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A Cost-Benefit Analysis of Typhoid Fever Immunization Programmes in an Indian Urban Slum Community

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ABSTRACT

Many economic analyses of immunization programmes focus on the benefits in terms of public-sector cost savings, but do not incorporate estimates of the private cost savings that individuals receive from vaccination. This paper considers the implications of Bahl *et al*.'s cost-of-illness estimates for typhoid immunization policy by examining how community-level incidence estimates and information on distribution of costs of illness among patients and the public-health sector can be used in the economic analysis of vaccination-programme options. The findings illustrate why typhoid vaccination programmes may often appear to be unattractive to public-health officials who adopt a public budgetary perspective. Under many plausible sets of assumptions, public-sector expenditure on typhoid vaccination does not yield comparable public-sector cost savings. If public-health officials adopt a societal perspective on the economic benefits of vaccination, there are many situations in which different vaccination programmes will make economic sense. The findings show that this is especially true when public decision-makers recognize that (a) the incidence of typhoid fever is underestimated by blood culture-positive cases and (b) avoided costs of illness represent a significant underestimate of the actual economic benefits to individuals of vaccination.

***Key words*:** Typhoid fever; Cost-benefit analysis; Costs and cost analysis; Cost of illness; Vaccination; Typhoid-paratyphoid vaccines; Slums; Urban health; India

INTRODUCTION

Globally, there are an estimated 16 million cases of typhoid fever annually, causing 600,000 deaths mainly in developing countries (1). The World Health Organization recommends establishing typhoid fever vaccination programmes in endemic areas, and the Vi polysaccharide vaccine against typhoid fever has been shown to be effective, inexpensive, and well-tolerated (1). However, resources for implementing new and existing immunization programmes in developing countries are scarce, and the addition of new vaccines to current immunization schedules has logistical and financial difficulties (2). Many countries have concluded that they cannot afford to add new vaccines (e.g. against hepatitis B) to their Expanded Programme on Immunization (EPI), and public-health resources are under constant pressure to be redirected to other interventions.

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In their study of an urban slum (Govindpuri) in New Delhi, India, Sinha *et al*. found that the incidence of typhoid fever in children aged five years and below was much higher than expected (3). Using household survey data from the same population, Bahl *et al*. generated the first estimates of costs of illness associated with typhoid fever at the community level in a developing country (4). Results of their study showed that the costs of illness per episode of typhoid fever were the highest in 2-5-year old children and that both hospitalization and clinical resistance to ciprofloxacin dramatically increased the cost of illness. Finally, Bahl *et al*. showed that the distribution of costs between private individuals and the public sector varies by age group (4). The public sector in India is estimated to bear 70% of costs of illness in 2-5-year old children. In all other age groups, the majority of costs of illness are borne by private households.

Many economic analyses of immunization programmes focus on the benefits in terms of public-sector cost savings, but do not incorporate estimates of the private cost savings that individuals receive from vaccination. This paper considers the implications of Bahl *et al*.'s cost-of-illness estimates for typhoid immunization policy by examining how community-level incidence estimates and information on the distribution of costs of illness among patients and the public-health sector can be used in the economic analysis of vaccination-programme options.

Economic analysis of vaccination programmes

Policy analyses of immunization programmes typically seek to answer the question: which immunization programme generates the best health outcomes per dollar spent by the public-health system? Health outcomes are commonly measured in terms of avoided cases, avoided deaths, and/or avoided costs. These analyses help decision-makers select programmes that maximize health benefits with a given budget. Economic analyses of immunization programmes typically measure the benefits of those programmes using avoided costs of illness (5-7)

Drummond *et al*. emphasize that the results of economic analyses will vary depending on the perspective assumed by the analyst (8). Most policy analyses of vaccination programmes take a public-sector budgetary perspective, i.e. they only look at avoided public-sector budget costs, or costs borne by healthcare providers, to measure vaccination benefits (5-7). Only a few take a societal perspective and measure the total costs of illness as the sum of avoided public and private costs (9). To the best of our knowledge, none of the previous economic analyses of vaccination programmes in the literature has explicitly compared the public-sector budget perspective with the societal perspective (public plus private costs avoided) using actual field data from a developing country.

This study uses estimates of both public and private costs of illness due to typhoid fever to analyze the economic and public-health impacts of three kinds of publicly-financed immunization programmes (school-based vaccination, targeted vaccination of pre-school children aged 2-5 years, and vaccination of the general population). We illustrate the difference between looking at the results of the economic analysis from a public budgetary perspective only and a fuller accounting of the economic benefits that includes cost savings to private individuals. We report the sensitivity of cost-benefit results to changes in three main sources of uncertainty: (a) the incidence of typhoid fever in the community, (b) the average cost of vaccination, and (c) the proportion of the total economic benefits represented by avoided costs of illness.

