RESEARCH LETTER

BCG protects against tuberculosis irrespective of HIV status: a matched case-control study in Mwanza, Tanzania

While BCG vaccine protects against severe tuberculosis (TB) in children, its effect against adult TB is questionable. Furthermore, it is not known if HIV co-infection modifies the effect of BCG. Among 352 pairs of Tanzanian TB cases and matched controls, the BCG scar was associated with a reduced risk of TB (OR 0.3, 95% CI 0.2 to 0.7, p=0.005), irrespective of HIV status (interaction, p=0.623). In stratified analysis by HIV status and adjusted for age, diabetes and sociodemographic factors, the BCG scar was associated with TB among both HIV-negative (0.3, 0.1;0.5, p<0.001) and HIV-positive (0.1, 0.02;0.95, p=0.045) participants. There was a similar effect across all age groups (data not shown), indicating a long-term BCG effect.

The BCG efficacy in 14 prospective trials and 12 case-control studies was 50%, ranging from a zero effect to 80%, and a recent case-control study from India among 412 pairs of cases and controls reported a protective effect of BCG vaccination (OR 0.47, 95% CI 0.35 to 0.63). The variations in the observed protective efficacy have been explained as potential differences in the BCG vaccine strains used, the application methods, pre-existing immunity induced by environmental non-tuberculous mycobacteria, or latent TB infection. Our study was not a vaccine efficacy study, but aimed to examine the association between the presence of a BCG scar and developing active TB disease, but the OR of 0.3 does reflect a high efficacy. Since not all BCG-vaccinated individuals develop a BCG scar, the presence of a BCG scar, rather than information on BCG vaccination, might better predict protection, since this indicates that an immunological reaction has actually taken place.

This is the first study providing evidence strongly suggesting that BCG vaccination may prevent TB among both HIV-infected and uninfected participants. We do not have data on the time of HIV infection in the current population, but due to the inclusion criteria (age >15 years), and since most patients were antiretroviral-treatment naïve, the majority of the HIV infected must have contracted the infection in adulthood.

In conclusion, BCG vaccination seems to have an overall protective effect on the risk of developing active TB, and importantly, the effect is similar among HIV-uninfected and HIV-infected adults.

### Table 1  Predictors of pulmonary tuberculosis with OR and 95% CI based on 352 pulmonary tuberculosis cases and 352 controls (n=704)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Crude* OR (95% CI)</th>
<th>p</th>
<th>Multivariable† OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG scar</td>
<td>0.3 (0.2 to 0.5)</td>
<td>&lt;0.001</td>
<td>0.3 (0.2 to 0.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>HIV infection</td>
<td>9.0 (5.4 to 15.1)</td>
<td>&lt;0.001</td>
<td>9.6 (4.7 to 19.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>3.0 (1.9 to 4.8)</td>
<td>&lt;0.001</td>
<td>2.4 (1.2 to 4.8)</td>
<td>0.017</td>
</tr>
<tr>
<td>Alcohol</td>
<td>3.0 (2.1 to 4.3)</td>
<td>&lt;0.001</td>
<td>2.8 (1.6 to 5.2)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Univariate conditional logistic regression for matched case-control groups.
†Multivariable conditional logistic regression for matched case-control groups including all covariates from table and adjusted for age, tribe, marital status, occupation, religion and diabetes status.
REFERENCES
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John Changalucha, Daniel R Witte, Aase B Andersen and Henrik Friis

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