A cost-benefit analysis of typhoid fever immunization programmes in an Indian urban slum community

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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
Three typhoid fever immunisation programmes based on the Vi polysaccharide vaccine were examined. The programmes were:

- a mass vaccination campaign (assumed to reach 80% of the total population),
- a school vaccination campaign (assumed to reach 80% of 6- to 19-year-olds), and
- a targeted vaccination campaign for pre-school children (assumed to reach 80% of this age group).

The Vi polysaccharide vaccine was administered in one dose, as an injection, with revaccination recommended after 3 years. The government fully paid for all programmes.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals eligible for typhoid fever immunisation, depending on the programme considered.

Setting
The setting was the community. The economic study was carried out in India.

Dates to which data relate
The effectiveness and resource use data were gathered from November 1995 to October 1996. The price year was 1996.

Source of effectiveness data
The effectiveness evidence was derived from a published study (Sinha et al. 1999, see 'Other Publications of Related Interest' below for bibliographic details) and authors’ assumptions.

Link between effectiveness and cost data
The costing was carried out on the same sample of patients as that used in the clinical study. It was unclear whether it
was carried out prospectively or retrospectively.

**Study sample**
There were limited details on sample selection and sample characteristics since much of the data had been published separately. The population of the study area was divided into clusters of 70 households, and 26 of such clusters were randomly selected for active twice-weekly surveillance. The residents in the remaining household clusters were kept under only passive surveillance. The overall study sample comprised 19,585 individuals. There were 1,123 in the age group 0 - 2 years, 2,011 in the age group 2 - 5 years, 8,370 in the age group 5 - 19 years, and 8,081 in the age group older than 19 years.

**Study design**
The design of the study was unclear. Participating clusters were randomly selected. Blood specimens for cultures were obtained from all children aged less than 5 years who had fever (temperature higher than 38 degrees C), identified through active or passive surveillance. Older children and adults had to have had continuous fever for at least 3 days before a blood specimen was obtained for culture. No details of the length of follow-up were given.

**Analysis of effectiveness**
The primary outcome measure was the annual incidence observed in the study population. It would appear that all of the individuals included in the study were accounted for in the analysis. Two different estimates were obtained, one including individuals with active surveillance and another one based on blood culture-confirmed cases detected by both active and passive surveillance, plus estimates of "clinical typhoid".

**Effectiveness results**
In the group of individuals receiving active surveillance, the overall annual incidence (per 1,000 person-years) was 9.8 for all ages, 13.6 in the age group 0 - 2 years, 34.9 in the age group 2 - 5 years, 11.7 in the age group 5 - 19 years, and 1.1 in the age group older than 19 years.

As an alternative estimate, the overall annual incidence (per 1,000 person-years) was estimated also in the group of individuals receiving active plus passive surveillance and "clinical diagnosis". This was 17.5 for all ages, 24.5 in the age group 0 - 2 years, 53.1 in the age group 2 - 5 years, 19.3 in the age group 5 - 19 years, and 6 in the age group older than 19 years.

**Clinical conclusions**
The clinical data were used to estimate the benefits of the three programmes.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions to derive some clinical estimates.

**Estimates of effectiveness and key assumptions**
The vaccine efficacy was 70% and lasted 3 years. To estimate the number of cases of typhoid fever avoided, it was assumed that the vaccine coverage rate was 100%.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the number of typhoid fever cases avoided with the three vaccination programmes in comparison with no vaccination. This was obtained by an algorithm based on the annual incidence of typhoid fever, vaccine efficacy and vaccine coverage rate.
Direct costs

The health services included in the economic evaluation were vaccine costs (e.g. vaccine dose, syringe, safety box and labour) and costs associated with typhoid fever such as public and private costs. Public costs included outpatient visits, hospitalisations, laboratory tests, and medicines. Private costs referred to medical costs (out-of-pocket expenditures on consultation fees, laboratory tests and medicines) and non-medical costs (out-of-pocket expenditures on transportation, special foods and drinks, and other items). All vaccine costs assumed that the existing cold-chain and central administrative structure would have sufficient capacity for the programme to be added, without additional investment.

The perspective of the public sector and the patients was adopted in the analysis of direct costs. The costs and resources used were estimated from a published study (Bahl et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details). Discounting was relevant, as the costs were incurred during a long timeframe, and a 10% discount rate was applied. The unit costs were not presented separately from the quantities of resources used. The price year was 1996.

Statistical analysis of costs

The costs were treated deterministically.

Indirect Costs

The indirect costs (i.e. days of work missed by all household members because of typhoid fever) were included in the analysis because a societal perspective was considered. The costs were derived from a monetary value of lost productivity. Both the quantities of resources used and unit costs were estimated from a published study (Bahl et al. 2004). The price year was 1996. The unit costs were not presented separately from the quantities of resources used. An annual discount rate of 10% was applied.

Currency

The costs were estimated in Indian rupees (INR) and converted into US dollars ($). The conversion rate was $1 = INR 35.5.

Sensitivity analysis

Three types of sensitivity analyses were carried out to examine the robustness of the base-case costs and cost-effectiveness results to variations in uncertain data. For example, the estimates of the ex-ante cost of illness (public and private costs associated with typhoid fever) and the incidence of typhoid fever.

