. Utility Calculations

**Table K: This table shows how we calculate the number of quality adjusted life years (QALYs) accrued at death by someone who does not have tuberculosis, and the number accrued by someone who dies prematurely from TB. The case fatality ratio (CFR), life expectancy (LE) and utilities are taken from Mears et al.[12], the population estimates are taken from Office for National Statistics[30], and the caseloads are taken from the London TB register. The final three columns are calculated. The QALYs at this LE is calculated by summing the age-specific healthy utilities up until the gender-specific life-expectancy given in that row. From these columns we can calculate the values of $A_H = 72.4$ and $A_{TB} = 52.1$ given in Mears et al.**

| Age | CFR (%) | LE (men) | LE (women) | Utility with no TB | Male population, 2015 | Female population, 2015 | Cases in London , 2015 | QALYs/year up to this age | QALYs at this LE (men) | QALYs at this LE (women) |
|---|---|---|---|---|---|---|---|---|---|---|
| **0-4** | 0.3 | 78 | 82.1 | 0.94 | 324,404 | 308,866 | 254 | 0.94 | 69.83 | 72.7 |
| **5-9** | 0.2 | 73.5 | 77.5 | 0.94 | 289,083 | 276,855 | 177 | 0.94 | 70.18 | 72.98 |
| **10-14** | 0.2 | 68.5 | 72.5 | 0.94 | 241,496 | 231,172 | 347 | 0.94 | 70.18 | 72.98 |
| **15-19** | 1.2 | 63.5 | 67.6 | 0.94 | 240,789 | 227,381 | 890 | 0.94 | 70.18 | 73.05 |
| **20-24** | 1.2 | 58.7 | 62.6 | 0.94 | 284,353 | 290,053 | 2152 | 0.94 | 70.32 | 73.05 |
| **25-29** | 1.2 | 53.9 | 57.7 | 0.94 | 410,745 | 421,885 | 3040 | 0.94 | 70.46 | 73.12 |
| **30-34** | 1.2 | 49 | 52.8 | 0.91 | 441,020 | 420,357 | 2670 | 0.938 | 70.53 | 73.19 |
| **35-39** | 1.2 | 44.3 | 47.9 | 0.91 | 378,059 | 358,584 | 1995 | 0.934 | 70.74 | 73.26 |
| **40-44** | 1.2 | 39.6 | 43.1 | 0.88 | 319,017 | 308,709 | 1522 | 0.929 | 70.95 | 73.37 |
| **45-49** | 4.8 | 34.9 | 38.3 | 0.86 | 293,289 | 296,029 | 1323 | 0.923 | 71.16 | 73.5 |
| **50-54** | 4.8 | 30.3 | 33.6 | 0.83 | 261,918 | 271,143 | 1019 | 0.915 | 71.44 | 73.695 |
| **55-59** | 4.8 | 25.9 | 29.1 | 0.82 | 213,163 | 219,039 | 840 | 0.908 | 71.86 | 74.02 |
| **60-64** | 4.8 | 21.7 | 24.6 | 0.81 | 166,398 | 178,540 | 659 | 0.900 | 72.42 | 74.345 |
| **65-69** | 17.6 | 17.7 | 20.4 | 0.8 | 147,623 | 163,020 | 527 | 0.893 | 73.12 | 74.865 |
| **70-74** | 17.6 | 14.1 | 16.4 | 0.78 | 103,809 | 121,884 | 481 | 0.886 | 74.02 | 75.515 |
| **75-79** | 17.6 | 10.8 | 12.6 | 0.75 | 85,856 | 103,614 | 382 | 0.878 | 75.125 | 76.295 |
| **80-84** | 17.6 | 8 | 9.4 | 0.7 | 59,937 | 79,369 | 242 | 0.869 | 76.555 | 77.465 |
| **85-89** | 17.6 | 5.8 | 6.7 | 0.65 | 32,967 | 52,762 | 138 | 0.858 | 78.375 | 78.96 |
| **90-** | 17.6 | 4.2 | 4.6 | 0.65 | 15,586 | 34,939 | 43 | 0.846 | 80.585 | 80.845 |