Background

Vi polysaccharide vaccine

The Vi polysaccharide vaccine is administered in one dose, as an injection, with revaccination recommended after three years (1). In most countries, it is indicated for use in adults and children aged over 24 months, while its efficacy in very young children needs to be determined (1). Studies in endemic areas have found that the efficacy of the Vi vaccine ranges from 55% to 75% (1,10). The Vi vaccine has a well-established safety profile with low incidence of mild side-effects, whether it is administered alone or with other vaccines (1).

Study population

The study area is a poor, densely-populated urban slum located in Kalkaji, New Delhi, India. The socioeconomic characteristics of the sample are described in the paper of Bahl *et al*. (4). Sinha *et al*. reported that the annual incidence of typhoid fever among all 0-40-year old residents was 9.8 per 1,000 persons, and the annual incidence in children aged less than five years was 27.3 cases per 1,000 persons (3). These are among the highest incidence rates of typhoid fever reported anywhere in the world.

Research design and fieldwork

The population of the study area was divided into clusters with 70 households in each, and 26 such clusters were randomly selected for active twice-weekly surveillance for detection of cases with typhoid fever (3). The residents in the remaining household clusters were kept under only passive surveillance at health facilities and neighbouring practitioners for detection of fever cases.

Blood specimens for culture were obtained from all children, aged less than five years, who had fever (temperature >38 °C), identified through active or passive surveillance. Older children and adults had to have had continuous fever for at least three days before a blood specimen was obtained for culture. These methods have been described in detail previously (3).

In the study population, a total of 98 cases of culture-positive typhoid fever and 31 of culture-positive paratyphoid were identified through both active and passive surveillance. Ninety-four culture-negative cases exhibiting a characteristic clinical syndrome were also treated as typhoid fever. This 'clinical' typhoid syndrome was defined as continuous high fever for seven days or more with no other obvious causes and no response to three days of anti-malarial therapy. A diagnosis of 'clinical' typhoid was made earlier, i.e. after five days of fever, if the patient additionally had bradycardia or splenomegaly. Bahl *et al*. estimated the costs of illness for blood culture-positive *Salmonella enterica* serotype Typhi, blood culture-positive *S. enterica* serotype Paratyphi, and 'clinical typhoid' cases (4).

Measurement and calculation of costs of illness

Data to calculate the private costs of illness were collected through weekly in-person interviews conducted in the patient's home (4). Private, or patient, costs of illness are the sum of direct medical, direct non-medical, and indirect costs. Direct medical costs included out-of-pocket expenditure on consultation fees, laboratory tests, and medicines. Non-medical direct costs measured out-of-pocket expenditure on transportation, special foods and drinks, and other items. Indirect costs were calculated as the product of days of work missed by all household members and a monetary value of lost productivity. [Over the course of the study period from November 1995 to October 1996, the exchange rate between the Indian rupee and the US dollar fluctuated between INR 34.32 and 36.59 per US$. For the costs of illness presented in this study, we have assumed an average exchange rate over the period of US$ 1=INR 35.5. All costs are expressed in 1996 US$.] Public costs of illness, or non-patient costs, were defined as the costs borne by institutions or the public sector. Public costs were the sum of costs of outpatient visits or hospitalization in government hospitals, and laboratory tests and medicines provided free of charge to the patient.

Ex-ante costs of illness

The estimates of *ex-ante* costs-of-illness are the product of the average cost of illness and the disease incidence; they represent the per-capita expected annual losses due to typhoid fever. Table 1 presents these estimates for the entire study population and by age group. These point estimates represent averages around which the population's *ex-ante* costs of illness will be distributed. The private *ex-ante* costs of illness are the costs that households should expect to incur; the public *ex-ante* costs of illness are the costs that the public health-care system should expect to incur.

The total private and public *ex-ante* costs were higher for children aged 2-5 years (US$ 4.34) than those for children aged 0-2 year(s) (US$ 0.70), individuals aged 5-19 years (US$ 0.90), and adult (US$ 0.06) subjects. Given that the average daily wage rate for an adult is US$ 1.97, these estimates imply that households could expect to lose two days' wages in the next year because of typhoid fever in 2-5-year old children and less than one-half day's wage due to typhoid fever affecting household members in other age groups.

