

## Sensitivity and specificity of BCG scar reading in Brazil

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### SUMMARY

In a cross sectional survey within a community trial of BCG efficacy evaluation in Brazil, trained teams inspected children's upper arms and obtained information on BCG vaccination from guardian letters and vaccination cards. Nurses re-examined the sub-sample of children blindly. High agreement was found between the two scar readings (Kappa = 0.839). High sensitivity and low specificity was observed when guardian or card in-

formation was the gold standard. Sensitivity remained high when guardian and card information agreed. When disagreement occurred, sensitivity remained high and specificity was very low. BCG scar is a good indicator of BCG vaccination.

**KEY WORDS:** validation; sensitivity, specificity, BCG vaccine; BCG scar

ONE OF THE methodological challenges of observational studies of the efficacy of BCG against tuberculosis is the ascertainment of past BCG vaccination.<sup>1</sup> Most studies relied on BCG scar as the main indicator of BCG vaccination, particularly in developing countries,<sup>2-4</sup> reflecting an assumption that scar examination was a valid measure of past BCG vaccination.<sup>2</sup>

BCG usually leads to development of a scar which can be recognised by its aspect and location in the lower insertion of the right deltoid. However, scar reading is not perfect: BCG vaccine can fail to leave a visible scar, the scar can disappear with time, and scars from other causes can look like a BCG scar. Studies have in general found BCG scar reading to be a highly sensitive indicator of BCG vaccination, with sensitivity sometimes varying with age at vaccination and time since vaccination.<sup>2</sup> Other factors assumed to modify sensitivity include vaccine potency, application techniques, and variation in the ability to read scars.

The few studies which have evaluated specificity of BCG scar reading found a range of between 52%<sup>5</sup> and 97%.<sup>6</sup>

This paper reports a validity study of BCG scar reading. This is an important issue because non-differential low sensitivity and specificity would lead to underestimation of vaccine efficacy when scarring is the main indicator of past BCG vaccination.

### MATERIALS AND METHODS

The investigation presented in this paper was conducted as part of an effectiveness trial in Brazil to evaluate the impact of a second BCG dose at school age.<sup>7</sup> Data were collected by a team of 14 interviewers who were trained by two nurses from the Brazilian Ministry of Health Tuberculosis Control Programme and supervised by a graduate nurse. The team visited all the trial's schools, and collected personal data from the school's registry using a standardised form. Letters were sent to all guardians asking whether their children had received BCG (and when), and requesting that they send their children's vaccination card to the school. The children had their right upper arm inspected for a BCG scar. No other areas were examined, as in Brazil vaccination in this site is standard. The scar reading was classified as present (one or two scars), absent, or doubtful. A representative sub-sample from all teams (but also for convenience of access) was selected for repeated reading. Trained nurses, blinded to the first reading and to the information from card and/or letter, re-examined these children. The Kappa coefficient was calculated using standard methods. All children with two doses of BCG on scar reading, vaccination card or guardian information, as well as those with a doubtful scar reading or with impossible information (such as date

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**Table 1** Sensitivity and specificity of scar reading using guardian information or vaccination card as gold standard, Salvador, Brazil, 1996–1997

Scars	Guardian information			Vaccination card		
	1 dose	0 dose	Total	1 dose	0 dose	Total
Present	12 733	1 019	13 752	2 634	155	2 789
Absent	1 318	1 210	2 528	44	51	95
Total	14 051	2 229	16 280	2 678	206	2 884
Sensitivity	90.6% (95%CI 90.2–91.1)			98.4% (95%CI 97.9–98.8)		
Specificity	54.3% (95%CI 52.2–56.4)			24.8% (95%CI 19.0–31.2)		

CI = confidence interval.

of vaccination before date of birth), were excluded. Age was grouped in tertiles. Sensitivity and specificity were estimated using three separate gold standards: guardian information, card information, and agreement between parental and card information.<sup>8</sup>

## RESULTS

A total of 72 926 children had a scar reading. We excluded 39 who had two scars, six who had a doubtful readings, 570 with missing information on scar and 200 with missing information on age. The remaining 72 111 were included in the study: 12 117 (16.8%) had no scar and 59 994 (83.2%) had one scar. Of the children included in the analysis, 18 984 (26.3%) had information from the guardian's letter. We excluded 2592 children because the letters had incomplete data and another 112 because the guardian's letter reported that the child had received two doses of BCG. Only 3155 (4.3%) children presented their vaccination card for examination; of these, 271 were excluded because of incomplete information, leaving 2884 children in the analysis of card data.

The proportions of children with a BCG vaccination were 86.3% and 92.9%, respectively, when guardian information and vaccination card were the information source. The sex distribution and the mean age were similar in these groups.

Repeated reading was performed on 1739 children: agreement in scar reading between supervisor and interviewer was good (Kappa = 0.84,  $P < 0.001$ ).

When guardian information was used as the gold standard, the sensitivity of scar reading was 90.6% (95%CI 90.2–91.1) and the specificity 54.3% (95%CI

52.2–56.4). The sensitivity obtained using the card as the gold standard was 98.4% (95%CI 97.9–98.8) and the specificity was 24.8% (95%CI 19.0–31.2) (Table 1).

