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The Cost-Effectiveness of Typhoid Vi Vaccination Programs: Calculations for Four Urban Sites in Four Asian Countries

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Abstract

The burden of typhoid fever remains high in impoverished settings and increasing antibiotic resistance is making treatment costly. One strategy for reducing the typhoid morbidity and mortality is vaccination with the Vi polysaccharide vaccine. We use a wealth of new economic and epidemiological data to evaluate the cost-effectiveness of Vi vaccination against typhoid in sites in four Asian cities: Kolkata (India), Karachi (Pakistan), N. Jakarta (Indonesia), Hue (Vietnam).

We estimate that a vaccination program targeting all children (2–14) would cost US\$189, US\$232, and US\$712 per DALY averted in Kolkata, Karachi, and N. Jakarta. These programs would be considered “very cost-effective” under a wide range of assumptions. Community-based vaccination programs that also target adults in Kolkata and Jakarta are less cost-effective because incidence is lower in adults than children, but are also likely to be “very cost-effective.” Any type of program in Hue, Vietnam would not be cost effective (US\$3,924 per DALY averted for a program targeting children 5–14 years old) because of the low typhoid incidence there.

Although the study does not address the important question of whether the social economic benefits of vaccination exceed the social costs, Vi vaccination programs targeting children in the sites in Kolkata, Karachi and N. Jakarta look to be attractive investments. They would be among the better half of interventions for Asia compiled by the Disease Control Priorities Project, although health policymakers will want to carefully compare the cost effectiveness of Vi vaccination with other public health priorities.

Key Words: typhoid vaccination, cost effectiveness, Kolkata, Karachi, Jakarta, Hue

1. Introduction

Typhoid fever, caused by the bacterium *Salmonella enterica serovar Typhi* (hereafter referred to as *S. typhi*), is transmitted through contaminated food or water and characterized by high fever, chills, nausea, headaches, and malaise, and sometimes delirium.¹ The global burden of typhoid fever was estimated at 21 million cases and more than 200,000 deaths in 2000 and south-central Asia is believed to have the highest incidence rates.² The true burden of disease is thought to be higher because of under-reporting and inadequate surveillance.² Resistance to antibiotics is a growing problem.¹ Ochiai et al.³ reported multi-drug resistance to first line antibiotics (chloramphenicol, ampicillin, and co-trimoxazole) of up to 67% in *S. typhi* isolates in a surveillance study in Karachi, Pakistan and rates of naladixic acid resistance (indicating reduced effectiveness of ciprofloxacin and other fluoroquinolones) of 44% to 59% in Hue, Vietnam; Kolkata, India; and Karachi, Pakistan. Griffin⁴ reported that 14% of typhoid patients in a Delhi slum in 1998 did not respond to a 10-day course of ciprofloxacin, and Bahl et al.¹ found that the cost of illness for persons with typhoid that did not respond quickly to antibiotics was five times higher than for those who were successfully treated.

Although improvements in water and sanitation infrastructure and food hygiene could reduce the disease burden and lessen the threat of antibiotic resistance, another strategy to reduce typhoid cases in the near term is vaccination with new-generation vaccines in high-risk areas. The Vi polysaccharide vaccine is given as an injection and requires only 1 dose.¹ The best available estimates indicate the Vi vaccine is safe and 65% protective, with protection lasting at least 3 years.^{5, 6, 7} This vaccine is internationally licensed for children 2 years of age and older.^{8, 9} The liquid formulation of the live oral vaccine (Ty21a) is also licensed for children 2 years and older. This vaccine requires 3–4 doses at closely spaced intervals and is more expensive than the Vi polysaccharide vaccine.¹ Newer Vi-based vaccines are under development in which Vi polysaccharide is chemically conjugated to a recombinant exotoxin protein (Vi-rEPA, or the “Vi conjugate”) or another carrier protein. Unlike the Vi vaccine, these conjugate vaccines have the potential to protect children under 2 because they induce a T cell-dependent immune response in young children.^{1, 10} Trials have shown the Vi-rEPA vaccine is safe and effective

(almost 90% after 4 years) in children aged 2–5,^{1, 11} but no studies have yet tested the vaccine in children under 2.

Because health resources are limited in many areas where typhoid is endemic, it is important for local, national, and global health policymakers to evaluate the economic attractiveness of typhoid vaccination programs in relation to other possible health interventions. The goal of this paper is to report on detailed cost effectiveness analyses of Vi polysaccharide vaccination programs against typhoid fever in four urban settings in four Asian countries using a wealth of new data collected by the Diseases of the Most Impoverished (DOMI) program.

There are relatively few published economic evaluations of typhoid vaccination programs. Papadimitropoulos et al.¹² examined the cost-effectiveness of 2 types of typhoid vaccines (Ty21a and Vi polysaccharide) for travelers. They found that neither vaccine was cost-effective unless travelers were going to areas with very high incidence rates (200 cases/million travelers) or expected to be in very close personal contact with local inhabitants. Bahl et al.¹³ examined incidence (through both active and passive surveillance) and cost-of-illness in an urban slum in Delhi, India. They found total mean costs of illness were roughly the same across age groups (~\$100 per case in US\$1996), though the public share of costs was much higher for preschool children (aged 2–5), largely because these children were more likely to be hospitalized. Mean annual expected, or “ex-ante,” costs were on the order of US\$0.11–\$0.22 for adults and US\$3.42–\$5.22 for preschool children (US\$1996).