The distribution of *ex-ante* costs between private individuals and the public sector varies widely by age group. The private costs are greater than public costs for all age groups except 2-5-year old children. In the 2-5-year age group, however, public-sector costs (US$ 3.32) are over three times greater than patient costs (US$ 1.04). The *ex-ante* public costs of illness are so high for 2-5-year old children because of the high incidence of typhoid fever in this age group and the relatively high rates of hospitalization. The private *ex-ante* costs are also high for this age group because of lost wages due to adult caretaking. The *ex-ante* public cost for adults is zero, indicating that typhoid fever in adults imposes little burden on the public sector. Considering all age groups, however, expected public costs (US$ 0.48) are roughly comparable to expected patient costs (US$ 0.42). The *ex-ante* cost of illness increases significantly for patients who exhibit antibiotic resistance and patients who were hospitalized (4). These results underscore the benefits of typhoid prevention in areas with antibiotic resistance and poor case treatment [See the paper by Bahl *et al*. (4) for more details, including sensitivity analyses conducted by varying assumptions on daily wages, the non-patient costs of outpatient visits, and the daily hospitalization costs].

vaccination campaign]. The third is a targeted vaccination campaign for pre-school children aged 2-5 years, which is assumed to reach 80% of this age group. All three programmes are assumed to be fully paid for by government, i.e. no user-fees are charged.

Vaccine benefits

We measure the outcomes of each of the three publicly-funded vaccination programmes in three different ways: (a) The number of typhoid fever cases avoided, calculated as the product of the incidence rate, cohort population, vaccine effectiveness, and vaccine coverage, i.e. the percentage of the population in an age cohort that is vaccinated; (b) Public-sector cost savings, estimated as the costs of illness avoided by public healthcare providers; and (c) Total public and private costs of illness avoided. We assume that the Vi vaccine is 70% effective for three years.

Table 1. Incidence of typhoid fever, *ex-ante* costs of illness, and vaccine benefits, by age group (70% effectiveness)

Age (years) group	Population of Govindpuri	Annual incidence (per 1,000 person-years)	Annual *ex-ante* costs of illness (US$)			Per-capita vaccine benefits, discounted over 3-year period (US$)			Expected number of cases of typhoid fever prevented with 100% vaccine coverage
		Blood +ve typhoid from active surveillance	Private	Public	Total	Private	Public	Total	
0-2	1,123	13.6	0.45	0.25	0.70	NA	NA	NA	NA
2-5	2,011	34.9	1.04	3.32	4.34	1.81	5.79	7.55	147
5-19	8,370	11.7	0.59	0.31	0.90	1.03	0.54	1.57	206
>19	8,081	1.1	0.06	0.00	0.06	0.10	0.00	0.10	19
All ages	19,585	9.8	0.42	0.48	0.90	0.74	0.83	1.57	372
Age (years) group		Blood +ve typhoid from active plus passive surveillance and 'clinical' diagnoses							
0-2	1,123	24.5	0.79	0.45	1.24	NA	NA	NA	NA
2-5	2,011	53.1	1.58	5.04	6.62	2.75	8.78	11.52	224
5-19	8,370	19.3	0.99	0.48	1.49	1.72	0.83	2.60	339
>19	8,081	6	0.31	0.03	0.34	0.54	0.05	0.59	102
All ages	19,585	17.5	0.79	0.45	1.24	1.27	1.52	2.80	665

NA=Indicates that there are no vaccine benefits in the 0-2-year age group because the Vi polysaccharide vaccine is not indicated for this age group

MATERIALS AND METHODS

Policy interventions

We estimate the costs and benefits of three different public-sector vaccination programmes in the study area. The first is a mass vaccination campaign that is assumed to reach 80% of the total population in the study area. The second is a school vaccination campaign that is assumed to reach 80% of the 6-19-year old individuals [We do not have data on what percentage of school-age children are enrolled in schools. We assume that the vaccine would be made available to any child in this target age group, whether they attend school or not, via the health posts established for the

The first outcome measure is simply a non-monetarized count of the number of typhoid fever cases avoided by a vaccination programme. It is presumably of interest to both public-sector decision-makers and private individuals. However, from an economic perspective the benefits must be compared with the costs, and it is difficult to make such comparisons when the costs are measured in monetary units and the benefits are not. The second outcome measure is of particular interest to public-sector decision-makers who focus on the financial cost savings to the public-health budget. The third outcome measure reflects a broader societal perspective, combining both public and private-sector cost savings. Increases in all three measures indicate better programme performance.

We measure the economic benefits of the Vi vaccine by the avoided *ex-ante* cost of illness. If the vaccine were 100% effective in preventing typhoid fever, the expected benefits of the vaccine could be estimated by the present value of the *ex-ante* cost of illness avoided during the three years of protection. We calculate the present value of total vaccine benefits over the assumed three-year period of vaccine effectiveness by:

$$PV_B = \sum_{j=1}^{m} n_j \sum_{i=1}^{3} \frac{(\text{Public COI}_j + \text{Private COI}_j)}{(1+r)^i} \quad (1)$$

Where, PV_B=present value of the stream of vaccine benefits to the vaccinated population; Public COI_j=annual *ex-ante* public-sector costs of illness avoided by vaccinating an individual in age cohort j (assuming that the vaccine is 70% effective); Private COI_j=annual *ex-ante* private costs of illness avoided by vaccinating an individual in age cohort j (assuming that the vaccine is 70% effective); n_j=number of individuals vaccinated by the programme in age cohort j; m=number of age cohorts; i=number of years the vaccine is effective; and r=real discount. The vaccine benefits are reported in Table 1.