In order to calculate $A_H$ from this table, we take the product of the "Population" and "QALYs at this LE" columns, divided by the total population, to get the QALYs at death for both men and women. We then take the sum of these, weighted by the population of each group to get $A_H$. To calculate $A_{TB}$, we take the product of the "CFR", "Cases in

London" and "QALYS/year up to this age" columns and the midpoint of the age ranges, and divide by the product of the "Cases in London" and "QALYS/year up to this age" columns




142

143 **Figure 1: Summary of incremental cost-effectiveness ratios and 95% confidence intervals (shaded region)**
144 **for different levels of transmission from contacts if we use utility scores given in Mears et al. (c and d) as**
145 **opposed to Jit et al. (a and b) The comparator is no screening. The dashed horizontal line indicates the**
146 **£30000/QALY cost-effectiveness threshold and the dotted horizontal line the £20000/QALY threshold.**
147 **The solid horizontal line indicates when contact tracing becomes cost-saving. GBP = pounds sterling, ETB**
148 **= non-pulmonary, non-laryngeal tuberculosis, PTB = pulmonary or laryngeal tuberculosis, QALY =**
149 **quality-adjusted life years, ICER = incremental cost-effectiveness ratio**

## 7. Sensitivity of ICER

**Table L: Sensitivity of the ICER to each parameter. The numbers presented are the square of the correlations of each parameter value with the ICER across all 10000 parameter sets. A higher number indicates the given parameter explains a greater proportion of the uncertainty in the ICER. The shading indicates the correlation; deeper shading indicates a higher correlation. $r$ = number of new infections per PTB case per month infectious. ETB = non-pulmonary and non-laryngeal tuberculosis, LTBI = latent *M.Tb* infection, PT = preventive therapy, PTB = pulmonary or laryngeal tuberculosis, QALY = quality-adjusted life years, ICER = incremental cost-effectiveness ratio.**

| | r=0 | | r=1 | | r=2 | |
|---|---|---|---|---|---|---|
| | ETB indexes | PTB indexes | ETB indexes | PTB indexes | ETB indexes | PTB indexes |
| Number of contacts screened, ETB index | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Number of contacts screened, PTB index | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Yield of active tuberculosis, ETB index | 0.05 | 0.00 | 0.08 | 0.00 | 0.09 | 0.00 |
| Yield of active tuberculosis, PTB index | 0.00 | 0.02 | 0.00 | 0.02 | 0.00 | 0.02 |
| Proportion of contacts with ETB, ETB index | 0.00 | 0.00 | 0.03 | 0.00 | 0.11 | 0.00 |
| Proportion of contacts with ETB, PTB index | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 | 0.02 |
| Yield of LTBI, ETB index | 0.00 | 0.00 | 0.01 | 0.00 | 0.00 | 0.00 |
| Yield of LTBI, PTB index | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Probability of starting PT, ETB index, adult contact | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Probability of ending PT, ETB index, adult contact | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Probability of starting PT, PTB index, adult contact | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Probability of ending PT, PTB index, adult contact | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Probability of starting PT, ETB index, adult contact | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Probability of ending PT, ETB index, adult contact | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Probability of starting PT, PTB index, adult contact | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Probability of ending PT, PTB index, adult contact | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Efficacy of PT, adult | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| Efficacy of PT, child | 0.02 | 0.03 | 0.03 | 0.04 | 0.02 | 0.03 |
| Probability of developing disease ever | 0.03 | 0.03 | 0.07 | 0.12 | 0.13 | 0.28 |
| Symptomatic period, passively detected PTB cases | 0.01 | 0.03 | 0.01 | 0.04 | 0.02 | 0.05 |
| Symptomatic period, contact traced PTB cases | 0.06 | 0.16 | 0.11 | 0.26 | 0.14 | 0.31 |
| Symptomatic period, PTB cases | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Symptomatic period, passively detected ETB cases | 0.01 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Symptomatic period, contact traced ETB cases | 0.60 | 0.56 | 0.48 | 0.38 | 0.30 | 0.15 |
| Symptomatic period, passively detected cases | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |

## 8. Pleural TB

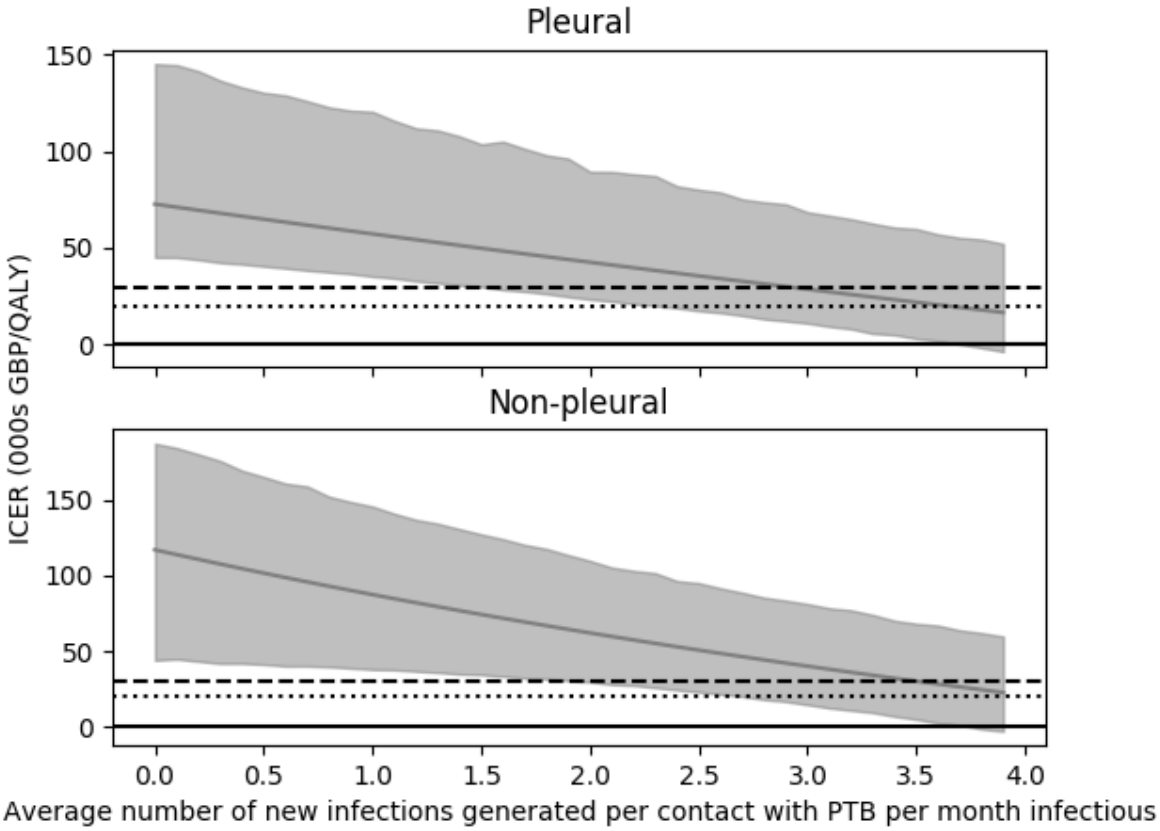



**Figure 2: Summary of incremental cost-effectiveness ratios and 95% confidence intervals (shaded region) for different levels of transmission from contacts of cases with pleural (but non-pulmonary and non-laryngeal) TB (upper panel) and with non-pleural, non-laryngeal, non-pulmonary TB (bottom panel). The comparator is no screening. The dashed horizontal line indicates the £30000/QALY cost-effectiveness threshold and the dotted horizontal line the £20000/QALY threshold. The solid horizontal line indicates when contact tracing becomes cost-saving. GBP = pounds sterling, ETB = non-pulmonary, non-laryngeal tuberculosis, PTB = pulmonary or laryngeal tuberculosis, QALY = quality-adjusted life years, ICER = incremental cost-effectiveness ratio**