Under a range of vaccine cost estimates, Poulos et al.¹⁴ found that immunizing preschool children against typhoid fever in the same (high-incidence) slum in Delhi would actually be cost-saving to the public sector. They also found that immunizing other age groups would likely pass a social cost-benefit test when privately-borne costs of illness were counted as benefits of vaccination. Using a contingent valuation approach in Hue, Vietnam, Canh et al.¹⁵ provided a more complete picture of the private economic benefits of a Vi typhoid vaccine. They found that the private benefits that would accrue to the average household in Hue (with 5.6 household members), if all household members received a Vi vaccine, ranged from US\$21–\$27. They found that a vaccination program without user fees would most likely

pass a social cost-benefit test, but that there was also significant potential for the program to be self-financing through user fees.

This previous work on the economic attractiveness of typhoid vaccination programs can be greatly enriched using the results of recent research from the Diseases of the Most Impoverished (DOMI) Program. The DOMI program, administered by the International Vaccine Institute, involved a number of parallel activities, including epidemiological studies, economic studies, and investigation of the feasibility of vaccine technology transfer. It represents a unique set of site-specific economic and epidemiological data.

2. Methods

a. Sites

The sites included in this analysis correspond to the areas with typhoid fever surveillance studies reported in Ochiai et al.³ In Kolkata (India), we model the effects of vaccinating two densely populated urban slums—Tiljala (Wards 59,60) and Narkeldanga (Wards 29,30)—with a combined population of about 185,000 people. We do not analyze programs to vaccinate the entire city. Similarly, we examine programs in two impoverished municipal sub-districts in North Jakarta, Indonesia, with a total population of 161,000 (Tanjung Priok and Koja). Hue is a regional capital in central Vietnam with a population of 280,000 consisting of both urban areas and semi-urban areas at the periphery of the city. The disease surveillance studies included the entire city,³ so we assume vaccinations would occur city-wide in Hue. In Karachi (Pakistan), we examine programs targeting three squatter settlements (Hijrat Colony, Sultanabad and Bilal Colony), with a combined population of 102,000.

Our results pertain only to the cost effectiveness of vaccination in these specific locations and cannot be extrapolated to the country-level. Nonetheless, the cost-effectiveness model that we use could be readily modified to include other locations, or nation-wide programs.

b. Modeling approach

Our analysis employs standard cost-effectiveness methods used by the Disease Control Priorities Project¹⁶ and WHO’s CHOICE project.¹⁷ We first assess the baseline burden of disease in terms of cases, deaths, and disability-adjusted life years (DALYs) for each of the four urban sites. Because we use DALYs for our health outcome measure, we incorporate reductions in morbidity from vaccination (years of life lost to disability or YLD) as well as reductions in typhoid mortality (years of life lost or YLL). Following convention, we use uniform age weights that apply the same value to an extra year of life regardless of the age of its recipient. To calculate the number of life years saved from mortality reductions, we use country-specific life expectancies (*LE*) from WHO life tables and discount life years using a 3% real (i.e., net of inflation) discount rate.^{16, 17} Equations 1–4 below show the calculation of DALYs avoided:

$$\text{DALYs avoided per year in age group } i = \text{YLL avoided per year} + \text{YLD avoided per year} \quad (1)$$

$$\text{YLD}_i \text{ avoided per year} = [((1-\text{CFR}_i) \cdot \text{Eff} \cdot \text{Cover}_i \cdot N_i \cdot I_i) \cdot \text{Length} \cdot \text{DALY weight}] \quad (2)$$

$$\text{YLL}_i \text{ avoided per year} = [((\text{CFR}_i \cdot \text{Eff} \cdot \text{Cover}_i \cdot N_i \cdot I_i) / 0.03) \cdot (1 - \exp(-0.03 \cdot \text{LE}_i))] \quad (3)$$

$$\text{Total DALYs avoided in age group } i = \sum_{t=0}^{Dur} (\text{DALYs avoided per year}_i) / (1 + 0.03)^t \quad (4)$$

where *i* indexes the age group targeted, *Eff* is the effectiveness of the vaccine, *Cover* is the percentage of the age group who would be vaccinated if the vaccine were provided free, *CFR* is the case fatality rate, *Length* is the disease’s average duration (i.e., number of days sick with typhoid), *N* is the number of people in age group *i*, *Dur* is the vaccine’s duration, and *I* is the group’s typhoid incidence.

We examine three types of typhoid Vi vaccination programs. All three options involve campaigns rather than routine immunizations because the Vi vaccine is not effective in children younger than 2 and cannot be included in the infant EPI schedule. The first two options involve school-based vaccination since typhoid incidence is typically highest in this age group. The first school-based option (Option 1) would target only children 5–14 years old actually attending school. The second school-based

option (Option 2) would target all children who are old enough to receive the vaccine safely (2 years) but younger than 15 years. We assume that mothers could bring younger children (2–4 years old) to the school for vaccination. The third type of program (Option 3) would target adults as well as eligible children and would require a community-based vaccination campaign. For all three program options, we assume a one-period model, i.e., we estimate the costs of immunizing the target population in year 1, and compare these costs with the effects on disease burden over the duration of the vaccine’s effectiveness (3 years). Because the Karachi disease surveillance studies did not include adults, we only evaluate the school-based options (Options 1 & 2) in this site. Similarly, disease surveillance in Hue included only 5–18-year-olds so we evaluate only a school-based option for children 5–14 years old (Option 1).