We assume the real (i.e. net of inflation) discount rate to be 10%.

Vaccine costs

Field data on the costs of running the three different kinds of Vi vaccination programmes in this study population are not available. However, recent estimates of the cost of typhoid vaccination in Viet Nam have been prepared for the International Vaccine Institute based on data from a vaccination trial conducted in Hue, Viet Nam, in 2003. These cost estimates reflect the financial recurrent cost of resources that would be required to conduct a new Vi vaccination programme in Viet Nam. The per-unit vaccination cost was calculated by dividing the total reported expenditure on several cost items (e.g. vaccine dose, syringe, safety box, labour) by the number of vaccinations given. The estimates represent the 'incremental' costs of providing the typhoid vaccine to the target population in the sense that they assume that the existing cold-chain and central administrative structure have sufficient capacity to add the programme without the requirement of investing in additional capacity. The direct recurrent costs are estimated to range from US$ 0.79 to 1.58 per vaccine depending upon the assumptions made about the amount and value of the labour input needed for the vaccination programme (Stewart J. Personal communication, 2004). These per-unit vaccine costs are assumed to reflect the full costs of vaccine acquisition and delivery, including the opportunity costs of resources used in vaccine provision. From a societal cost-benefit perspective, one should add to these recurrent cost estimates the private costs to an individual in terms of transportation and time spent to obtain the vaccine.

Although there are numerous reasons why vaccination costs in India and Viet Nam may differ, we believe that these cost estimates of vaccination for Viet Nam are likely to be generally representative of costs that one would expect in urban India. However, to address the uncertainties in the cost estimates, we conduct our cost-benefit analysis using five assumed values for the per-capita cost of vaccination (V_c): US$ 0.75, US$ 1.00, US$ 1.50, US$ 2.00, and US$ 3.00.

Comparing costs and benefits

We compare the costs and benefits of the three vaccination programmes using five different metrics. First, we present a standard cost-effectiveness ratio: the dollars spent by the public sector on vaccination per typhoid fever case avoided:

$$\frac{\sum_{j=1}^{m} n_j V_c}{\text{Total typhoid fever cases avoided}} \quad (2)$$

Second, we present a ratio of the public-sector treatment cost savings per dollar spent by the public sector on vaccination:

$$\frac{\sum_{j=1}^{m} n_j \sum_{i=1}^{3} (\text{Public COI}_j)/(1+r)^i}{\sum_{j=1}^{m} n_j V_c} \quad (3)$$

Our third cost-effectiveness ratio combines the three types of data in the first two cost-effectiveness ratios (i.e. the number of typhoid cases avoided, the costs of the vaccination programme, and the public-sector cost savings).

It is the public dollars spent on vaccination minus the public-sector cost savings per typhoid fever case avoided:

$$\frac{\left[\sum_{j=1}^{m} n_j\ V_c\right]-\left[\sum_{j=1}^{m} n_j \sum_{i=1}^{3}(\text{Public COI}_j)\big/(1+r)^i\right]}{\text{Total number of typhoid fever fever cases avoided}} \quad (4)$$

This cost-effectiveness ratio shows the net cost to the public sector of avoiding a typhoid fever case, taking into account the fact that the costs to the public sector of vaccination are partially offset by reduced public-sector treatment costs. The numerator is, thus, the net effect on the public-health budget of avoiding a typhoid case. If the public-sector cost savings are greater than the vaccination programme costs, this numerator will be negative, implying that vaccination both reduces the public-health budget and saves typhoid cases, and is a win-win policy intervention.

Fourth, we calculate the total net benefits in the study area of each vaccination programme from the public-sector budgetary perspective:

$$\left[\sum_{j=1}^{m} n_j \sum_{i=1}^{3}(\text{Public COI}_j)\big/(1+r)^i\right]-\left[\sum_{j=1}^{m} n_j\ V_c\right] \quad (5)$$

Fifth, we calculate the net benefits of each vaccination programme from the societal perspective:

$$\sum_{j=1}^{m} n_j \sum_{i=1}^{3} \frac{(\text{Public COI}_j + \text{Private COI}_j)}{(1+r)^i}-\left[\sum_{j=1}^{m} n_j\ V_c\right] \quad (6)$$

