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.

Health technology
A universal Bacillus Calmette-Guerin (BCG) vaccination programme to prevent tuberculosis (TB) in Japanese infants was compared with no vaccination.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 1.2 million infants born in 1996 in locations across Japan.

Setting
The setting was the community and primary care. The economic study was carried out in Japan.

Dates to which data relate
The effectiveness data were taken from literature published between 1993 and 1998. The resource use data were estimated from literature published between 1996 and 1999. The price year was not stated.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies.

Modelling
A mathematical model was used to calculate the cost and number of immunisations required to prevent one case of TB.

Outcomes assessed in the review
The following outcomes were used as input parameters to the model:

- vaccine efficacy against TB;
- vaccine efficacy against TB-meningitis;
- the duration of BCG vaccine effectiveness;
- the number of infants born in 1996 in Japan;
the number of infants vaccinated against BCG in 1996;
the proportion of vaccinated infants;
the proportion of purified protein derivative (PPD) positive infants;
the TB incidence among the cohort in Japan for two age groups, 0 to 4 years and 5 to 9 years;
the hypothetical incidence of TB among the unvaccinated; and
the hypothetical incidence of TB among the vaccinated.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported. The authors reported that they mainly used published reports of meta-analyses of data.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
The estimates for the input parameters to the model were derived from 7 published studies.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The results of the outcomes used as input parameters to the model were as follows:

the vaccine efficacy against TB was 40 to 80%;
the vaccine efficacy against TB-meningitis was 64 to 86%;
the duration of the BCG vaccine’s effectiveness was 10 years;
the number of infants born in Japan in 1996 was 1.2 million;
the number of infants vaccinated against BCG in 1996 was 1.15 million;
the proportion of vaccinated infants was 0.955;
the proportion of PPD-positive infants was 0.1034;

the TB incidence among the cohort in Japan was 2.2 per 100,000 in the 0- to 4-year age group, and 1.1 per 100,000 in the 5- to 9-year age group;

the hypothetical incidences of TB among the unvaccinated and vaccinated were not reported.

**Measure of benefits used in the economic analysis**
The measure of benefit used in the economic analysis was the number of TB cases avoided.

**Direct costs**
The analysis included the costs of a vaccination programme. These were derived from actual expenditure data on the BCG vaccination programme in Kyoto. The cost of the programme included the costs of the PPD testing kit, the BCG vaccines, the injection materials and the personnel. The costs of treating side effects of BCG vaccination and follow-up of PPD positive cases were also included. These were derived from published reports and expert opinion. The costs were discounted at a rate of 5%. The price year was not reported.

**Statistical analysis of costs**
No statistical analysis of the costs was conducted.

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
US dollars ($). The exchange rate was Yen 110 = $1.

**Sensitivity analysis**
A series of one-way sensitivity analyses were performed in order to test the robustness of the results. The parameters varied were the duration of BCG protection, TB incidence, vaccine coverage and the discount rate.

**Estimated benefits used in the economic analysis**
The total number of TB cases averted was 111 for a vaccine efficacy rate of 40%, 228 for a vaccine efficacy rate of 60%, and 542 for a vaccine efficacy rate of 80%.

**Cost results**
The authors reported that the total cost associated with the vaccination programme was $19.5 million. This does not appear to include the cost of treating children with TB infection. The costs associated with no vaccination were not reported.

**Synthesis of costs and benefits**
The costs and the benefits were synthesised by dividing the costs of the vaccination by the number of TB cases averted. This equates to an incremental cost-effectiveness ratio if it is assumed that the costs of the no vaccination programme are zero.

The cost per TB case averted was $175,682 for a vaccine efficacy rate of 40%, $85,348 for a vaccine efficacy rate of 60%, and $35,950 for a vaccine efficacy rate of 80%.
The sensitivity analysis showed that changing the duration of BCG protection from 10 to 5 years increased the cost and the number of immunisations to 37 to 39% above the baseline values. In addition, the TB incidence rate showed considerable regional variation and, if it was reduced to half the baseline value, the cost and the number of immunisations to prevent a single case of TB would be doubled. The authors also stated that cost-effectiveness was improved by higher vaccine coverage and when discounting was omitted. It was also reported that the cost per TB case averted by universal vaccination was likely to exceed the cost to treat a single patient with TB infection.

Authors' conclusions
The cost per case of tuberculosis (TB) prevented was heavily dependent on vaccine efficacy and the duration of protection. The cost was high when compared with the cost of treating one child who has developed TB.

CRD COMMENTARY - Selection of comparators
The choice of the comparator used was justified on the grounds that some countries with a low TB incidence do not have a universal vaccination strategy. However, the authors noted that these countries do have a policy of vaccination for high-risk groups. This latter policy was not included in the evaluation. You should decide if a no vaccination policy is common in your own setting.

Validity of estimate of measure of effectiveness
The authors did not report whether a systematic review of the literature had been undertaken, or the sources searched and the strategies used. The methods used to assess the validity of the primary data sources, and the validity and relevance of the data to the analysis, were not reported. In addition, the methods used to extract the data and assess its quality, and to combine data from more than one source to generate estimates of individual input parameters, were also not provided. The authors appear to have used the data from the available studies selectively. They did not report any investigation of the impact of differences between the primary studies.

Validity of estimate of measure of benefit
The estimation of benefits was proxied by a single effectiveness estimate, the number of TB cases averted. This measure does not quantify the impact of BCG side effects, or the impact of TB on mortality or the long-term health status. The authors reported that BCG side effects can occasionally be life threatening. They went on to note that TB-related mortality has not recently been identified in children in Japan, and used this fact to justify not using survival as the measure of health benefit. The analysis might be biased if BCG side effects or TB significantly reduce life expectancy or health status.

Validity of estimate of costs
Not all the categories of cost relevant to the perspective adopted were included in the analysis. The analysis did not include the costs of the no vaccination comparator. Nor did it include the costs of the health service and public health costs for the identification and treatment of TB. It is unclear whether the exclusion of these costs would under- or overestimate the incremental costs of a universal vaccination policy.

The costs and the quantities were not reported separately. The resource use and cost data were derived from published literature and actual expenditure data. The methods used to review the cost literature were not reported. The authors did not report the value of all the cost parameters included in the model. No statistical analysis was performed, but one-way sensitivity analyses of the effectiveness parameters and the discount rate were conducted. The authors did not test the sensitivity of the results to variation in the cost input parameters.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, and addressed the issue of generalisability to other settings. As the authors acknowledged, the main limitation of their study was that the data used were mainly derived from meta-analyses of studies conducted in countries other than Japan. The authors stated that the
efficacy of the BCG vaccine in Japan might be different from that determined from meta-analyses conducted in other countries.

**Implications of the study**
The authors conclude that the cost per case of TB prevented is heavily dependent on vaccine efficacy and the duration of protection. In addition, the cost is high in comparison to the cost of treating one child who has developed TB. The authors state that the high overall average of TB incidence in Japan is due to a high incidence among the elderly, and this does not necessarily justify continuing the universal vaccination of children. Further, the authors state that since the TB incidence rates vary considerably by region, a BCG vaccination programme could be devised for each region on the basis of incidence data. Further research is required to evaluate the cost-effectiveness of selective vaccination for high-risk groups.

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