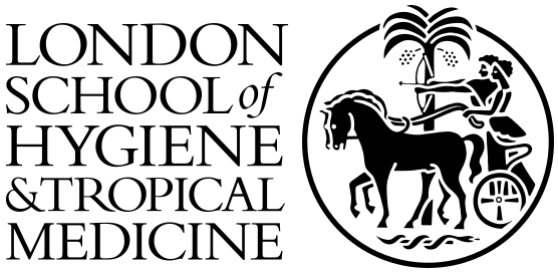

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Letter to the Editor

Single-dose rifampicin and BCG to prevent leprosy

Dear Editor,

The MALTALEP trial compared the efficacy of bacillus Calmette–Guérin (BCG) vaccination followed by single-dose rifampicin (SDR) with BCG vaccination alone in preventing leprosy in household contacts and next-door neighbours of newly diagnosed leprosy patients in Bangladesh (Richardus et al., 2019). It was a large, well designed cluster randomised controlled trial (RCT) and 14,988 contacts of 1552 new leprosy patients were randomised to receive either BCG alone (7378) or BCG followed by SDR (7609) 8–12 weeks later. Participants were followed for 2 years.

The primary outcome of the RCT recorded in the Netherlands Trial Register (NTR3087) and reported in the peer-reviewed protocol was "New cases of leprosy among the contacts of index cases" and " . . . the number of new leprosy patients emerging from the contact groups" respectively (Richardus et al., 2013). There were no significant differences between the proportions of contacts who developed leprosy following the interventions at one or two years. This is an important negative finding and in keeping with the findings of the COLEP RCT of SDR (Moet et al., 2008). The COLEP trial identified that the short-term benefits of SDR were only significant in more distant contacts of index cases.

A secondary data analysis was planned to "define special groups at risk for developing leprosy" and "No significant differences of interest were found" (Richardus et al., 2013). The authors discuss the non-significant 42% reduction in the number of new cases of paucibacillary leprosy in those who received SDR after one year. We were surprised that the significant number of individuals who developed multibacillary (MB) leprosy in the SDR group by 2 years was not similarly discussed. The odds of having developed MB leprosy at the two year follow up point were 3.68 (95% CI: 1.03–13.21) in the group randomised to receive BCG and SDR compared to BCG alone. Table 6 states that only one of 11 new cases of MB leprosy diagnosed after completion of the intervention was slit-skin smear positive. The clinical relevance of the increased numbers of MB patients should be discussed including information about nerve function impairment. The COLEP trial did not show any significant difference in the amount of MB disease between the SDR and placebo groups during two or four years of follow up (Moet et al., 2008).

The MALTALEP study shows that SDR after BCG does not have a significant protective effect against leprosy in household and next-door neighbour contacts compared to BCG alone. This replicates the finding from the larger COLEP study. Data from the BCG arm of the current study were compared with the placebo arm of the COLEP study to infer that the protective effect of BCG is doubtful in Bangladesh.

We agree with Richardus et al. that the current evidence does not support the use of BCG followed by SDR for the contacts of leprosy patients (Richardus et al., 2019) and with WHO that the evidence for BCG alone is conflicting with no evidence of benefit (2018a).

The incomplete understanding of the transmission of *Mycobacterium leprae* and dev elopment of disease hamper the discovery of an effective strategy for prevention. The administration of SDR to contacts of individuals diagnosed with leprosy is recommended by WHO without providing criteria to determine who is a contact (2018b).

The evidence for SDR as a strategy to prevent leprosy or achieve the target of zero transmission of *M. leprae* remains limited.

Conflict of interest

None.

Funding source

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Ethical approval

None.

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