Limitations of methods

Several limitations of these benefit-cost calculations need to be emphasized. First, it has been shown both theoretically and empirically that the *ex-ante* cost of illness underestimates the benefits of disease prevention (11). The *ex-ante* private cost of illness does not incorporate (a) the expected pain and suffering due to typhoid fever, (b) the risks of mortality, or (c) the costs individuals may incur for activities that prevent typhoid fever. [Willingness-to-pay (WTP) for the Vi vaccine is a more comprehensive measure of the benefits of reducing the risk of typhoid fever. Individuals' expressed WTP for the Vi vaccine would likely reflect the reduction in *ex-ante* cost of illness, avoided pain and suffering, avoided disability, and the avoided costs of activities to prevent typhoid fever]. To explore the sensitivity of our results to the magnitude of this underestimation of total economic benefits, we multiply *ex-ante* cost-of-illness (public + private) estimates by a 'COI correction factor'–α, that we vary from 1 (no correction) to 4 (which implies that avoided costs of illness represent 25% of the total economic benefits).

Second, the actual incidence of typhoid fever in the study area is difficult to estimate. To show the sensitivity of these cost-benefit calculations to changes in the incidence of typhoid fever in the study population, we use two estimates of incidence. First, we use a conservative estimate based on blood culture-confirmed cases detected by active surveillance (9.8 cases per 1,000). Second, we use a higher estimate based on blood culture-confirmed cases detected by both active and passive surveillance, plus estimates of 'clinical typhoid' (17.5 cases per 1,000).

Third, this analysis only considers the efficiency of alternative Vi vaccine programmes, not the efficiency of typhoid fever immunization programmes relative to other public-health programmes, such as EPI, polio eradication, or prevention of malaria or HIV/AIDS. The magnitude of Vi vaccine benefits relative to other health interventions will determine the priority placed on typhoid fever immunization programmes relative to other public-health programmes. This study also does not compare the efficiency of Vi vaccine programmes with other health interventions for typhoid fever, including water and sanitation improvements, changes in case treatment, or other vaccines for typhoid fever.

RESULTS

Panel A in Table 2 presents the results for the five different metrics for comparing costs and benefits of the mass vaccination programme for different per-unit vaccine costs, assuming an incidence rate in the study area based on blood culture-positive cases detected from active surveillance. Panels B and C show the same set of results for a school-based immunization programme and a pre-school vaccination programme respectively. There are a number of interesting findings from these calculations.

If one looks only at the public cost of avoiding a typhoid fever case (first cost-effectiveness ratio, metric 1), mass vaccination (Panel A) and school-based vaccination (Panel B) look similar. However, pre-school vaccination (Panel C) looks much more attractive. At a per-unit vaccine cost of US$ 1, the public vaccine cost per typhoid case avoided is about US$ 50 for mass vaccination and US$ 41 for school vaccination, but only about US$ 14 for a targeted vaccination programme for pre-school children.

An examination of the second metric (public treatment cost savings per dollar spent on vaccination) shows that from a public-sector budgetary perspective, the mass vaccination and school vaccination programmes do not look attractive at most per-unit vaccine costs, i.e. a dollar spent on vaccination yields less than a dollar reduction in public-sector treatment cost savings. However, a dollar spent on vaccinating 2-5-year old children yields more than a dollar reduction in public-sector treatment cost savings at all vaccine costs shown.

From the perspective of the net public cost per typhoid case avoided (metric 3), both mass vaccination and school vaccination look attractive at low to moderate vaccine costs. For example, at a per-unit vaccine cost of US$ 1, the net public cost of avoiding a case of typhoid is US$ 6 for mass vaccination and US$ 19 for school-based vaccination. Pre-school vaccination is much more attractive. At all per-unit vaccine costs shown, this intervention saves money and typhoid fever cases; in effect, the reduction in typhoid fever cases in this age cohort can make money for the public sector.

If one looks at the net benefits to the public sector (metric 4), the distinction between the three vaccination programmes is most stark. Mass vaccination and school-based vaccination have negative net benefits at almost all vaccine costs. The pre-school vaccination programme has high net public benefits at all vaccine costs shown in Table 2.

From an economic perspective, the net societal benefits (metric 5) are the most important results. In terms of net societal benefits, mass vaccination looks attractive at low to moderate vaccine costs (net societal benefits are positive for mass vaccination at a per-unit vaccine cost of US$ 1.50, but become negative at higher per-unit vaccine costs reported in Table 2). School-based vaccination has slightly lower net societal benefits than mass vaccination. On the other hand, the pre-school vaccination programme has positive net societal benefits at all the per-unit vaccine costs shown in Table 2.