For the cost of illness, the authors stated that the values used in the base-case analysis could have been underestimated. Thus, public and private costs associated with typhoid fever were multiplied by a correction factor, ranging from 0 (no correction) to 4 (implying that avoided costs of illness represent 25% of the total economic benefit). An alternative, higher estimate of the incidence of typhoid fever was based on individuals receiving active plus passive surveillance and "clinical diagnosis".

Estimated benefits used in the economic analysis

Using incidence rates based on blood culture-positive cases detected from active surveillance, the number of cases avoided over no immunisation was 297 with mass vaccination, 165 with school-based vaccination, and 118 with pre-school vaccination.

Cost results

With a vaccine price ranging from $0.75 to $3:

the ratio of public sector treatment cost-savings per dollar spent by the public sector on vaccination ranged from 1.17 to 0.29 with mass vaccination, from 0.72 to 0.18 with school-based vaccination, and from 7.72 to 1.93 with pre-school vaccination.
vaccination (higher ratios represent higher benefits);

the net public benefits (public benefits minus public costs) ranged from $1,844 to -$31,388 with mass vaccination, from -$1,410 to -$16,477 with school-based vaccination, and from $8,102 to $4,483 with pre-school vaccination; and

the net societal benefits (total benefits minus public costs) ranged from $12,213 to -$21,018 with mass vaccination, from $5,485 to -$9,581 with school-based vaccination, and from $10,942 to $7,323 with pre-school vaccination.

In general, the pre-school immunisation programme was the best strategy in terms of net (public or societal) benefits, followed by the school-based immunisation programme. As expected, the net benefits decreased as the cost of the vaccine increased (although for the pre-school immunisation programme, the resultant savings were higher than the costs at all vaccine prices).

**Synthesis of costs and benefits**

Incremental cost-effectiveness ratios were calculated to combine the costs and benefits of each vaccination strategy with no vaccination.

With a vaccine price ranging from $0.75 to $3, the public cost per case avoided ranged from $37.25 to $149 with mass vaccination, from $30.53 to $122.10 with school-based vaccination, and from $10.23 to $40.93 with pre-school vaccination.

With a vaccine price ranging from $0.75 to $3, the public cost minus public benefit per case avoided ranged from -$6.20 to $105.55 with mass vaccination, from $8.57 to $100.15 with school-based vaccination, and from -$68.72 to -$38.02 with pre-school vaccination.

Looking at the public cost per case avoided, the pre-school immunisation programme was more attractive than the mass immunisation programme and the school-based immunisation programme. A similar conclusion could be reached when considering only the public treatment cost-savings per dollar spent on vaccination, the net public cost per typhoid case avoided, or the net benefits to the public sector.

When net societal benefits were considered, both mass vaccination and school-based vaccination were attractive at low vaccine prices (although the net societal benefits were modest for school-based vaccination). The pre-school vaccination programme had substantial net societal benefits at all vaccine prices.

The sensitivity analysis showed that all immunisation programmes were sensitive to variations in disease incidence. The use of a higher incidence estimate improved the cost-effectiveness and net benefit estimates of all programmes.

When the estimate of the cost of illness was changed, all three vaccination programmes led to net benefits if incidence was based on active surveillance of blood culture-positive and clinical typhoid fever, and the per-unit vaccine cost was less than $3. Even if incidence was based only on blood culture-confirmed cases detected with active surveillance, all vaccination programmes remained economically attractive at a per-unit vaccine cost of $3 for a correction factor of 2. The pre-school vaccination programme remained attractive at all per-unit vaccine costs.

**Authors' conclusions**

From a public sector perspective, mass vaccination and school-based vaccination programmes for typhoid fever could be unattractive even in settings with very high incidence rates. Only the pre-school immunisation programme appears attractive from this perspective. However, using a societal perspective and with high incidence rates, all vaccination programmes could represent good value for money in developing countries.

**CRD COMMENTARY - Selection of comparators**

The selection of the comparator (no immunisation programme) was appropriate as it represented the standard of care in several developing countries. The three proposed vaccination programmes represented three feasible immunisation options for typhoid fever. You should decide whether they are valid comparators in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness evidence came from a published study, and there was limited information on the design and characteristics of the study. Thus, it was difficult to assess the validity of the primary source. Participating households were identified using a random process. The length of follow-up was not explicitly stated and the use of a comparator was not clear. Other clinical estimates were derived from authors' hypotheses. The key variable, incidence of disease, was varied in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It is comparable only with the benefits of similar health interventions.

Validity of estimate of costs
The cost analysis relied on a published cost-of-illness study. Extensive details on the categories of costs used and the different perspectives adopted in the study were reported. However, the unit costs and the quantities of resources used were not presented separately, and only the total costs were reported. The analysis focused on the distinction between public and private costs. The price year was reported, which aids reflation exercises in other settings. The costs were treated deterministically but cost-of-illness estimates were corrected for in the sensitivity analysis. Due to the uncertainty surrounding vaccine cost, all cost results were presented for five vaccine prices.

Other issues
The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. However, some sensitivity analyses were carried out around the key estimates, which enhanced the external validity of the study. The study results referred to a setting with a high incidence of typhoid fever and this was reflected in the authors' conclusions.

Implications of the study
The study results suggested that if government adopted a societal perspective on the economic benefits of vaccination, typhoid fever immunisation programmes could be efficient in settings of high incidence of disease and if decision-makers recognised that avoided costs of illness represent a significant underestimate of the actual economic benefits to individuals of vaccination.

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Other publications of related interest


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