Supplementary File

Title: “The incidence of tuberculosis and the influence of surveillance strategy on tuberculosis case-finding and all-cause mortality - a cluster randomized trial in Indian neonates vaccinated with bacillus Calmette-Guérin”

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Content:

1. Verbal autopsy questionnaire.
2. Stratified cluster randomization (table).
3. Socioeconomic and clinical characteristics of children admitted on suspicion of tuberculosis (table).
Survey of Deaths – Palamaner, India
Verbal Autopsy Form - 1
NEONATAL DEATH (age: 0--28 days)

Name of Head of Household………………………………………Name of deceased………………………………………

Section 1: General Information

Location
1. Town/ village: Name _______________________________________ Rural (1) / Urban (2) ☐
2. Address ………………………………………………………………………………………………………………………………………
………………………………Pincode……………………………Tel: ……………………………Mobile…………………………

Details of Respondent

2. Name of respondent ______________________________________

3. Relationship of respondent with deceased
   1. Son/ daughter 2. Brother/ sister (>18 years) 3. 
   4. Mother/ father 5. 6. 
   10. Other relative 11. Neighbour/ no relation 99. Unknown

4. Did the respondent live with the deceased during the events that led to death?
   1. Yes 2. No 9. Unknown

5. Respondent’s age (in completed years) _______________________

6. Respondent’s sex
   1. Male 2. Female

7. Respondent’s education
   1. Illiterate 2. Literate without formal education 3. Below primary 
   4. Primary 5. Middle 6. Secondary/ class10 
   7. Hr Sec/Class XII/Pre-univ 8. Graduate and above 9. Other

Details of deceased baby

8. Age __________ days

9. Sex
   1. Male 2. Female

10. Marital status

11. Religion

12. Name of mother of deceased ______________________________________

Details of Death

14. Date of death (yyyy/mm/dd): ____________________________ / __________ / __________

15. Place of death

16. Was the death registered?
   1. Yes 2. No 9. Unknown

17. What did the respondent think this baby died of?
   (Allow the respondent to tell about illness in his/ her own words): ______________________________________
Section 2: Neonatal Death

18A. Did baby die from an injury or accident?
   1. Yes  
   2. No  

18B. If yes, what kind of injury or accident?
   1. Road traffic accident  
   2. Falls  
   3. Fall of objects  
   4. Burns  
   5. Drowning  
   6. Poisoning  
   7. Bite/sting  
   8. Natural disaster  
   9. Homicide/assault  

If baby died of injury or accident  
   Skip to Q41

Details of Mother’s Health (Pregnancy and Delivery)

19. Was baby a single or multiple birth?
   1. Single  
   2. Multiple birth  
   9. Unknown

20. Where was baby born?
   1. Home  
   2. Health facility  
   3. Other  
   9. Unknown

21. Who attended the delivery?
   1. Trained traditional birth attendant  
   2. Untrained traditional birth attendant  
   3. Midwife/nurse  
   4. Allopathic Doctor  
   5. Ayurvedic/Homeopathy/Unani Doctor  
   6. None  
   7. Other  
   9. Unknown

22. How many months long was the pregnancy?

23A. Was there any complication during the pregnancy or during labour?
   1. Yes  
   2. No  

23B. If yes, what complications occurred? (circle all that apply)
   1. Mother had fits  
   2. Excessive bleeding before/during delivery  
   3. Waters broke 1 day or more before contractions started  
   4. Prolonged/difficult labour (12 hours or more)  
   5. Operative delivery  
   6. Child delivered feet first  
   7. Mother ill throughout this period  
   8. Mother had fever  
   9. Other (write in narrative)  
   99. Unknown

24. Did the mother receive 2 doses of tetanus toxoid during pregnancy?
   1. Yes  
   2. No  
   9. Unknown

Details of Baby after Birth

25. Did the baby stop “moving” in the womb before labour?
   1. Yes  
   2. No  
   9. Unknown

26. Were there any bruises or signs of injury on his/her body after the birth?
   1. Yes  
   2. No  
   9. Unknown

27. Did baby have any deformity at birth?
   1. Yes (Write site in narrative)  
   2. No  
   9. Unknown

28. What was his/her size at birth?
   1. Small  
   2. Average  
   3. Larger than average  
   9. Unknown

29A. Did baby cry normally at birth?
   1. Yes  
   2. No  

29B. If yes, did baby stop being able to cry?
   1. Yes  
   2. No  

29C. If yes, how long (days) after birth did baby stop crying?
   1. Yes  
   2. No  

30A. Was baby able to suckle normally after birth?
   1. Yes  
   2. No  
   9. Unknown
30B. If yes, did s/he stop being able to suck in a normal way?
1. Yes    2. No    9. Unknown

30C. If yes, how long (days) after birth did s/he stop sucking?