Table 2. Impacts and economic analyses of mass immunization programme, school-based immunization programme, and pre-school immunization programme by vaccine cost (based on incidence of blood culture-positive typhoid fever from active surveillance)

Programmes and programme metrics	Vaccine cost (US$)				
	0.75	1	1.5	2	3
Panel A: Mass immunization programme					
Number of cases avoided	297	297	297	297	297
Public cost/cases avoided (US$/case)	37.25	49.67	74.50	99.33	149.00
Public benefits (US$)/public cost (US$)	1.17	0.87	0.58	0.44	0.29
(Public cost–public benefit)/cases avoided (US$/case)	-6.20	6.22	31.05	55.88	105.55
Net public benefits (=public benefits–public costs) (US$)	1,844	-1,849	-9,233	-16,618	-31,388
Net societal benefits (=total benefits–public costs) (US$)	12,213	8,521	1,136	-6,249	-21,018
Panel B: School-based immunization programme					
Number of cases avoided	165	165	165	165	165
Public cost/cases avoided (US$/case)	30.53	40.70	61.05	81.40	122.10
Public benefits (US$)/public cost (US$)	0.72	0.54	0.36	0.27	0.18
(Public cost–public benefit)/cases avoided (US$/case)	8.57	18.75	39.10	59.45	100.15
Net public benefits (=public benefits–public costs) (US$)	-1,410	-3,084	-6,433	-9,781	-16,477
Net societal benefits (=total benefits–public costs) (US$)	5,485	3,811	463	-2,885	-9,581
Panel C: Pre-school immunization programme					
Number of cases avoided	118	118	118	118	118
Public cost/cases avoided (US$/case)	10.23	13.64	20.47	27.29	40.93
Public benefits (US$)/public cost (US$)	7.72	5.79	3.86	2.89	1.93
(Public cost–public benefit)/cases avoided (US$/case)	-68.72	-65.31	-58.48	-51.66	-38.02
Net public benefits (=public benefits–public costs) (US$)	8,102	7,700	6,896	6,091	4,483
Net societal benefits (=total benefits–public costs) (US$)	10,942	10,540	9,736	8,931	7,323

As shown in Table 3, the cost-benefit results for all of these five metrics are sensitive to the assumptions one makes about the incidence of typhoid fever in the study population. Experienced epidemiologists are confident that estimating the incidence using the number of blood culture-positive cases detected even from active surveillance will result in a significant underestimate

Table 3. Impacts and economic analysis of mass immunization programme, school-based immunization programme, and pre-school immunization programme by vaccine cost (based on incidence of blood culture-positive typhoid fever from active plus passive surveillance plus 'clinical' typhoid fever)

Programmes and programme benefits	Vaccine cost (US$)				
	0.75	1	1.5	2	3
Panel A: Mass immunization programme					
Number of cases avoided	532	532	532	532	532
Public cost/cases avoided (US$/case)	20.81	27.75	41.62	55.50	83.25
Public benefits (US$)/public cost (US$)	1.81	1.36	0.90	0.68	0.45
(Public cost–public benefit)/cases avoided (US$/case)	-16.80	-9.87	4.01	17.88	45.63
Net public benefits (=public benefits–public costs) (US$)	8,943	5,251	-2,134	-9,519	-24,288
Net societal benefits (=total benefits–public costs) (US$)	28,669	24,977	17,592	10,207	-4,562
Panel B: School-based immunization programme					
Number of cases avoided	271	271	271	271	271
Public cost/cases avoided (US$/case)	18.50	24.67	37.01	49.35	74.02
Public benefits (US$)/public cost (US$)	1.11	0.83	0.56	0.42	0.28
(Public cost–public benefit)/cases avoided (US$/case)	-2.06	4.11	16.44	28.78	53.45
Net public benefits (=public benefits–public costs) (US$)	560	-1,114	-4,462	-7,811	-14,507
Net societal benefits (=total benefits–public costs) (US$)	12,381	10,707	7,359	4,011	-2,686
Panel C: Pre-school immunization programme					
Number of cases avoided	179	179	179	179	179
Public cost/cases avoided (US$/case)	6.73	8.97	13.45	17.94	26.90
Public benefits (US$)/public cost (US$)	11.70	8.78	5.85	4.39	2.93
(Public cost–public benefit)/cases avoided (US$/case)	-71.99	-69.75	-65.26	-60.78	-51.81
Net public benefits (=public benefits–public costs) (US$)	12,915	12,512	11,708	10,904	9,295
Net societal benefits (=total benefits–public costs) (US$)	17,332	16,930	16,126	15,321	13,713

of typhoid fever in the population. If one includes the blood culture-positive cases from active plus passive surveillance and the 'clinical' typhoid cases in the calculation of the incidence rate, the cost-benefit results for all three vaccination programmes look much better. The net societal benefits (metric 5) of all three vaccination programmes are positive even at a high per-unit vaccine cost of US$ 2. Importantly, the net public benefits (metric 4) are still negative for mass vaccination if the vaccine costs are US$ 1.50 or higher and are negative for school-based vaccination if vaccine costs are US$ 1 or higher. Pre-school vaccination looks even more attractive from both public and societal perspectives at all vaccine costs.