We consider the costs of the vaccine program options from a public sector financial perspective. Vaccine manufacturing/acquisition costs and delivery costs (discussed below) are assumed to be borne by the government (public) sector and we assume there are no user fees collected from vaccine recipients. We reduce vaccination program costs by the cost of illness that would have been borne by the public sector if the vaccination program had not been implemented, again using a real discount rate of 3%.¹⁷ We call the result after this subtraction “net public cost.” In practice, public treatment cost savings may be difficult to convert to cash to pay for vaccination programs.

We report the commonly used thresholds for “cost-effective” and “very cost-effective” that compare the net public cost per DALY to per capita income.^{17, 18} A “very cost-effective” intervention is assumed to be one with a cost-effectiveness ratio less than per capita GDP, and a “cost-effective” intervention is one with a ratio less than three times per capita GDP.¹⁹ Satisfying these thresholds is probably a necessary but not a sufficient condition for a vaccination program option to be attractive from an economic perspective. Financial resources for health are limited in these settings and other interventions that also qualify as “highly cost-effective” may have even more attractive cost-effectiveness ratios. Furthermore, our cost effectiveness analysis should not be confused with a full accounting of all the social benefits and costs of the program options. We return to this limitation of cost-effectiveness analyses in the concluding section of the paper.

c. Construction of Base Case and Sensitivity Analysis

The first step in our cost-effectiveness analysis is to calculate the cost-effectiveness ratios of the three program options for the “base case” set of parameter values presented in Table 1. We then investigate the impact of uncertainty in the parameters with two types of sensitivity analysis. The first examines the impact of varying a few of the most important parameters (cost per fully vaccinated individual, incidence, and case fatality rates) individually while keeping all other parameters at their base case values. The second sensitivity analysis uses a probabilistic Monte Carlo framework that allows all uncertain parameters to vary simultaneously. The lower and upper bounds for each parameter are presented in brackets in Table 1. We used Crystal Ball, a Microsoft Excel plug-in, to run the simulations. The results presented used 10,000 draws from triangular parameter probability functions for most variables, with low and high ends of the distribution set to the uncertainty bounds, and the peak of the triangle (the most likely value) set to the base case value. For the duration of the vaccine’s effectiveness, we use a discrete probability function where the probability of the vaccine having the base case duration (3 years) is 0.5, and the probability of the vaccine protecting 1 year less or 1 year more is 0.25 each.

d. Model Parameters

i. *Epidemiological parameters*

Data on baseline typhoid incidence come from a recent compilation of multi-year surveillance in each of the four DOMI sites.³ The observed typhoid incidence is generally highest in school-aged children (5–14), ranging from 0.26 cases per 1,000 in Hue to 4.9 cases per 1,000 in Kolkata (Table 1). With the exception of Karachi, observed incidence in young children is lower than incidence in school-aged children, and adult incidence is still lower (in the two sites with adult surveillance data). Overall, Kolkata and Karachi represent the sites with highest incidence, Hue has the lowest incidence, and North Jakarta falls in between. Although blood-culture tests for identification of *S. typhi* isolates are still considered the gold standard due to their high specificity, they are known to produce false negatives in

32–70% of samples.³ For our base case models, we follow Ochiai et al.³ and double the incidence rates in Table 1 to account for this. For uncertainty analysis, we use the 95% confidence intervals from Ochiai et al.³ (shown in brackets in Table 1).

We use 65% as the base case for vaccine efficacy, ranging from 55–75% in the uncertainty analysis.^{8,9} Although indirect (herd) protection may reduce cases even further, we include only direct protection in our analysis because reliable empirical evidence of herd protection from typhoid vaccination is not available. We assume the duration of the vaccine's protection ranges from 2 years to 4 years, with a base case value of 3 years.^{8,9}

According to the WHO,²⁰ the case fatality rate (CFR) for typhoid cases treated with antibiotics is about 1%. CFR without treatment can range from 4% to 10%.²⁰ The CFR in a January 2005 outbreak in Congo was 0.5% (214 deaths in 42,564 cases).²¹ Crump, Luby, and Mintz² use 1% based on "conservative estimates from hospital-based typhoid fever studies, mortality data from countries with reliable national typhoid fever surveillance systems that employ blood culture confirmation of cases, and expert opinion." Parry et al.¹ also list 1% as a good estimate, though they report fatality rates of 30–50% in parts of Papua New Guinea and Indonesia. For our analysis, a mean case fatality rate for typhoid of 1% is assumed for all four study sites, with lower and upper bounds of 0.5% to 3% for the uncertainty analysis (Table 2).

Parry et al.¹ reported a range of "mean fever clearance times" with different antibiotics from 4 to 7 days, increasing to a mean of 9 days in "clinical failures" or cases where antimicrobials were not initially successful. Treatment times can increase to 21 days if third-line antibiotics (e.g., cephalosporins) are necessary.¹ We assume the average typhoid case lasts 1 week, with lower and upper bounds of 4 days and 3 weeks.

