

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).
4. Sensitivity analyses of TB case-finding rates (table).
5. Causes of death (table).

Name of Head of Household Name of deceased

Section 1: General Information

Unique ID No.

Location

1. **Town/ village:** Name Rural (1) / Urban (2)

Address

.....Pincode.....Tel:Mobile.....

Details of Respondent

2. **Name of respondent**

3. **Relationship of respondent with deceased**

1. <i>Wife/ husband</i>	2. Brother/ sister (>18 years)	3.
4. Mother/ father	5.	6.
7. <i>Brother-in-law /sister-in-law</i>	8. Parent-in-law	9. Grandparent
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
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5. **Respondent's age (in completed years)**

6. **Respondent's sex**

1. Male	2. Female
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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
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10. **Marital status**

11. **Religion**

1. Hindu	2. Muslim	3. Christian	4. Others
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12. **Name of mother of deceased**

Details of Death

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

15. **Place of death**

1. Home	2. Health centre	3. Other place	9. Unknown
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16. **Was the death registered?**

1. Yes	2. No	9. Unknown
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17. **What did the respondent think this baby died of?**
 (Allow the respondent to tell about illness in his/ her own words):

Survey of Deaths – Palamaner, India
Verbal Autopsy Form - 1
NEONATAL DEATH (age: 0--28 days)

Section 2: Neonatal Death

18A. Did baby die from an injury or accident?

1. Yes 2. No → **Skip to Q19** 9. Unknown → **Skip to Q19**

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 | 10. | 11. | 99. Unknown |

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 → **Skip to Q24** 9. Unknown

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 → **Skip to Q30A** 9. Unknown → **Skip to Q30A**

29B. If yes, did baby stop being able to cry?

1. Yes 2. No → **Skip to Q30A** 9. Unknown → **Skip to Q30A**

29C. If yes, how long (days) after birth did baby stop crying?

30A. Was baby able to suckle normally after birth?

1. Yes 2. No **Skip to Q31** 9. Unknown → **Skip to Q31**

NEONATAL DEATH (age: 0--28 days)

30B. If yes, did s/he stop being able to suck in a normal way?

1. Yes

2. No → Skip to Q31

9. Unknown → Skip to Q31

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 → Skip to Q34A

9. Unknown → Skip to Q34A

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

34A. Did baby have any difficulty with breathing?

1. Yes

2. No → Skip to Q35A

9. Unknown → Skip to Q35A

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

35A. Did baby have fast breathing?

1. Yes

2. No → Skip to Q36

9. Unknown → Skip to Q36

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 → Skip to Q38A

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 → Skip to Q39

9. Unknown → Skip to Q39

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

48.

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.

Large empty box with horizontal dotted lines for writing the narrative.

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 -----

Cooperation of the respondent: 1. High 2. Medium 3. Low

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

(this section is to be filled by a trained physician coder)

Medical Certificate of Death																															
Cause of death	<table style="width: 100%; border: none;"> <tr> <td style="width: 15%;">Part I</td> <td style="width: 70%;"></td> <td style="width: 15%; text-align: center;">I</td> </tr> <tr> <td>Immediate cause of death</td> <td>(a)</td> <td></td> </tr> <tr> <td></td> <td style="text-align: center;"><i>due to, or as a consequence of</i></td> <td></td> </tr> <tr> <td>Antecedent causes, if any, giving rise to the immediate cause (a) above, stating the <u>Underlying Cause</u> last</td> <td>(b)</td> <td></td> </tr> <tr> <td></td> <td style="text-align: center;"><i>due to, or as a consequence of</i></td> <td></td> </tr> <tr> <td></td> <td>(c)</td> <td></td> </tr> <tr> <td></td> <td></td> <td style="text-align: center;">II</td> </tr> <tr> <td>Part II</td> <td colspan="2"></td> </tr> <tr> <td>Other significant conditions contributing to the death but not causally related to the immediate cause (a) above</td> <td colspan="2">.....</td> </tr> <tr> <td></td> <td colspan="2">.....</td> </tr> </table>	Part I		I	Immediate cause of death	(a)			<i>due to, or as a consequence of</i>		Antecedent causes, if any, giving rise to the immediate cause (a) above, stating the <u>Underlying Cause</u> last	(b)			<i>due to, or as a consequence of</i>			(c)				II	Part II			Other significant conditions contributing to the death but not causally related to the immediate cause (a) above	
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Underlying Cause of Death (ICD-10) -----	<table border="1" style="border-collapse: collapse; width: 100%; height: 20px;"> <tr> <td style="width: 25%;"></td> <td style="width: 25%;"></td> <td style="width: 25%;"></td> <td style="width: 25%;"></td> </tr> </table>				
Keywords					
Certainty of Diagnosis: 1. Definite 2. Possible 3. Probable	<table border="1" style="border-collapse: collapse; width: 30px; height: 40px;"> <tr> <td style="width: 100%;"></td> </tr> <tr> <td style="width: 100%;"></td> </tr> </table>				
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.