Just as epidemiologists are confident that the incidence of typhoid fever is significantly higher than indicated by blood culture-confirmed cases, economists are confident that the avoided private costs of illness are a significant underestimate of the actual economic value of risk reduction that a typhoid vaccine provides to individuals. Figure 1 shows how the net societal benefits of the three vaccination programmes change for different 'correction factors' for the magnitude of this underestimation of economic benefits, assuming an incidence rate based on blood culture-positive cases detected with active surveillance. Figure 2 shows the same results for an incidence rate based on blood culture-confirmed and 'clinical' typhoid fever. Note that the lines representing the mass immunization and school-based programmes are so close that they cannot be distinguished from one another.

In both the figures, the area lying above the lines representing the mass immunization and school-based programmes represents combinations of COI correction factors and vaccine prices for which programme benefits are greater than programme costs. In this region, all programmes make economic sense. The area lying between the two lines shown on each graph represents combinations of COI correction factors and vaccine prices for which the pre-school programme benefits are greater than the pre-school programme costs—costs exceed benefits for the other two programmes. The area lying below the line representing the pre-school programme represents combinations of COI correction factors and vaccine prices for which programme benefits are less than programme costs for all three vaccination programmes.

These sensitivity analyses show that, for moderate values of this economic correction factor (1.5-2.0), all three vaccination programmes easily pass a societal cost-benefit test if incidence is based on active surveillance of blood culture-positive and clinical typhoid fever, and the per-unit vaccine cost is less than US$ 3. Even if incidence is based only on blood culture-confirmed cases detected with active surveillance (Fig. 1), all three vaccination programmes still pass a societal cost-benefit test at a per-unit vaccine cost of US$ 3 for a correction factor of 2. The pre-school vaccination programme easily passes a societal cost-benefit test at all per-unit vaccine costs shown even if the avoided public and

Fig. 1. Net societal benefits by COI correction factor and per-unit vaccine cost: sensitivity analysis (Incidence of blood culture-positive typhoid fever from active surveillance)

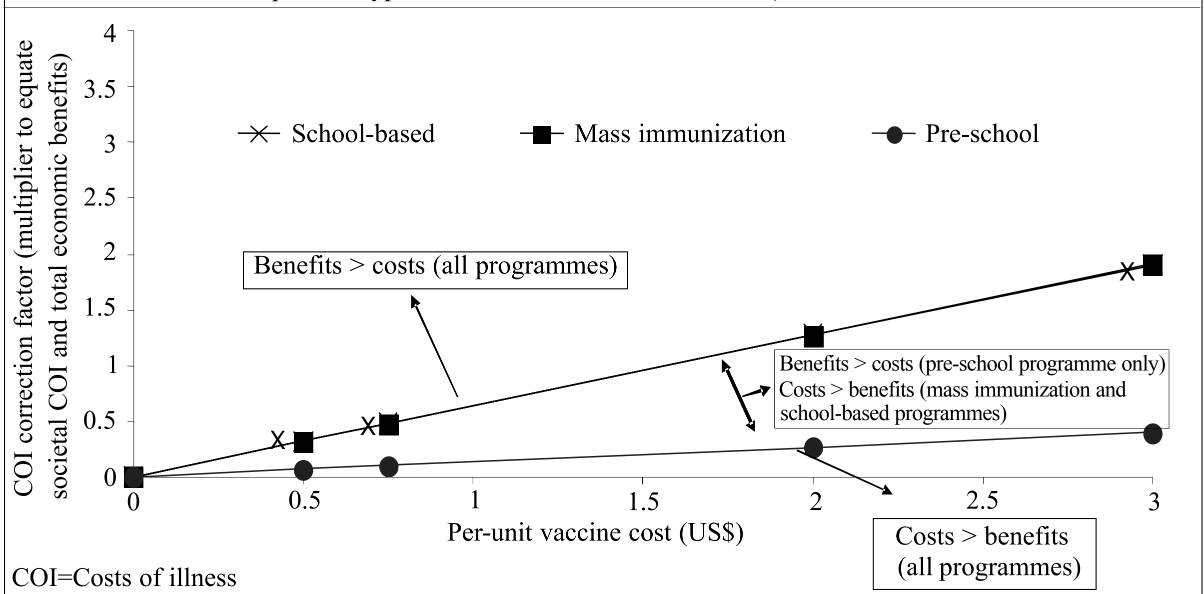
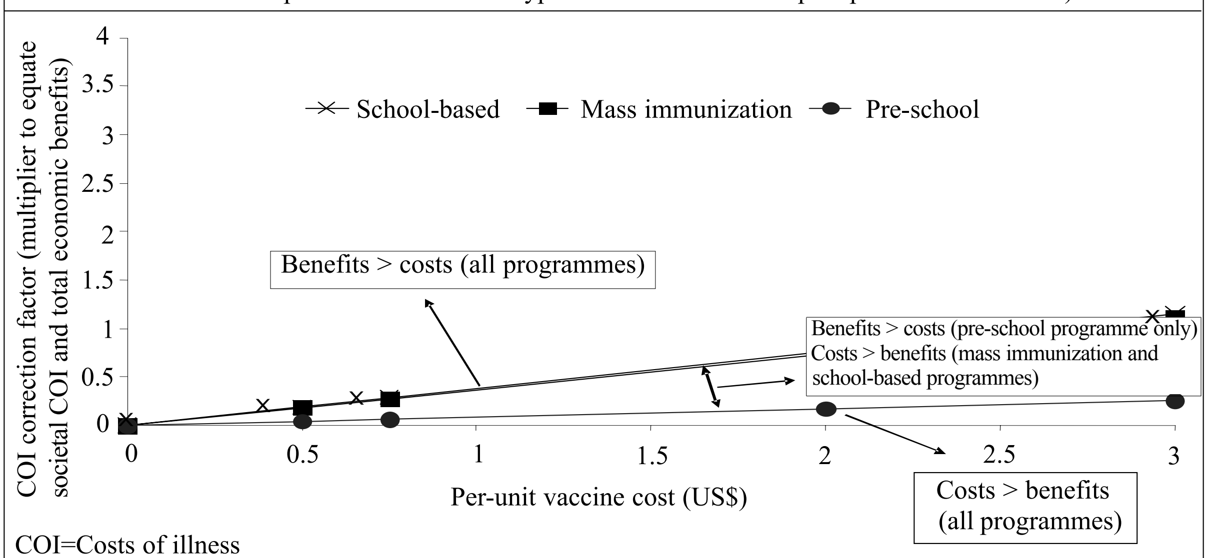