31. Was there any breathing effort/gasping at birth?
1. Yes    2. No    9. Unknown

Details of Sickness

32. For how many days was baby sick before death?

33A. Did baby have fever?
1. Yes    2. No    9. Unknown

33B. If yes, how many days did the fever last?

34A. Did baby have any difficulty with breathing?
1. Yes    2. No    9. Unknown

34B. If yes, for how many days did the difficulty with breathing last?

35A. Did baby have fast breathing?
1. Yes    2. No    9. Unknown

35B. If yes, for how many days did the fast breathing last?

36. Did baby have in-drawing of the chest?
1. Yes    2. No    9. Unknown

37A. Did baby have cough?
1. Yes    2. No    9. Unknown

37B. If yes, for how many days did the cough last?

38A. Did baby have diarrhoea (use local term)?
1. Yes    2. No    9. Unknown

38B. If yes, for how many days was the diarrhoea (use local term)?

39. Did baby have any vomiting?
1. Yes    2. No    9. Unknown

40. Did baby have redness around, or discharge from, the birth cord stump?
1. Yes    2. No    9. Unknown

41. Did baby have areas of skin that were red, hot or peeling?
1. Yes    2. No    9. Unknown

42. Did baby have a skin rash with blisters containing pus?
1. Yes    2. No    9. Unknown

43. Did baby have yellow eyes or skin?
1. Yes    2. No    9. Unknown

44. Did baby have spasms or fits (convulsions)?
1. Yes    2. No    9. Unknown

45. Did baby become unresponsive or unconscious?
1. Yes    2. No    9. Unknown

46. Did baby have a bulging fontanelle (describe)?
1. Yes    2. No    9. Unknown

47. Did the baby's body feel cold when touched?
1. Yes    2. No    9. Unknown
Section 3: Written Narrative (in Local Language)

Please describe the symptoms in order of appearance, health care services used, and history of similar episodes. Enter the results from reports of the investigations if available.

Section 5: Supporting information

49. Antenatal card (Yes =1; No = 2)
50. Immunization card (Yes =1; No = 2)
51. Investigation slip (Yes =1; No = 2)
52. Prescription(s) (Yes =1; No = 2)
53. Discharge summary (Yes =1; No = 2)
54. Death certificate (Yes =1; No = 2)
55. Tablet strip or medicine container (Yes =1; No = 2)

Name of the Interviewer


Date of Study Consent for cause of death (yyyy/mm/dd): __ __ __ __/ __ __ / __ __
Date of Interview (yyyy/mm/dd): __ __ __ __/ __ __ / __ __

Result: (1) Completed: (2) Respondent Not Available: (3) Refused: (4) Partially Completed
<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Part I</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate cause of death</td>
<td>(a) ........................................................................... <em>due to, or as a consequence of</em></td>
<td></td>
</tr>
<tr>
<td>Antecedent causes, if any, giving rise to the immediate cause (a) above, stating the Underlying Cause last</td>
<td>(b) ........................................................................... <em>due to, or as a consequence of</em></td>
<td></td>
</tr>
<tr>
<td>Part II</td>
<td>II</td>
<td></td>
</tr>
<tr>
<td>Other significant conditions contributing to the death but not causally related to the immediate cause (a) above</td>
<td>....................................................................................</td>
<td></td>
</tr>
</tbody>
</table>

**Underlying Cause of Death (ICD-10)**: .................................................................

**Keywords**: .................................................................................................

**Certainty of Diagnosis**: 1. Definite 2. Possible 3. Probable

**Quality of narrative**: 1. High 2. Medium 3. Low

**Name of the M.O.**: .................................  
**Date of diagnosis**: (yyyy/mm/dd): __ __  __ __/ __ __ / __ __
Supplementary 2. Assignment of Population units to Active and Passive Surveillance based on a matrix of size and level of development, which resulted in 8 different strata. Information relevant to this stratification was based on village level questionnaires that captured information on accessibility (roads and transport), infra-structure including electricity and village level facilities for shopping, education and health care facilities. Each stratum had its own randomization list.