## 9. UK born versus non-UK born

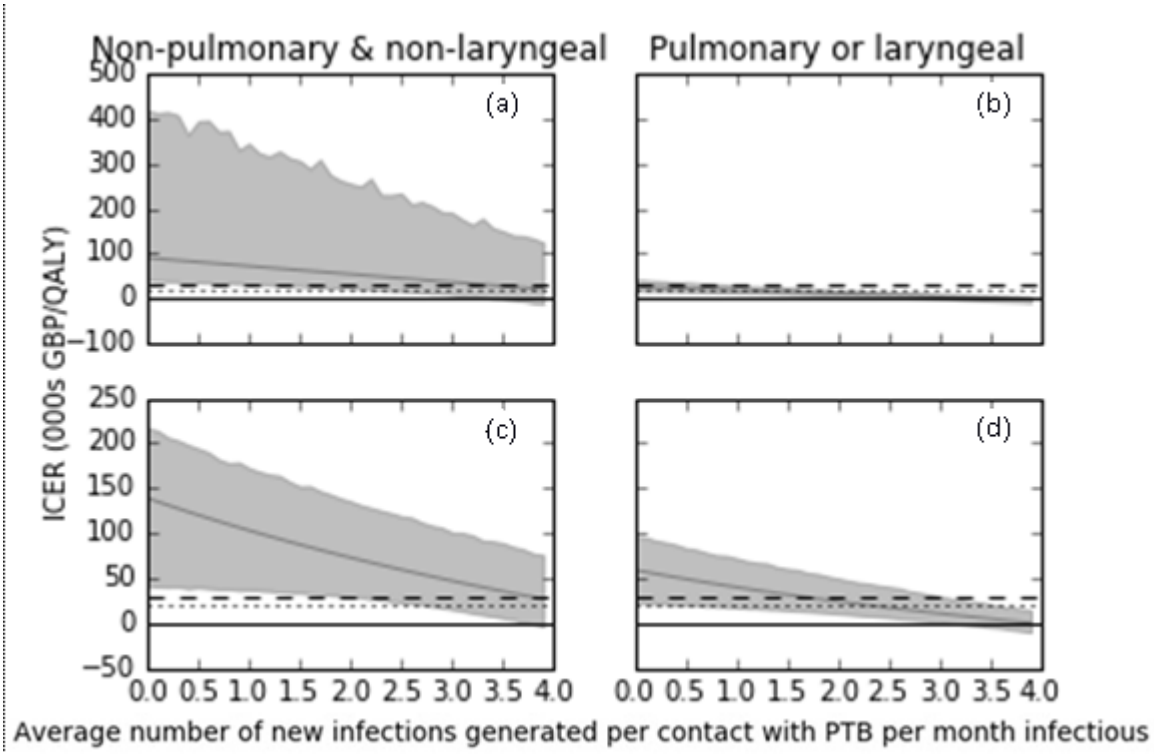



**Figure 3: Summary of incremental cost-effectiveness ratios and 95% confidence intervals (shaded region) for different levels of transmission from contacts of UK-born cases (a and b) and of non-UK born cases (c and d) The comparator is no screening. The dashed horizontal line indicates the £30000/QALY cost-effectiveness threshold and the dotted horizontal line the £20000/QALY threshold. The solid horizontal line indicates when contact tracing becomes cost-saving. GBP = pounds sterling, ETB = non-pulmonary, non-laryngeal tuberculosis, PTB = pulmonary or laryngeal tuberculosis, QALY = quality-adjusted life years, ICER = incremental cost-effectiveness ratio**

Table M: Estimates of parameters calculated from the LTBR for UK born cases. All parameters are chosen from a normal distribution. Parameters which are not different between UK born and non-UK born are not included in this table. ETB = non-pulmonary and non-laryngeal tuberculosis, PTB=Pulmonary or laryngeal tuberculosis. LTBI = latent M.Tb infection, LTBR = London TB report, PT = preventive therapy, TB = tuberculosis