We use a mean DALY weight of 0.27, which lies within a range of weights for somewhat similar diseases (malaria, Japanese encephalitis, dengue, upper respiratory infections).¹⁷ The lower bound and upper bounds are those for dengue fever (0.08) and neurological sequelae of malaria (0.47).

ii. *Cost-of-illness*

The DOMI project's economic studies provide data on the costs of illness from contracting typhoid fever, both to the public sector and to individuals.²² Because we take a public sector financial perspective, we focus here on public cost of illness (COI) rather than private COI, although both are needed to evaluate whether an investment in typhoid vaccines would pass a social cost-benefit test. Public COI is estimated from data obtained from facilities-based studies (both hospitals and outpatient settings) using a micro (i.e., bottom-up) costing approach²² and applying the rates of hospitalization obtained from the disease surveillance studies to get average weighted costs.

iii. *Demand for typhoid vaccines*

DOMI also conducted studies of private vaccine demand that estimated the quantity of typhoid vaccines demanded by households as a function of price.^{15, 23–25} These studies provide an estimate of anticipated coverage levels for different ages given the provision of a free vaccine. The quantity of typhoid vaccines demanded at a price (user charge) of 0 was estimated from responses to questions posed to respondents in contingent valuation surveys. These estimates of vaccine demand at a 0 price were adjusted to account for the effect of giving respondents time to think about their answers. Several studies of private demand for cholera and typhoid vaccines have found that respondents who were given the opportunity to consider the vaccine scenario overnight expressed more certainty about their responses and lower willingness to pay.^{23, 24, 26, 27} We adjust coverage levels in the four sites to reflect the average effect of time to think from these studies (without this adjustment, coverage levels would be 10–15% higher). For sensitivity analysis, we further vary these time-to-think-adjusted estimates by +/- 20% of their base value. Furthermore, we assume that 80% of people would be informed of the vaccination campaign through a social marketing campaign. We do not vary the percentage of people informed of the program in the sensitivity analysis because it has little effect on the ratio of costs to disease-reduction benefits.

iv. *Vaccine costs*

The social cost of a typhoid vaccination program is composed of three main components: (1) the cost of acquiring vaccines from the manufacturer; (2) the cost of delivering and administering the vaccine to the target population; and (3) the time and pecuniary costs incurred by household members to travel to the vaccination outpost and to wait to receive the vaccine. Following standard practice, we do not include the third cost component in our estimate of the costs of a vaccination program. Neither of the first two cost components is known with certainty. They depend on a number of factors for which there is little information in the published vaccine cost literature. For the cost estimates used in this paper we rely on data collected on vaccination costs during the Vi demonstration projects in the DOMI study sites and a recent review and analysis of this literature by Lauria and Stewart.²⁸

The acquisition cost depends largely on whether or not manufacturing technology has been transferred to local producers. This type of technology transfer has been successfully accomplished in Vietnam, where the locally produced Vi vaccine is sold to the public sector for around US\$0.56 per dose in 2007 dollars.²⁹ Several private sector Indian producers have also acquired the technology and have offered prices to the public sector of \$0.45 per dose or less for multi-dose vials.³⁰ As a base case, we assume that all countries can purchase Vi vaccine from one of these developing country manufacturers at a price of US\$0.45 per dose. We add 15% to the price (\$0.067 per dose) to cover customs, insurance, and freight based on the average percentage used by UNICEF.²⁸ Furthermore, we assume 10% wastage of vaccines (adding US\$0.052 after customs, freight, and insurance have been added). We therefore use a total base case acquisition cost, including the cost of wastage, customs, freight, and insurance, of US\$0.57 per dose. We use the same base case acquisition cost for all sites, including Vietnam and India, which already have local production, because the cost of customs, freight, and insurance are within the overall margin of error. We vary this acquisition cost in the sensitivity analysis from US\$0.4 to US\$0.8 per dose.²⁸

Delivery costs depend on a number of factors including the type of campaign (routine vs. school-based vs. community-based) and the size of the target population; the type of facilities used (existing

health clinics vs. temporary vaccination outposts) and their operating hours; the number of health workers required, the efficiency with which they are deployed, and their wage rates; the number of doses required; whether the vaccine is administered alone or with other vaccines; cold storage requirements; and the scope of the information and education campaign directed at the target population. Lauria and Stewart²⁸ find some evidence that there may be economies of scale in delivery for densely populated urban areas but diseconomies of scale (i.e., average delivery costs increase with larger numbers of people vaccinated) in rural areas. They also find diseconomies of scale in their analysis of delivery cost data from a survey of 30 studies of EPI programs in Africa and Asia in the 1980s and 1990s.³²

Delivery costs in the published literature vary widely, even for similar programs (e.g., EPI vaccinations). The reviews of both Walker and Fox-Rushby³³ and Pegurri et al.³⁴ found that most economic evaluations of vaccine lacked transparency in the calculation of costs. Walker and Fox-Rushby³³ found that many studies also overlooked donated costs such as vaccines, supplies, equipment, and volunteer time. Furthermore, many economic evaluations assume that the vaccination programs can be readily implemented through existing health infrastructure (typically the country's EPI vaccination program) with minimal additional delivery costs.³⁵ This will generally not be the case with typhoid vaccination programs, since typhoid affects mainly older children and Vi would need to be provided in campaigns outside of the infant EPI schedule. Countries may, however, follow the WHO's recommendation to harmonize Vi vaccination with school-based diphtheria or tetanus vaccination.