Level of development	Size of the Population units based on population							
	Small < 500		Medium 500-1000		Large >1000			
	Active	Passive	Active	Passive	Active	Passive	Active	Passive
Rural – Low development	119	119	60	59	6	6		
Rural – High development	32	31	53	53	20	22		
Urban					7	5		
Units by size and type of surveillance	151	150	113	112	33	33		

Supplementary 3. Socioeconomic and clinical characteristics of 746 children admitted into the Case verification ward on suspicion of tuberculosis and consenting for per protocol investigations. In total 749 children were admitted. (Data lacking for 3 participants).

	Surveillance			*OR/Estimate (95%CI)
	Total (N=746) n (%)	Active (N=638) n (%)	Passive (N=108) n (%)	
<i>Socioeconomic characteristics</i>				
Age (in months)				
Mean (min-max)	14.3 (0-36)	13.3 (0-35)	20.3 (0-36)	7.31 (6.20-8.42)
St.error	0.24	0.23	0.79	
<i>Clinical characteristics</i>				
Cough \geq 2 weeks				
Yes	142 (19.1)	128 (20.1)	14 (13.0)	0.58 (0.30-1.12)
Fever \geq 2 weeks				
Yes	81 (10.9)	74 (11.6)	7 (6.5)	0.82 (0.36-1.87)
Failure to thrive ¹				
Yes	562 (75.7)	505 (79.5)	57 (53.3)	4.12 (2.52-6.72)
Known TB exposure				
Yes	95 (12.8)	73 (11.5)	22 (20.4)	0.30 (0.17-0.56)
Chest X-ray ²				
Abnormal TB	11 (1.5)	9 (1.4)	2 (1.9)	0.76 (0.14-4.18)
Abnormal not TB	20 (2.7)	16 (2.5)	4 (3.7)	0.25 (0.07-0.87)
Tuberculin Skin Test (TST)				
\geq 10mm	74 (10.3)	39 (6.3)	35 (36.1)	0.26 (0.14-0.48)
Weight for age Z score < -2				
Underweight	354 (50.2)	309 (50.7)	42 (43.8)	0.89 (0.56-1.41)
Height for age Z score < -2				
Stunted	197 (28.0)	162 (26.7)	35 (36.5)	0.91 (0.56-1.47)
Weight for Height Z score < -2				
Malnourished	305 (43.4)	268 (44.2)	37 (38.5)	0.99 (0.62-1.59)

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.

Assumptions	Active surveillance (N=2215)			Passive Surveillance (N=2167)			Active vs passive p-value	Overall (N=4382) Case-finding rate ratio (95% CI)
	TB cases	py	Case finding rate/100 py (95% CI)	TB cases	py	Case finding rate/100 py (95% CI)		
Participants lost to follow-up do not have TB and are censored at the last visit of contact.	10	4164	2.4 (1.2, 4.4)	3	3997	0.75 (0.15, 2.2)	0.06	3.19 (0.82, 18.09)
Participants lost to follow-up do not have TB and have completed the study.	10	4183	2.4 (1.1, 4.4)	3	4114	0.73 (0.15, 2.1)	0.05	3.27 (0.84, 18.53)
Participants lost to follow-up have TB and length of follow-up as in the primary analysis.	48	4166	11.5 (8.5, 15.3)	63	3998	15.8 (12.1, 20.2)	0.1	0.73 (0.49, 1.08)
Participants lost to follow-up have TB and are censored at the last visit of contact.	48	4164	11.5 (8.5, 15.3)	63	3997	15.8 (12.1, 20.2)	0.1	0.73 (0.49, 1.08)
Participants lost to follow-up have TB and have completed the study..	48	4183	11.5 (8.5, 15.2)	63	4114	15.3 (11.8, 19.6)	0.13	0.75 (0.50, 1.11)

Supplementary 5. Causes of death (neonatal and postnatal causes pooled) as distributed within the active and passive surveillance arms.

	Surveillance			OR (95%CI)*
	Total (N=4382)	Active (N=2215)	Passive (N=2167)	
	n(%)	n(%)	n(%)	
<i>Total number of deaths</i>	120 (2.7)	49 (2.2)	71 (3.3)	0.68 (0.47-0.98)
<i>Causes of death</i>				
Intrapartum birth complications/Prematurity/Asphyxia ¹	12 (10.9)	5 (10.6)	7 (11.1)	0.68 (0.22-2.16)
Drowning/Injuries/Poisoning ¹	7 (6.4)	2 (4.3)	5 (7.9)	0.37 (0.07-1.94)
Sepsis ¹	8 (7.3)	3 (6.4)	5 (7.9)	0.43 (0.08-2.20)
Pneumonia/Respiratory infection ¹	27 (24.5)	7 (14.9)	20 (31.7)	0.34 (0.14-0.80)
Gastroenteritis ¹	16 (14.5)	10 (21.3)	6 (9.5)	1.66 (0.60-4.59)
Meningitis/CNS infection ¹	11 (10.0)	7 (14.9)	4 (6.3)	1.81 (0.53-6.19)
Congenital anomalies/non-infectious liver/renal disease/cancer ¹	18 (16.4)	9 (19.1)	9 (14.3)	1.05 (0.40-2.73)
SIDS/non-infectious causes ¹	11 (10.0)	4 (8.5)	7 (11.1)	1.03 (0.26-4.14)
Verbal autopsy data not available	10 (8.3)	2 (4.1)	8 (11.3)	0.27 (0.06-1.28)

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. ¹percentages are calculated based on children with available data from verbal autopsy (N=110).