### Supplement 4 - Results of the TB contact investigation processes from published studies included in the review

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<thead>
<tr>
<th>Country</th>
<th>Results / conclusions</th>
<th>Author</th>
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| Angola    | . Of the 124 TB contact children studied, active TB was diagnosed in 70 cases (56.5%), including 22 TB-infected (17.7%) and 32 (25.8%) TB-exposed cases.  
. TB-HIV co-infection was diagnosed in 14 children with active TB (20%) and two TB exposed children.  
. Seven per cent of the active TB cases were asymptomatic.  
. Of the 124 children studied, all 14 HIV-infected children died.  
. After six months of follow-up, 7/22 (31.8%) TB-infected children had progressed to active TB, as did 3/32 (9.4%) of the exposed ones. | Fortunato [18]  |
| Guinea-Bissau | . Children < 5 years of age exposed to an adult with intrathoracic TB had 66% higher mortality than unexposed children (HR 1.66, 95% CI 1.2 to 2.3).  
. Higher MR for children living in the same family as a TB case (HR 2.15, 95% CI 1.3 to 3.7) than children living in the same house but not belonging to the same family as the TB case (HR 1.51, 95% CI 1.0 to 2.2).  
. Mortality was increased eightfold (HR 7.82, 95% CI 2.1 to 30) for children whose mothers had TB.  
. The risk of death was particularly increased from 6 months following exposure (HR 2.16, 95% CI 1.5 to 3.2), and the highest rate of excess mortality was found in children aged 3-4 years.  
. Excess mortality was highest among children with close contact with an adult with sputum-positive pulmonary TB (HR 1.90, 95% CI 1.1 to 3.2), but contact with a sputum-negative case was also associated with increased mortality (HR 1.55, 95% CI 1.0 to 2.3).  
. There was a high overall adherence rate to preventive therapy with isoniazid as 79% of the prescribed doses were taken.  
. Of the 820 children enrolled in the study: 21% were lost to follow up, and active TB was diagnosed in two children after 3 and 5 weeks of isoniazid preventive therapy (IPT).  
. Individually, 83% of the children took > 60% of the prescribed doses, while 65% took > 80%.  
. In all, 51% of the children completed more than six consecutive months of IPT.  
. Migration and travelling accounted, respectively, for 41% and 17% of the missed doses.  
. Children aged >5 years old were significantly more likely to be fully adherent than those under five years (P = 0.003). | Gomes [13]  
Gomes [20]  |

Note: TB = tuberculosis; HIV = human immunodeficiency virus; MR = mortality rate; HR = hazard ratio; IPT = isoniazid preventive therapy (to be continued)
Results of the TB contact investigation processes from published studies included in the review (continuation)

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| Guinea-Bissau | . The IPT children had a mortality rate ratio (MRR) of 0.30 (95%CI 0.1 to 1.2) compared with community controls. The MRR comparing exposed children with and without IPT was 0.21 (0.0 to 1.1).  
. The relative mortality in IPT children compared with community controls in 2005–2008 differed significantly from the relative mortality of exposed untreated children compared with the community controls in 1996–1998 (test of interaction, p=0.01).  
. In 2005–2008, exposed children on IPT had 70% lower mortality than the community control children, though not significantly.  
. The 66% excess mortality found for children exposed to TB in 1996-1998 was reduced in the cohort of children receiving IPT from 2005 to 2008.  
. Both MRR of 0.30 among children who received IPT and the overall MRR of 0.71 for all exposed children in the 2005–2008 period were significantly lower than the previously observed MRR of 1.66.  
. Of the 287 children examined, 25 (9%) were reported healthy, while 262 (91%) had at least one symptom at home (mainly cough, fever, chest pain and rhinitis).  
. Overall, the number of children with concomitant HIV infection or AIDS was 9 (3%), while the total number of hospitalized patients was 56 (20%).  
. Tuberculosis was diagnosed in 44 (15%) patients. Of which 35 (80%) pulmonary TB and 12 extrapulmonary TB (3 of them having both pulmonary and extrapulmonary disease).  
. Of the hospitalized children, three patients (7%) died during treatment;  
. Low mortality (7%) was observed among children diagnosed and treated for tuberculosis. | Gomes [14] |
| Bosa [19]     | Patients with pulmonary tuberculosis differed significantly from their household contacts and healthy controls in sociodemographic and anthropometric aspects (except for ethnicity). The prevalence of malnutrition was 5% for household contacts and healthy controls and 51% among patients with pulmonary tuberculosis. | Patsche [15] |

Note: IPT = isoniazid preventive therapy; TB = tuberculosis; HIV = human immunodeficiency virus; AIDS = acquired immunodeficiency syndrome; MRR= mortality rate ratio

(to be continued)
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| Moçambique| . The minimum community-based incidence rate of TB (confirmed\(^1\) plus probable\(^2\) cases) was 470 of 100.000 person-year (95% confidence interval: 343–629 of 100.000) and 135/100.000 person-years (95% CI: 72-232 of 100.000) for confirmed TB cases.\(^3\)  
  . HIV co-infection was present in 44% of the TB cases.  
  . Twenty-one per cent of all presumptive TB cases had a chest x-ray compatible with TB.  
  . Non-TB mycobacteria were isolated in 27% of all cultures of presumptive TB cases.  
  . The percentage of confirmed cases among TB cases was highest for those <1 year (40% vs 29% and 22% among children with 1–2 and 2–3 years, respectively), and statistically significantly lower for HIV–TB coinfected cases (10% vs 44%, P = 0.02).  
  . Confirmed cases appeared to be more symptomatic at enrollment than the probable cases (53.8% vs 15.6% presenting with ≥1 TB symptom, respectively, P < 0.001).  
  . Probable cases had a higher proportion of HIV infection (P = 0.01), positive TST (P = 0.001) or BCG scarring (P = 0.08) when compared with confirmed cases.  
  . HIV-infected children were six times more likely to have TB disease than uninfected ones (odds ratio: 8.4; 95% CI: 4–17).  
  . A total of 217 TB cases aged <3 years were diagnosed in the period 2006–2010, with a pooled incidence rate of 251 per 100000 people (95% CI 227–276 per 100000). During the 2011-2012 period, 57 TB cases aged <3 years initiated anti-TB treatment, equivalent to an incidence rate of 615 per 100000 people (95% CI 466–797 per 100000). The estimated case detection rate (CDR) was 40.8% (95% CI 36.6–45.1%), and 41.8% (95% CI 37.2–46.4%) after correction.  
  . The HIV prevalence among the study population was 47% and 46% during the 2006-2010 and 2011-2012 periods, respectively.  
  . During the 2011-2012 period, fewer patients aged <1year initiated anti-TB treatment (8.8% versus 35.9%), more TB cases were extrapulmonary (12.3% versus 7.4%) and the treatment success rate was significantly better (82.5% versus 67.3%; p=0.025). | López-Varela [17] |

Note: TB = tuberculosis; HIV = human immunodeficiency virus; BCG = Bacille Calmette-Guérin; TST = tuberculin skin test

\(^1\) Confirmed TB cases – children presented compatible symptoms with tuberculosis plus positive culture for *Mycobacterium tuberculosis*.

\(^2\) Probable TB cases – children with (1) compatible symptoms unresolved at last clinical follow-up visit (before any TB treatment initiation) plus (2) compatible CXR (for children with ≥1 CXR, the latter was used given the likelihood of seeing resolving pneumonias) plus (3) at least one of the following: TB exposure, positive TST or positive response to TB treatment.

\(^3\) Presumptive TB cases – children < 3 years of age with compatible TB signs or symptoms.