The only published estimate of delivery costs for typhoid vaccines is from a cost-benefit analysis for a slum community in India, although it is based on a personal communication about an unpublished study in Vietnam.¹⁴ The authors use a delivery cost estimate of US\$0.9–\$1.7 (in 2007 dollars). Lauria and Stewart²⁸ review data from 22 vaccine cost studies in low and middle income countries, including unpublished cost data from several DOMI vaccine trials, and find that the median delivery cost per dose (after removing four outliers) is US\$0.8 (mean US\$1.1), with estimates ranging from US\$0.10 to US\$5.7 per dose. Because delivery costs in middle income countries tend to be twice those in low income

countries,^{18, 36} Lauria and Stewart's best judgment is that delivery costs are on the order of US\$0.5 per dose for low income countries and US\$1.0 per dose for middle income countries.

We follow a commonly-used convention in the cost-effectiveness literature (see Sinha et al.³⁷ for a recent example) and assume that delivery costs are captured in a constant marginal cost per vaccinated individual rather than including fixed (i.e., set-up) costs. This implies constant returns to scale in vaccination. We assume that the marginal delivery cost per dose is the same for a school-based program (Options 1 and 2) as for a community-based vaccination program (Option 3). It is possible that average delivery costs for school-based programs may be lower than for community-based programs because there may be other school-based programs a vaccination program shares costs with, because health staff time might be used more efficiently, and because less social marketing might be needed. We feel, however, that the body of evidence is not strong enough to warrant the use of different delivery costs for our program options.

For India, Pakistan, and Vietnam, low-income countries with gross national incomes per capita on the order of US\$800–\$900, we use Lauria and Stewart's estimate of US\$0.5 per dose for delivery costs. For the sensitivity analyses, we base the uncertainty ranges on the 16 studies for low-income countries reviewed by Lauria and Stewart. The 12.5%–87.5% confidence interval (obtained by dropping the two highest and two lowest delivery cost estimates) is US\$0.3–US\$2.5 per dose, which we use as the uncertainty bounds. For Indonesia, a middle-income country with a GDP per capita of US\$1,800, we use Lauria and Stewart's estimate of delivery costs for middle income countries of US\$1.0 per dose. Because their study only included six middle-income countries and because costs are assumed to be twice as high in middle income countries, we derive the uncertainty range by doubling the range described above for low-income countries, or US\$0.6–US\$5.0 per dose.

3. Results

a. Base case

Option 1—School-based vaccination targeting only school-age children

The main difference in cost-effectiveness results among the four sites and within a program option stems from differences in baseline typhoid incidence (Table 3). In Option 1 (targeting only children 5–14 years old who attend school), a program in the two urban slums in Kolkata has the most attractive cost-effectiveness (CE) ratio (US\$189 per DALY averted). We estimate that about 20,100 school children would be vaccinated at a total cost of US\$21,530, preventing 384 typhoid cases over 3 years. Preventing these 384 cases would reduce public expenditures on treating typhoid by only US\$1,493 (with savings in years 2 and 3 discounted at 3%), for a net public cost of \$20,032. None of the programs examined in any of the four sites would be “cost saving” because expected public sector treatment cost savings are much less than vaccination program costs for the base case and for the entire range of plausible vaccine cost estimates.

Compared to the Kolkata slums, the three settlements in Karachi have a somewhat lower baseline incidence among school-aged children and a lower public COI per case. As such, the costs per DALY avoided are higher for Option 1 in Karachi (US\$232 per DALY). The two sub-districts in North Jakarta have lower incidences than both the Kolkata or Karachi sites and higher delivery costs per dose, yielding ratios of \$712 per DALY averted for Option 1. However, programs targeting school children would be considered “very cost-effective” in all three of these sites because the costs per DALY are less than per capita GDP (shown for reference in the bottom row of Table 3).

The incidence is an order of magnitude lower in Hue than the other three sites, so the CE ratio for Option 1 is an order of magnitude higher (US\$3,924 per DALY avoided). This program would not be considered “cost-effective.”

Option 2—School-based vaccination targeting school-age and younger children

Option 2 is a school-based program that would make vaccines available to all children (aged 2–14) in the study sites. Because children must still be old enough to be safely vaccinated (≥ 2 yrs), the difference between Options 1 and 2 is simply adding young children (aged 2–4.9 yrs old) to Option 1. The main effect of adding young children, then, is to increase the number of vaccinations, the number of cases avoided, and the total costs. For example, Option 2 for the two Kolkata slums would vaccinate 5,402 more children than Option 1, avoiding 72 more typhoid cases but costing \$5,780 more in total program costs. Because these effects move in parallel, the difference in cost-effectiveness ratios is very small. In Kolkata, Option 2 has a net public cost of US\$202 per DALY avoided vs. US\$189 for Option 1. Including young children is only slightly less cost-effective than Option 1, because young children have a lower baseline incidence than school children in Kolkata (3.4 per 1000 vs. 4.9 per 1000 in school children, see Table 1). This is also true in North Jakarta, where Option 2 is slightly less cost effective than Option 1 (US\$735 per DALY vs. US\$712). The opposite is true in Karachi, where young children have higher incidence than school children, so Option 2 is slightly more cost effective than Option 1 (US\$211 per DALY vs. US\$232 in Option 1).

