Observational study to estimate the changes in the effectiveness of bacillus Calmette–Guérin (BCG) vaccination with time since vaccination for preventing tuberculosis in the UK

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Scientific summary

BCG effectiveness for TB prevention in UK

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Scientific summary

Background

Until recently, there was no evidence that protection against tuberculosis (TB) by bacillus Calmette–Guérin (BCG) vaccination lasted for > 10 years. In the past few years, studies in Brazil and the USA (in Native Americans) have suggested that protection from BCG vaccination against TB can last for several decades in some populations. These findings were interesting and we conducted this research to add to this body of evidence and to determine its relevance to the UK.

Establishing the duration of protection from BCG vaccination against TB is of relevance given the higher disease risks in young adults and the increase with age in the proportion of TB cases that are pulmonary, the main source of onward transmission. We carried out two case–control studies of the duration of protection of BCG vaccination: one of infant BCG vaccination and one of school-aged BCG vaccination. The studies took advantage of the UK's long-standing universal school-aged BCG vaccination programme and the changes introduced in 2005, when school-aged vaccination was discontinued and the programme of selective vaccination of high-risk (usually ethnic minority) infants was enhanced.

Methods

We carried out two case–control studies in England of cases of TB and population-based control subjects (controls), frequency matched for age. One study involved those in minority ethnic groups who were eligible for infant BCG vaccination 1–19 years earlier. The other involved those who were UK born and white, and who were eligible for school-aged BCG vaccination 10–29 years earlier. TB cases included in both studies were drawn from among those notified in the years 2003–12 to the UK national Enhanced Tuberculosis Surveillance system. Controls were recruited from the community in the areas where sampled cases had arisen. BCG vaccination status was established based on BCG records when available, scar reading (inspection of both arms) and BCG history (recall of vaccination). Information on potential confounders (including demographic and social variables) was collected from cases and controls using face-to-face computer-assisted interviews. We studied vaccine effectiveness as a function of time since vaccination, using a case–cohort analysis based on Cox regression.

Results

In the study of infant BCG vaccination, vaccination status was based on available vaccination records as there was poor concordance between vaccination records and either a history of BCG vaccination or scar reading. For infant vaccination, in the subset with vaccine records, a protective effect was seen for up to 10 years following vaccination [< 5 years since vaccination: vaccine effectiveness (VE) 66%, 95% confidence interval (CI) 12% to 85%; 5–10 years since vaccination: VE 76%, 95% CI 44% to 89%], but there was weak evidence of an effect 10–15 years after vaccination (VE 36%, 95% CI negative to 76%; $p = 0.361$). The analyses of the protective effect of infant BCG vaccination were adjusted for several confounding variables, including birth cohort and ethnicity. Adjusting only for ethnicity, sex and birth cohort, for which there were fewer missing data (on covariates), gave weak evidence of effectiveness (VE 50%, 95% CI negative to 78%; $p = 0.096$) 10–15 years after vaccination. The high infant BCG vaccine uptake in this high-risk ethnic minority study population and the sparsity of vaccine record data in the later periods precluded further assessment. These results may be modified when methods to deal with missing data are further explored.

After school-aged BCG vaccination, a protective effect of 51% (95% CI 21% to 69%) was found 10–15 years after vaccination and a protective effect of 57% (95% CI 33% to 72%) was found 15–20 years after vaccination, beyond which time protection appeared to wane. Ascertainment of vaccination status was based on self-reported history and scar reading.

Conclusions

Although the findings for infant BCG vaccination in a population at high risk for TB are insufficient to conclude that the protection extends beyond 10 years, the evidence is stronger for a moderate protective effect for up to 20 years after school-aged BCG vaccination in the native white population. The findings are consistent with the limited literature available.

This new evidence may be useful when making decisions on TB vaccine programmes (e.g. the timing of the administration of improved TB vaccines, if they become available) and for cost-effectiveness studies.

Methods to deal with missing record data in the infant study could be explored, including the use of scar reading.

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