<table>
<thead>
<tr>
<th>Size of the Population units based on population</th>
<th>Small &lt; 500</th>
<th>Medium 500-1000</th>
<th>Large &gt;1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>Passive</td>
<td>Active</td>
<td>Passive</td>
</tr>
<tr>
<td>Rural – Low development</td>
<td>119</td>
<td>119</td>
<td>60</td>
</tr>
<tr>
<td>Rural – High development</td>
<td>32</td>
<td>31</td>
<td>53</td>
</tr>
<tr>
<td>Urban</td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Units by size and type of surveillance</td>
<td>151</td>
<td>150</td>
<td>113</td>
</tr>
<tr>
<td>Surveillance</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>--------------</td>
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</tr>
<tr>
<td></td>
<td>Total (N=746)</td>
<td>Active (N=638)</td>
<td>Passive (N=108)</td>
</tr>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td><strong>Socioeconomic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (min-max)</td>
<td>14.3 (0-36)</td>
<td>13.3 (0-35)</td>
<td>20.3 (0-36)</td>
</tr>
<tr>
<td>St.error</td>
<td>0.24</td>
<td>0.23</td>
<td>0.79</td>
</tr>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough ≥ 2 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>142 (19.1)</td>
<td>128 (20.1)</td>
<td>14 (13.0)</td>
</tr>
<tr>
<td>Fever ≥ 2 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>81 (10.9)</td>
<td>74 (11.6)</td>
<td>7 (6.5)</td>
</tr>
<tr>
<td>Failure to thrive¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>562 (75.7)</td>
<td>505 (79.5)</td>
<td>57 (53.3)</td>
</tr>
<tr>
<td>Known TB exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>95 (12.8)</td>
<td>73 (11.5)</td>
<td>22 (20.4)</td>
</tr>
<tr>
<td>Chest X-ray²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal TB</td>
<td>11 (1.5)</td>
<td>9 (1.4)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Abnormal not TB</td>
<td>20 (2.7)</td>
<td>16 (2.5)</td>
<td>4 (3.7)</td>
</tr>
<tr>
<td>Tuberculin Skin Test (TST) ≥ 10mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>74 (10.3)</td>
<td>39 (6.3)</td>
<td>35 (36.1)</td>
<td></td>
</tr>
<tr>
<td>Weight for age Z score &lt; -2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>354 (50.2)</td>
<td>309 (50.7)</td>
<td>42 (43.8)</td>
</tr>
<tr>
<td>Height for age Z score &lt; -2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stunted</td>
<td>197 (28.0)</td>
<td>162 (26.7)</td>
<td>35 (36.5)</td>
</tr>
<tr>
<td>Weight for Height Z score &lt; -2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malnourished</td>
<td>305 (43.4)</td>
<td>268 (44.2)</td>
<td>37 (38.5)</td>
</tr>
</tbody>
</table>

Data are reported as number and percentages within parenthesis. 3-5% excluded in each analysis due to missing data. *OR and 95%CI estimates (mixed-effects logistic regression) or the regression coefficient with Std.Error and 95%CI estimates (mixed-effects linear regression) of the effect of active surveillance are shown (corrected for cluster-specific random effects and the fixed effects of age in months at the CVW visit, study-closure, gender, religion, father's education and fuel). Significant differences are bolded. ¹Crossing of two percentile lines; plateauing weight across two visits; or sustained growth below the 3rd percentile of weight-for-age on the WHO growth charts. ²Abnormal TB and Abnormal not TB X-rays are not overlapping.
Supplementary 4. Sensitivity analyses: TB case-finding rates by randomisation group.