Option 3—Community-based vaccination targeting adults and children

Community-based vaccination programs that target adults as well as children have less favorable cost-effectiveness ratios in the two sites with adult incidence data because incidence is lower in adults than in children. A community-based vaccination program targeting the two Kolkata slums would vaccinate many more people (91,000 people) than either of the first two options at a higher net public cost (US\$97,300, or US\$477 per DALY avoided). This ratio, however, would still meet the “very cost-effective” criterion. A community-based vaccination program in the two North Jakarta districts would vaccinate 46,000 people at a net public cost of US\$72,200. At US\$1,221 per DALY averted, this ratio is also “very cost-effective.”

b. Sensitivity analyses

Which model parameters have the largest effect on cost-effectiveness?

The five parameters that have the largest effect on the ratio of net public cost per DALY are vaccine cost, the case fatality rate, the vaccine's duration, the baseline incidence, and the vaccine's effectiveness. In almost all cases, the ratio is most sensitive to vaccine cost. Figures 1–3 show the one-way sensitivity analysis for cost, or the effect of varying only the cost parameter within the uncertainty range in Table 1 and leaving all other parameters at their base case value. For Option 1 (targeting school aged children only) in Kolkata, for example, the ratio varies from US\$119 per DALY avoided if the total cost per vaccinated person is US\$0.7 to US\$611 per DALY if the cost is US\$3.3 per person. Within the entire range of assumptions about vaccine cost, however, the program would be “very cost-effective.” This is true for Options 1 and 2 in both Kolkata and Karachi. Program Option 3 would be “very cost-effective” in Kolkata if the total cost per vaccinated person were less than US\$2.0. Options 1, 2, and 3 would be “very cost-effective” in North Jakarta if total vaccine costs were less than US\$3.8, US\$3.7, and US\$2.3. The program in Hue would not be “cost-effective” within the entire range of plausible vaccine cost estimates.

Table 4 shows the one-sensitivity analysis for the other parameters which have the largest effect on cost-effectiveness. For Options 1 or 2 in Kolkata, North Jakarta, and Karachi, the choice of individual parameter estimates does not change the overall assessment of whether the program is “very cost-effective”: the CE ratios for these programs in these locations are nearly always lower than GDP per capita. Similarly, within the entire assumed range of parameter estimates for Hue, the CE ratio is always larger than US\$800 per DALY, and “cost-effective” only for the highest value of case fatality rate (3%) or incidence (0.43 cases/1000).

Monte Carlo simulations

Finally, we allow all parameters to vary simultaneously in a Monte Carlo framework. Table 5 presents the median costs per DALY avoided, 95% confidence intervals, and probability that the net

public costs per DALY will be less than per capita GDP for all three program options. Again, programs targeting school-aged children only (Option 1), or targeting younger children as well (Option 2) in Kolkata, Jakarta and Karachi (Option 2) are the most attractive, and will certainly pass the GDP cost-effectiveness threshold. Programs in Hue will not pass this threshold due to the low typhoid incidence in this site.

4. Discussion

Our results indicate that typhoid vaccination programs targeting children (Options 1 or 2) have “very cost-effective” ratios in the high-incidence areas of Kolkata, Karachi, and N. Jakarta. The CE ratios in the Kolkata and Karachi slums (US\$189–US\$232 per DALY) are somewhat higher than recent estimates for country-wide pneumococcal vaccination (~US\$70 per DALY) in countries with the highest under 5 mortality rates.³⁷ Recent estimates for rotavirus, another enteric disease, ranged from US\$20–US\$638 per DALY in low income countries in Asia (when vaccination costs ranged from US\$2–US\$60 per course).³⁸

Although the CE ratios are quite sensitive to our estimated cost per vaccinated person, our conclusions hold across a range of plausible assumptions about vaccine cost, case fatality rate, incidence, and vaccine effectiveness. Comparing Options 1 and 2, the program targeting only school children (Option 1) has a slightly lower CE ratio in Kolkata and Karachi, but slightly higher ratio in Jakarta. On balance, we think the economic differences between Options 1 and 2 are minimal, and that there is a strong moral argument for including young children in a vaccination program.

Community-based vaccination programs that include adults as well as children have less favorable cost-effectiveness ratios because child incidence is greater than adult incidence in all sites. Still, community-based programs in Kolkata and N. Jakarta would be “very cost-effective.” We assume pre-schoolers can be vaccinated through a local school, which might be logistically challenging in practice. Because we assume the same delivery costs for school- and community-based vaccination programs, however, this assumption does not alter the cost-effectiveness ratios.

No program in Hue is likely to be cost-effective for any of the three program options. This conclusion is driven by the low typhoid incidence in Hue and holds across a range of plausible parameter values. Typhoid vaccination may, of course, be more attractive in other sites in Vietnam where incidence is higher. Lin,³⁹ for example, reported a blood culture confirmed incidence level (5.3 per 1000) among 5–9 year olds in Dong Thap province similar to that observed in Kolkata and Karachi.