Table 2 shows a total of 1705 records that have information from both guardian and vaccination card. The specificity of scar reading varied substantially depending on whether there was agreement between the card and the guardian. Specificity was high (84.6%) in children described by both guardian and card as not having received BCG, and very low (20%) when there was disagreement between card and guardian information. Sensitivity was very high (98%) when there was agreement, and remained relatively high (95%) when there was disagreement.

The sensitivity and specificity using either guardian information or card as the gold standard were not substantially different in each of the three age groups, although there was a tendency for the sensitivity to decrease and the specificity to increase with age.

Sensitivity (using card as the gold standard) by age at vaccination was 98.4% when children were vaccinated before 3 months of age, 99.3% when vaccination was between 3 months and one year, and 96.7% when after 1 year. This difference was not statistically significant (data not shown).

## DISCUSSION

This study contributes to our evolving understanding of the validity of BCG reading, and highlights the importance of the choice of the gold standard used.

The high agreement observed between repeated scar readings by different interviewers was reassuring.

**Table 2** Sensitivity and specificity of scar reading combining vaccination card and guardian information as gold standard, Salvador, Brazil, 1996–1997

Scar	Card yes guardian yes	Card yes guardian no	Card no guardian yes	Card no guardian no
Yes	1532	35	73	2
No	32	2	18	11
Sensitivity	98% (95%CI 97.1–98.6)		95% (95%CI 81.8–99.3)	
Specificity	N/A		20% (95%CI 12.2–29.5)	
			84.6% (95%CI 54.6–98.1)	

CI = confidence interval; N/A = not applicable.

ing. We found a high sensitivity of scar reading when using guardian information as a gold standard, and even higher when using vaccination card information. Our sensitivity estimates are as high as those obtained in Chingleput (98.5%).<sup>1,9</sup> This finding is consistent with the quality of the training for vaccination staff in Brazil during the last two decades. The BCG vaccine used in this country is based on the Moreau-Rio de Janeiro strain, confirmed by DNA studies to be biologically close to the Tokyo, Russian and Swedish strains, which are similar to the original BCG strain.<sup>10</sup>

There was a decrease in sensitivity with age at scar reading when the gold standard was guardian information, but not when the gold standard was the vaccination card, suggesting recall bias.

Finally, specificity was low when the card or guardian information was used in isolation, but was very high when the gold standard was agreement between guardian and card. A possible explanation for this is that neither guardian recall nor vaccination card are a good standard in isolation, as both are vulnerable to error: guardians can forget when vaccination was given, and children can receive a vaccine that is not written on the card. The recommendation for avoiding missed opportunities for vaccination is to vaccinate a child that does not have a card, record the vaccination on a new card, and eventually transfer all information to a single card. However, information is frequently not copied to the original card which the guardian may consider the 'real' card. The estimated high specificity when there was agreement between guardian and card suggests that scar reading may be a better indicator of BCG vaccination than either guardian or card information alone, at least in our setting. Unfortunately, in spite of our very large sample size, there were only 13 children in this category, and so we can only raise this as a hypothesis.

Based on the table provided by Fine et al.,<sup>2</sup> a study with sensitivity of 91% and specificity of 54% would provide an efficacy estimate of 50%, when, in fact, the true vaccine efficacy was 90%. However, since very high vaccine efficacy estimates have been reported in different studies in Brazil which used BCG scar reading as evidence of vaccination, it is unlikely that these estimates have been grossly underestimated.<sup>3,4</sup> These findings support the hypothesis that the specificity in this setting is much higher.

In conclusion, a BCG scar appears to be a very

good indicator of past BCG vaccination in this setting, and it is possible that absence of scar may be a better indication of lack of vaccination than guardian recall or vaccination card. BCG scar reading is a safe indicator of BCG history. Further studies of validity of scar reading should not avoid the issue of specificity.

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#### RÉSUMÉ

Il s'agit d'une enquête transversale au sein d'un essai d'évaluation d'efficacité du BCG dans la collectivité au Brésil. Des équipes entraînées ont examiné la partie supérieure des bras des enfants et ont obtenu des informations sur la vaccination par le BCG grâce à des lettres

provenant des tuteurs et aux cartes de vaccination. Des infirmières ont réexaminé à l'aveugle le sous-échantillon d'enfants. Nous avons observé une haute corrélation entre les deux lectures de cicatrice ( $Kappa = 0,839$ ). Si l'on prend comme «gold standard» l'information provenant

des tuteurs ou des cartes, on observe une forte sensibilité et une faible spécificité. La sensibilité persiste en cas d'accord entre les informations provenant du tuteur et

de la carte. En cas de désaccord, la sensibilité reste élevée et la spécificité est très basse. La cicatrice de BCG est un bon indicateur de la vaccination par le BCG.

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#### RESUMEN

Se trata de una encuesta transversal sobre la eficacia de la evaluación del BCG en Brasil. Personal entrenado examinó los antebrazos de los niños y obtuvo información de la vacuna BCG por cartas de los tutores y por las cartillas de vacunación. Las enfermeras reexaminaron subgrupos de niños a ciegas. Se encontró una correlación entre las lecturas de las dos cicatrices ( $Kappa = 0,839$ ). Se observó alta sensibilidad y baja especificidad cuando

la información de los tutores o de las cartillas de vacunación fue el criterio estándar. La sensibilidad permaneció alta cuando la información de los tutores y de las cartillas de vacunación coincidían. Cuando existían discrepancias, la sensibilidad permaneció alta y la especificidad fue muy baja. La cicatriz BCG es un buen indicador de la vacunación BCG.

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