RESEARCH ARTICLE

BCG Vaccination Reduces Risk of Tuberculosis Infection in Vaccinated Badgers and Unvaccinated Badger Cubs

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Reader Comments (4)

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Substitution of IGRA for less sensitive test format

Posted by bovinetb on **19 Jun 2013** at **09:42 GMT**

I note that in the diagnostics section of the article it says the following,

[START OF EXTRACT]
For our investigation of the direct effects of vaccination, we substituted the IGRA (PPDB – PPDA) results with those from an alternative, less sensitive, test format based on the use of specific M. bovis antigens ESAT-6 and CFP-10, because the performance of the former test may be compromised by BCG vaccination leading to reduced specificity [24], [25].
[END OF EXTRACT]

Would this substitution have resulted in an over-estimate of the impact of vaccination obtained through comparing the proportion of badgers found to be infected in controls and vaccinates given in Table S5 for the IGRA and triple test methods?

No competing interests declared.

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Subject Areas

Vaccination and im…
Infectious disease c…
Tuberculosis
Badgers
Wildlife
Cattle
Bovine tuberculosis
Mycobacterium bovis

RE: Substitution of IGRA (PPDB-PPDA) for less sensitive test format (IGRA, ESAT-6 & CFP-10)

stecarter replied to bovinetb on **20 Jun 2013** at **13:16 GMT**

The interferon gamma release assay based on ESAT-6 & CFP-10 antigens was used to test badgers in both treatment (vaccinated) and control (unvaccinated) groups. Therefore, the reported reduction in incidence of new positive cases among vaccinated badgers compared to unvaccinated badgers is valid.

Table S5 provides details of background prevalence of test-positive animals across the study site but cannot be used to test the effect of vaccination on the incidence of new cases.

Competing interests declared: I am the lead author of this paper.

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RE: RE: Substitution of IGRA (PPDB-PPDA) for less sensitive test format (IGRA, ESAT-6 & CFP-10)

bovinetb replied to stecarter on **20 Jun 2013** at **18:06 GMT**

Thank for you pointing out to me that the same assay was used in both groups.

In this instance I am most interested in how the vaccine will reduce the proportion of infected badgers in a real unscreened population containing both infected and uninfected individuals since this is what the vaccine is being used on when it is deployed. I am assuming (perhaps wrongly) that the numbers in Table S5 can be used to estimate this (subject to errors introduced by small sample size) by comparing the proportions in the vaccinates and controls for each year.

No competing interests declared.

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RE: RE: RE: Substitution of IGRA (PPDB-PPDA) for less sensitive test format (IGRA, ESAT-6 & CFP-10)

bovinetb replied to bovinetb on **20 Jun 2013** at **18:24 GMT**

I perhaps should also have said that I appreciate that infected badgers will remain infected after vaccination and that the initial proportion of infected badgers at the test site is considered to be very high. This will mean that when the vaccine is applied in other areas of the country the impact of initial infection is likely to be somewhat less. As such any measure obtained by comparing the proportions given in Table S5 will be subject to this unknown together with any other issues which I may have overlooked.

No competing interests declared.

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RE: RE: RE: Substitution of IGRA (PPDB-PPDA) for less sensitive test format (IGRA, ESAT-6 & CFP-10)

stecarter replied to bovinetb on **10 Sep 2013** at **13:53 GMT**

The prevalence estimates in Table S5 cannot be used to estimate the population-level effect of vaccination. The study design whereby some social groups in the population were administered the vaccine and some were not was appropriate for comparing the effect of the vaccine between vaccinated and unvaccinated individuals/groups, but is not appropriate for comparing the effect of vaccination between a vaccinated population and an unvaccinated population. Vaccination is likely to be more effective at reducing the force of infection in a population when deployed at all the accessible social groups in that population. This is how it is currently being deployed in part of Gloucestershire, England (Badger Vaccine Deployment Project) and in the IAA in Wales (IAA Badger Vaccination Project).

Competing interests declared: I am the lead author of this paper.

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RE: RE: RE: RE: Substitution of IGRA (PPDB-PPDA) for less sensitive test format (IGRA, ESAT-6 & CFP-10)

bovinetb replied to stecarter on **19 Sep 2013** at **20:10 GMT**

Thank you for taking the trouble to explain this to me.

I would like to confirm that I understand you correctly.

The following is how I understand it.

All individuals in the population referred to as vaccinates were vaccinated but they were surrounded by individuals who were not vaccinated. Hence the vaccinated individuals were subjected to a higher level of infection than they would have been if all accessible individuals in the area were vaccinated. This would have impacted on those vaccinates for which the protection provided by the vaccine was partial.

Having said this, in essence, complete social groups were vaccinated so it was only the interfaces between vaccinated and unvaccinated social groups where this could have made a difference and then only on the partially protected individuals who crossed this boundary. i.e a subset of a subset.

If this description of the situation is correct, although this may make a difference, should the effect of NOT vaccinating all social groups in the accessible area be considered to be of secondary importance rather than of primary importance?

No competing interests declared.

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RE: RE: RE: RE: RE: Substitution of IGRA (PPDB-PPDA) for less sensitive test format (IGRA, ESAT-6 & CFP-10)

bovinetb replied to bovinetb on **20 Sep 2013** at **20:18 GMT**

I think I can see at least one problem with the reply shown above.

Where I said "on the partially protected individuals who crossed this boundary" I should have said "on the partially protected individuals who crossed this boundary plus the badgers which they directly and indirectly infect".

No competing interests declared.

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RE: RE: RE: RE: RE: RE: Substitution of IGRA (PPDB-PPDA) for less sensitive test format (IGRA, ESAT-6 & CFP-10)

stecarter replied to bovinetb on **27 Sep 2013** at **08:54 GMT**

Irrespective of whether you attribute primary or secondary importance, the key point is that the study design was not appropriate for comparing the effect of vaccination on prevalence at the population level as, crucially, this was a single population containing both vaccinate and control groups. Consequently, the force of infection for vaccinate groups would have, on average, been greater than if the same number of contiguous groups had been applied the vaccine treatment. Conversely, the force of infection for control groups in this study would have, on average, been lower (due to their proximity to vaccinate groups and associated benefits through herd immunity) than if the control groups were a separate discrete population. The strength of this study was in determining the effect of vaccination on the incidence of infection, specifically the effect of vaccinating individual badgers on their subsequent risk of testing positive to TB. As you point out, differences in the force of infection are unlikely to be relevant for vaccinated individuals completely protected from acquiring infection, but we do not know what proportion (or if any) were completely protected. Similarly, we do not know the effect of repeated challenge on individuals that have received partial protection. From our data it is not possible to quantify to what extent the force of infection would have differed between vaccinate and control groups had the study been designed differently with a different objective. Hope this is helpful.

It might be useful for me to clarify how the vaccine treatment was allocated to social groups: Vaccination treatment was allocated at the social group level so all individuals captured from a “vaccinate” social group would have been vaccinated (although we would have only caught a proportion of animals from most groups each year) and individuals caught in the “control” groups were not vaccinated. We used a stratified randomisation process to allocate the treatments so that, as far as possible, group sizes and group prevalence were similar between vaccinates and controls (using baseline data collected in the first year before vaccination). This resulted in a patchwork effect whereby vaccinate groups may have been surrounded by other vaccinate groups, a mix of vaccinates and controls or control groups only and vice versa (see Figure S1 in the supporting information to the paper).

Competing interests declared: I am the lead author of the paper

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