In addition to asking the question of whether typhoid vaccination is cost-effective, a donor or policy maker might take a social cost-benefit perspective and ask whether the economic benefits of a vaccination program that provides vaccines for free exceed its economic costs. The cost-effectiveness approach presented in this paper avoids placing an economic value on preventing a case of typhoid, subsuming all economic benefits within the DALY metric and simply comparing the costs of preventing one more DALY across policy interventions. Although a DALY measure reflects both the (non-monetized) morbidity and mortality outcomes of the vaccination intervention, it may be undesirable to assume that the value of the risk reduction obtained from vaccination applies equally for heterogeneous populations in four different countries. A program with an unfavorable ratio of net public cost per DALY may still pass a social cost-benefit test, and vice versa.

A more comprehensive picture of economic costs and benefits would include at least the private cost-of-illness avoided (Table 6), including both financial costs (lost wages, payments for medicine) and the time and monetary costs individuals incur in traveling to a health clinic and waiting to be seen. In many settings privately borne COI is a substantial proportion of the total costs of illness.²² It would also include the value of mortality risk reductions. In a contingent valuation survey of cholera vaccines in Beira, Mozambique, 55% of respondents said that the most important benefit of the vaccine was reducing their risk of dying.²⁶ These types of benefits can be observed through labor hedonic studies or measured through stated preference techniques, where willingness-to-pay for a vaccine should incorporate ex-ante private COI and the benefits of mortality risk reduction, as well as other benefits that are more difficult to measure (risk aversion, pain and suffering).

Finally, a full a social cost-benefit perspective would also take account of the cost to vaccine recipients of traveling to the vaccination site and waiting to be seen.⁴⁰ In many instances, this cost may be substantial for adults. Although free vaccination is one strategy for helping the poor, where queues are long and vaccination clinics are inconveniently-located, the poor may not be able to afford time away from their work to bring their children to be vaccinated. In this paper, our cost-effectiveness analysis took a public financial perspective on vaccination costs that ignored these private costs. One might believe that benefits (for example mortality reductions, pain and suffering, and private COI) are adequately captured in the DALY measure of health outcome, but conventional approaches to cost-effectiveness analysis such as those used in this paper consistently miss these private costs to individuals.

Our analysis also ignores the potential to recover some or all of vaccination costs by asking users to share the costs through user fees. Government health resources are extremely limited in the countries in question and there may not be sufficient funds for the health ministries to pay for a typhoid vaccination program without an increase in per capita spending on health. In India, for example, public sector per capita spending on health was ~US\$ 4.5 in 2001–2002 according to the Indian Ministry of Health's National Health Accounts data.⁴¹ On a per capita basis, a typhoid vaccination program in the two slums that cost US\$1.1 per vaccinated individual would consume nearly a quarter of public sector health care spending. In addition, some donors may view their role as catalysts for health improvements in the short-run while expecting that local governments will eventually take over financial responsibility for the vaccination program in the medium term.⁴² This is particularly important for typhoid vaccines because the duration of protection is limited and re-vaccination must occur every 3 years to ensure continued protection. It may be possible to charge adults user fees that cross-subsidize vaccines for children.⁴³

Finally, the principal usefulness of cost-effectiveness analysis is not in comparing ratios with an absolute threshold such as per capita GDP, but rather in the ability to compare various policy interventions using a common metric. A donor or health policymaker interested in investing in typhoid vaccination programs in any of these four sites should carefully consider the burden of other diseases in each site and other health interventions that could improve health status. Information on the cost-

effectiveness of these other programs would ideally be site-specific, but the Disease Control Priorities project¹⁶ provides a useful compendium of the cost-effectiveness of a range of health interventions, particularly in identifying “neglected low-cost” health programs. Programs that achieve disease reductions for under \$1000 per DALY (Options 1 and 2 for Kolkata, Karachi and Jakarta, and Option 3 for Kolkata) are among the better half of interventions listed in Laxminarayan et al.⁴⁴ (Figure 2).

