Effectiveness and cost-effectiveness of first BCG vaccination against tuberculosis in school-age children without previous tuberculin test (BCG-REVAC trial): a cluster-randomised trial


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The study evaluated the effectiveness and cost-effectiveness of *Bacillus Calmette-Geurin* (BCG) vaccination in school age children without a previous tuberculin test and no BCG scarring. The authors concluded that vaccinating school age children without previous tuberculin test could confer moderate protection and save resources. The authors’ conclusions appear reasonable for Salvador, Brazil, but the effect of uncertainty on the results is unclear. Reporting was poor, and it is unclear whether the evaluation is generalisable beyond Salvador.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study evaluated the effectiveness and cost-effectiveness of *Bacillus Calmette-Geurin* (BCG) vaccination in school age children without a previous tuberculin test and no BCG scarring.

Interventions
Children in the trial either received BCG vaccine, or no vaccine.

Location/setting
Brazil/Public Health.

Methods
Analytical approach:
The economic evaluation was based on a large cluster randomised trial that administered BCG vaccine to children in urban public schools aged seven to 14 in Salvador and Manaus, Brazil. Recruitment was between October, 1996 and December, 1997 in Salvador, and between September, 1998 and December 1998 in Manaus. Cost-effectiveness evaluation was based on Salvador data only. The trial had nine years of follow-up. The authors stated that the analytical perspective was societal.

Effectiveness data:
The cluster randomised trial (Barreto, et al. 2002, see Other Publications of Related Interest) stratified schools by risk factors for tuberculosis and then randomised by the school. Neither patients nor health care workers receiving or administering the vaccines were blinded to allocation or treatment. However, the clinicians who monitored observed cases of tuberculosis after the trial were blinded to treatment allocation. The primary measure of effectiveness was incidence of tuberculosis in the study population. Children in the study were followed up passively relying on follow-up from the Brazilian Tuberculosis Control Programme with diagnosed patients matched to the study database. Patients lost to follow up were assumed to occur equally between the randomised interventions. Patients misclassified were assumed to occur equally between randomised interventions.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The primary measure of benefit in the economic evaluation was the tuberculosis incidence rate ratio.

Cost data:
The cost per BCG vaccination was from a meta-analysis of vaccination worldwide (Trunz, et al. 2006, see Other Publications of Related Interest). Hospital costs of tuberculosis were calculated from a Brazilian tuberculosis study in adults in Salvador (Costa, et al. 2005, see Other Publications of Related Interest). Total vaccine costs were calculated using the number needed to treat to prevent one case of tuberculosis. Adverse events of tuberculosis were not included in costs as the incidence of adverse events was very small. Hospitalisation costs were estimated assuming that 20% of all new tuberculosis patients were admitted to hospital and that drug resistant infection occurred in 10% of all patients. The average cost per case was calculated assuming 70% of the costs of hospitalisation were out-patient, 20% were in-patient, and 10% were due to drug resistant cases. Costs were expressed in 1997 US $, adjusted via the US consumer price index. Costs were discounted at a rate of 5% annually.

Analysis of uncertainty:
One-way sensitivity analyses were undertaken to measure the effect of varying vaccine effectiveness, vaccination cost, treatment cost, and baseline tuberculosis rate per 100,000 person years. Best- and worst-case scenario analyses were conducted. The best-case (for cost-effectiveness) scenario assumed high vaccine effectiveness, high tuberculosis rates, low vaccination costs, and high treatment costs; the worst-case (for cost-effectiveness) scenario had opposite assumptions.

Results
The cost-effectiveness of vaccination was calculated for Salvador only. Incidence of tuberculosis in the BCG arm was 54.9 per 100,000 person-years, while incidence was 72.7 per 100,000 person-years in the control arm. The tuberculosis incidence rate ratio controlled for demographic factors of vaccination versus no vaccination was 0.75 (95% CI 0.57 to 0.97). The costs of vaccinating 381 patients (the number needed to treat to prevent one case of tuberculosis), were lower than the costs of treating one tuberculosis patient with a ratio of vaccination costs to treatment costs of 0.69. So in Salvador, vaccination was more effective and less costly than no vaccination.

Uncertainty around vaccine effectiveness and vaccine costs had the largest effect on estimates of the ratio of treating and vaccination to prevent one case of tuberculosis. With all other parameters equal, vaccination was as expensive as treatment at vaccine effectiveness of 23.4% or a tuberculosis rate of 58.8 per 100,000 person-years. In the best-case scenario vaccination could be nine times less expensive than treatment. In the worst-case scenario, vaccination could be 11 times more expensive than treatment.

Authors' conclusions
The authors concluded that vaccinating school-age children without previous tuberculin test could confer moderate protection and save resources.

CRD commentary
Interventions:
The interventions appear appropriate and were sufficiently described.

Effectiveness/benefits:
The randomised controlled trial appeared well conducted. The study pragmatically used a public health system already in place to conduct follow-up of participants and took good care to validate the similarity of their clusters, the similarity of their randomised patients, and that unmasked original treatment had no effect on results. It appears that the study was generally methodologically sound, and reporting of methods was good. However, no loss to follow-up statistics were recorded, and the economic evaluation assumed no loss to follow-up. The authors acknowledge that this may lead to underestimation of the incidence of tuberculosis and may favour the cost-effectiveness of the vaccine. The cost-effectiveness calculations were based on Salvador data only. The effectiveness in Manaus was much smaller than in Salvador so the cost-effectiveness would also likely be less. Tuberculosis incidence was a useful measure of benefit as it captured the major health outcomes of this analysis. Quality-adjusted life-years would be useful to value the health outcome to the patient over time. No discounting was applied to benefits, as the measure of benefit was incidence rates.

Costs:
The methods for selecting the meta-analysis that determined vaccine cost were not reported. The study was a worldwide vaccination meta-analysis, but no demographic or methodological details were reported. The authors acknowledge some limitations of the choice of hospital costing study: the costing study was in adults, not children; and it did not include secondary cases that were prevented through vaccination. Another limitation of the costing study was that it used 1999 $ estimates, so it was not clear whether the costs expressed in it were representative of current practice. The authors assumed specific proportions of hospital costs were attributed to certain patient groups, but gave no justification for their assumptions. The authors excluded adverse events from costs but the authors justified this on the grounds of a very small incidence of adverse effects; it was unclear what effect this could have on the analysis. The reader should evaluate the potential cost of adverse events and secondary transmission savings of vaccination in their setting. It was not clear whether appropriate cost estimates have been used. Costs were expressed in 1997 $, which was unusual for a study published in 2011. The results may be slightly different using current prices.

Analysis and results:
There was no incremental analysis of results, but in the case of Salvador vaccination was less costly and more effective than no vaccination, so a cost-effectiveness ratio would not be calculated in any case. The sensitivity analyses report the effect of varying parameters on the ratio of costs rather than on cost-effectiveness, which would have been useful. The sensitivity analyses were useful but a probabilistic sensitivity analysis would also have been useful to evaluate the likelihood of vaccination being cost-effective given the uncertainty in the all of the parameter estimates. The analysis assumes that costs in Salvador would not be representative of costs in Manaus, it was unclear whether the results of the analysis have generalisability beyond Salvador. Not including secondary transmission in benefits and costs likely underestimates the benefits and cost savings of the vaccination strategy.

Concluding remarks:
The authors’ conclusions appear reasonable for Salvador, Brazil, but the effect of uncertainty on the results was unclear. Reporting was poor, and it is unclear whether the evaluation is generalisable beyond Salvador. It is also not clear how generalisable the results are to other areas in Brazil.

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