| Name of variable (units, if applicable) | Index case disease type | Symbol | Value | 95% Confidence intervals |
|---|---|---|---|---|
| **Number of contacts screened per index case** | ETB | $n_E$ | 2.82 | [2.52, 3.13] |
| | PTB | $n_P$ | 4.18 | [3.86, 4.50] |
| **Number of contacts found with TB per index case** | ETB | $Y_E$ | 0.0124 | [0, 0.027] |
| | PTB | $Y_P$ | 0.0920 | [0.0589, 0.125] |
| **Number of contacts found with LTBI per index case** | ETB | $y_E$ | 0.0870 | [0.0496, 0.124] |
| | PTB | $y_P$ | 0.446 | [0.360, 0.532] |
| **Proportion of contacts with LTBI that begin PT, adult contact** | ETB | $\theta_{a,E,B}$ | 0.606 | [0.500, 0.711] |
| | PTB | $\theta_{a,P,B}$ | 0.684 | [0.567, 0.801] |
| **Proportion of contacts starting PT that complete PT, adult contact** | ETB | $\theta_{a,E,C}$ | 0.881 | [0.798, 0.965] |
| | PTB | $\theta_{a,P,C}$ | 0.784 | [0.641, 0.927] |
| **Mean symptomatic period of PTB cases not found through contact tracing (days)** | N/a | $S_{P,\text{passive}}$ | 116 | [103, 128] |
| **Mean symptomatic period of PTB cases found through contact tracing (days)** | N/a | $S_{P,\text{traced}}$ | 55.2 | [35.2, 75.2] |
| **Mean symptomatic period of PTB cases (days)** | N/a | $S_{P,\text{overall}}$ | 113 | [101, 125] |
| **Mean symptomatic period of ETB cases not found through contact tracing (days)** | N/a | $S_{E,\text{passive}}$ | 173 | [136, 210] |
| **Mean symptomatic period of ETB cases found through contact tracing (days)** | N/a | $S_{E,\text{traced}}$ | 78.3 | [8.42, 148] |
| **Mean symptomatic period of all cases (days)** | N/a | $S_{\text{overall}}$ | 136 | [120, 152] |

183

184 **Table N: Estimates of parameters calculated from the LTBR for non-UK born cases. All parameters are chosen from a normal distribution. Parameters which are not different between UK**
185 **born and non-UK born are not included in this table. ETB = non-pulmonary and non-laryngeal tuberculosis, PTB=Pulmonary or laryngeal tuberculosis. LTBI = latent M.Tb infection, LTBR =**
186 **London TB report, PT = preventive therapy, TB = tuberculosis**

| Name of variable (units, if applicable) | Index case disease type | Symbol | Value | 95% Confidence intervals |
|---|---|---|---|---|
| **Number of contacts screened per index case** | ETB | $n_E$ | 2.46 | [2.36, 2.55] |
| | PTB | $n_P$ | 3.77 | [3.61, 3.93] |
| **Number of contacts found with TB per index case** | ETB | $Y_E$ | 0.0206 | [0.0120, 0.0291] |
| | PTB | $Y_P$ | 0.0945 | [0.0756, 0.113] |
| **Number of contacts found with LTBI per index case** | ETB | $y_E$ | 0.123 | [0.107, 0.140] |
| | PTB | $y_P$ | 0.479 | [0.430, 0.528] |
| **Proportion of contacts with LTBI that begin PT, adult contact** | ETB | $\theta_{a,E,B}$ | 0.606 | [0.500, 0.711] |
| | PTB | $\theta_{a,P,B}$ | 0.662 | [0.592, 0.732] |
| **Proportion of contacts starting PT that complete PT, adult contact** | ETB | $\theta_{a,E,C}$ | 0.881 | [0.798, 0.965] |
| | PTB | $\theta_{a,P,C}$ | 0.807 | [0.740, 0.873] |
| **Mean symptomatic period of PTB cases not found through contact tracing (days)** | N/a | $S_{P,\text{passive}}$ | 109 | [101, 118] |
| **Mean symptomatic period of PTB cases found through contact tracing (days)** | N/a | $S_{P,\text{traced}}$ | 86.5 | [61.9, 111] |
| **Mean symptomatic period of PTB cases (days)** | N/a | $S_{P,\text{overall}}$ | 108 | [100, 117] |
| **Mean symptomatic period of ETB cases not found through contact tracing (days)** | N/a | $S_{E,\text{passive}}$ | 182 | [166, 197] |
| **Mean symptomatic period of ETB cases found through contact tracing (days)** | N/a | $S_{E,\text{traced}}$ | 179 | [0, 364] |
| **Mean symptomatic period of all cases (days)** | N/a | $S_{\text{overall}}$ | 150 | [140, 160] |