<table>
<thead>
<tr>
<th>Assumptions</th>
<th>Active surveillance (N=2215)</th>
<th>Passive Surveillance (N=2167)</th>
<th>Active vs passive</th>
<th>Overall (N=4382)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TB cases  py</td>
<td>Case finding rate/100 py (95% CI)</td>
<td>TB cases  py</td>
<td>Case finding rate/100 py (95% CI)</td>
</tr>
<tr>
<td>Participants lost to follow-up do not have TB and are censored at the last visit of contact.</td>
<td>10 4164</td>
<td>2.4 (1.2, 4.4)</td>
<td>3 3997</td>
<td>0.75 (0.15, 2.2)</td>
</tr>
<tr>
<td>Participants lost to follow-up do not have TB and have completed the study.</td>
<td>10 4183</td>
<td>2.4 (1.1, 4.4)</td>
<td>3 4114</td>
<td>0.73 (0.15, 2.1)</td>
</tr>
<tr>
<td>Participants lost to follow-up have TB and length of follow-up as in the primary analysis.</td>
<td>48 4166</td>
<td>11.5 (8.5, 15.3)</td>
<td>63 3998</td>
<td>15.8 (12.1, 20.2)</td>
</tr>
<tr>
<td>Participants lost to follow-up have TB and are censored at the last visit of contact.</td>
<td>48 4164</td>
<td>11.5 (8.5, 15.3)</td>
<td>63 3997</td>
<td>15.8 (12.1, 20.2)</td>
</tr>
<tr>
<td>Participants lost to follow-up have TB and have completed the study.</td>
<td>48 4183</td>
<td>11.5 (8.5, 15.2)</td>
<td>63 4114</td>
<td>15.3 (11.8, 19.6)</td>
</tr>
</tbody>
</table>
Supplementary 5. Causes of death (neonatal and postnatal causes pooled) as distributed within the active and passive surveillance arms.

<table>
<thead>
<tr>
<th>Causes of death</th>
<th>Total (N=4382)</th>
<th>Active (N=2215)</th>
<th>Passive (N=2167)</th>
<th>OR (95%CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of deaths</td>
<td>120 (2.7)</td>
<td>49 (2.2)</td>
<td>71 (3.3)</td>
<td>0.68 (0.47-0.98)</td>
</tr>
<tr>
<td>Intrapartum birth complications/Prematurity/Asphyxia¹</td>
<td>12 (10.9)</td>
<td>5 (10.6)</td>
<td>7 (11.1)</td>
<td>0.68 (0.22-2.16)</td>
</tr>
<tr>
<td>Drowning/Injuries/Poisoning¹</td>
<td>7 (6.4)</td>
<td>2 (4.3)</td>
<td>5 (7.9)</td>
<td>0.37 (0.07-1.94)</td>
</tr>
<tr>
<td>Sepsis¹</td>
<td>8 (7.3)</td>
<td>3 (6.4)</td>
<td>5 (7.9)</td>
<td>0.43 (0.08-2.20)</td>
</tr>
<tr>
<td>Pneumonia/Respiratory infection¹</td>
<td>27 (24.5)</td>
<td>7 (14.9)</td>
<td>20 (31.7)</td>
<td><strong>0.34 (0.14-0.80)</strong></td>
</tr>
<tr>
<td>Gastroenteritis¹</td>
<td>16 (14.5)</td>
<td>10 (21.3)</td>
<td>6 (9.5)</td>
<td>1.66 (0.60-4.59)</td>
</tr>
<tr>
<td>Meningitis/CNS infection¹</td>
<td>11 (10.0)</td>
<td>7 (14.9)</td>
<td>4 (6.3)</td>
<td>1.81 (0.53-6.19)</td>
</tr>
<tr>
<td>Congenital anomalies/non-infectious liver/renal disease/cancer¹</td>
<td>18 (16.4)</td>
<td>9 (19.1)</td>
<td>9 (14.3)</td>
<td>1.05 (0.40-2.73)</td>
</tr>
<tr>
<td>SIDS/non-infectious causes¹</td>
<td>11 (10.0)</td>
<td>4 (8.5)</td>
<td>7 (11.1)</td>
<td>1.03 (0.26-4.14)</td>
</tr>
<tr>
<td>Verbal autopsy data not available</td>
<td>10 (8.3)</td>
<td>2 (4.1)</td>
<td>8 (11.3)</td>
<td>0.27 (0.06-1.28)</td>
</tr>
</tbody>
</table>

Data are reported as number and percentages within parenthesis. *OR and 95%CI estimates (mixed-effects logistic regression) of the effect of active surveillance are shown, corrected for cluster-specific random effects and the fixed effects of gender, religion, and father’s education. Significant differences are bolded. *percentages are calculated based on children with available data from verbal autopsy (N=110).