Fig. 2. Net societal benefits by COI correction factor and per-unit vaccine cost: sensitivity analysis (Incidence of blood culture-positive and 'clinical' typhoid fever from active plus passive surveillance)



private cost of illness overestimates the total economic benefits (implying $\propto<1$).

DISCUSSION

Immunizations not only prevent mortality and morbidity, they also reduce the expenditure of public and private resources, permitting increases in consumption or investments that improve individuals' standards of living. Despite these benefits, public immunization programmes must compete with other health interventions and other sectors for resources. Economic studies of immunization programmes often demonstrate the magnitude of benefits of immunization programmes in terms of public-sector budgetary cost savings, but only a few include the private cost benefits to individuals as well.

When attempting to conduct cost-benefit analyses of typhoid vaccination programmes, analysts confront major uncertainties in a number of key input parameters. Three of the most important parameters are: (a) the incidence of typhoid fever in the study population, (b) the per-unit vaccine cost, and (c) the magnitude by which avoided costs of illness underestimate the actual economic benefits of risk reduction that vaccination provides. The results presented in this paper illustrate the sensitivity of cost-benefit calculations to changes in these key assumptions.

The findings illustrate why typhoid vaccination programmes may often appear to be unattractive to public-health officials who adopt a public budgetary perspective. Under many plausible sets of assumptions, public-sector expenditure on typhoid vaccination does not yield comparable public-sector cost savings. Of course, public-health officials need not adopt this decision criterion. If public-health officials have the financial resources to spend on typhoid vaccination and adopt a societal perspective on the economic benefits of vaccination, including not only public cost savings but private cost savings as well, there are many situations in which different vaccination programmes will make economic sense. Our findings show that this is especially true when public decision-makers recognize that (a) the incidence of typhoid fever is significantly underestimated by blood culture-positive cases and (b) avoided costs of illness represent a significant underestimate of actual economic benefits to individuals of vaccination.

On the other hand, the results presented in this paper are illustrative for slum areas with very high incidence of typhoid fever. Typhoid vaccination programmes will look much less attractive from an economic point of view in locations with lower incidence of typhoid fever. For example, our results for a slum community in New Delhi are different from those of Vollaard *et al.*, who speculated that mass immunization against typhoid fever would not be appropriate in Jakarta, Indonesia (12).

Our cost-benefit calculations also illustrate the important differences between a public budgetary and a societal perspective on typhoid vaccination. From a public-sector budgetary perspective, under a wide array of conditions, mass vaccination and school-based vaccination programmes may appear to be unattractive even in a slum with very high incidence rates. This is, in large part, because standard policy interventions are not well-targeted from a public budgetary perspective. School vaccination misses the 2-5-year old children who impose high costs on the public-sector budget. Mass vaccinations would cover these 2-5-year old children, but spend resources vaccinating adults, who impose very low costs on the public-health budget.

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