References

1. Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid fever. *New England Journal of Medicine*. 2002;347(22):1770-82.
2. Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. *Bulletin of the World Health Organization*. 2004;82(5):346-53.
3. Ochiai RL, Acosta CJ, Danovaro-Holliday MC, Dong B, Bhattacharya SK, Agtini M, et al. A multicenter, population-based, prospective surveillance study of typhoid fever in 5 Asian countries: disease burden and implications for control. *Bulletin of the WHO*. 2007;accepted.
4. Griffin GE. Typhoid fever and childhood vaccine strategies (Commentary). *The Lancet*. 1998;354(9180):698.
5. Hessel L, Debois H, Fletcher M, Dumas R. Experience with Salmonella typhi Vi capsular polysaccharide vaccine. *European Journal of Clinical Microbiology and Infectious Diseases*. 1999;18:609-20.
6. Yang HH, Kilgore PE, Yang LH, Park J-K, Pan Y-F, Kim Y, et al. An outbreak of typhoid fever, Xing-An County, People's Republic of China, 1999: Estimation of the field effectiveness of Vi polysaccharide typhoid vaccine. *The Journal of Infectious Diseases*. 2001;183:1775-80.
7. Yang HH, Wu CG, Wie GZ, Gu QW, Wang BR, Wang LY, et al. Efficacy trial of Vi polysaccharide vaccine against typhoid fever in south-western China. *Bulletin of the WHO*. 2001;79(7):625-31.
8. Acosta C, Galindo C, Deen J, Ochiai R, Lee H, Seidlein Lv, et al. Vaccines against cholera, typhoid fever and shigellosis for developing countries. *Expert Opinion Biological Therapy*. 2004;12:1939-51.
9. Acharya I, Lowe C, Thapa R, Gurubacharya V, Shrestha M, Cadoz M, et al. Prevention of typhoid fever in Nepal with the Vi capsular polysaccharide of Salmonella typhi. A preliminary report. *New England Journal of Medicine*. 1987;317:1101-4.
10. Canh DG, Lin FK, Thiem VD, Trach DD, Trong ND, Mao ND, et al. Effect of dosage on immunogenicity of a Vi conjugate vaccine injected twice into 2- to 5-year old Vietnamese children. *New England Journal of Medicine*. 2004;72(11):6586-8.
11. Szu SC, Taylor DN, Trofa AC. Laboratory and preliminary clinical characterization of Vi capsular polysaccharide-protein conjugate vaccines. *Infection and Immunity*. 1994(4440-4444).
12. Papadimitropoulos V, Vergidis PI, Blitziotis I, Falagas ME. Vaccination against typhoid fever in travellers: a cost-effectiveness approach. *Clinical Microbiology and Infection*. 2004;10(8):681-3.
13. Bahl R, Sinha A, Poulos C, Whittington D, Sazawal S, Kumar R, et al. Costs-of-illness of typhoid fever in Indian urban slum community: implications for vaccination policy. *Journal of Health, Population and Nutrition*. 2004.
14. Poulos C, Bahl R, Whittington D, Bhan MK, Clemens JD, Acosta CJ. A cost-benefit analysis of typhoid fever immunization programs in an Indian urban slum community. *Journal of Health, Population and Nutrition*. 2004;22(3):311-21.
15. Canh DG, Whittington D, Thoa LTK, Utomo N, Hoa NT, Poulos C, et al. Household demand for typhoid fever vaccines in Hue, Vietnam. *Health Policy and Planning*. 2006:241-55.
16. Jamison DT, Breman JG, Measham A, Alleyne G, Claeson M, Evans DB, et al., editors. *Disease control priorities in developing countries*. 2nd. ed. Washington DC: The World Bank and Oxford University Press; 2006.
17. WHO. *Making choices in health: WHO guide to cost-effectiveness analysis*. Geneva, Switzerland: World Health Organization; 2003.
18. Bank W. *Investing in Health*. World Development Report. Washington DC: World Bank; 1993.
19. Fund IM. *World Economic Outlook database*. 2007.
20. WHO. Typhoid fever. 2007.
21. WHO. Typhoid fever, Democratic Republic of Congo. *Weekly epidemiological record*. 2005;80:30-1.

22. Poulos C, Riewpaiboon A, Stewart JF, Nyamete A, Guh S, Clemens J, et al. Cost of illness due to typhoid fever in five Asian countries. Manuscript, February 2007. 2007.
23. Whittington D, Sur D, Cook J, Chatterjee S, Maskery B, Lahiri M, et al. Private demand for cholera and typhoid vaccines in Kolkata, India. *World Development* (under review). 2007.
24. Cook J, Whittington D, Canh DG, Johnson FR, Nyamete A. The reliability of stated preferences for cholera and typhoid vaccines with time to think in Hue, Vietnam. *Economic Inquiry*. 2007;45(1):100-14.
25. Kim D, Canh DG, Poulos C, Thoa LTK, Cook J, Hoa NT, et al. Private demand for cholera vaccines in Hue, Vietnam. *Value in Health*. 2007;forthcoming.
26. Lucas M, Jeuland M, Deen J, Lazaro N, MacMahon M, Nyamete A, et al. Private demand for cholera vaccines in Beira, Mozambique. *Vaccine*. 2007;25(14):2599-609.
27. Islam Z, Maskery B, Nyamete A, Horowitz M, Yunus M, Whittington D. Private demand for cholera vaccines in rural Matlab, Bangladesh *Health Policy*. 2007;accepted.
28. Lauria D, Stewart J. Vaccination Costs: Working paper, UNC Envr Sci & Eng; 2007 July 2007.
29. Jodar L. Personal communication. 2007.
30. DeRoeck D. Personal communication. 2007.
31. UNICEF. Reference Vaccine Price List. 2001.
32. Brenzel L, Claquin P. Immunization programs and their costs. *Social Science and Medicine*. 1994;39(4):527-36.
33. Walker D, Mosquera NR, Penny ME, Lanata CF, Clark AD, Sanderson CFB, et al. Variation in the costs of delivering routine immunization services in Peru. *Bulletin of the World Health Organization*. 2004;82(9):676-82.
34. Pegurri E, Fox-Rushby JA, Damian W. The effects and costs of expanding the coverage of immunisation services in developing countries: a systematic literature review. *Vaccine*. 2005;23:1624-35.
35. Cookson S, Stamboulian D, Demonte J, Quero L, Arquiza CMD, Aleman A, et al. A cost-benefit analysis of programmatic use of CVD 103-HgR live oral cholera vaccine in a high-risk population. *International Journal of Epidemiology*. 1997;26(1):212-8.
36. Hinman AR. Economic aspects of vaccines and immunizations. . *C R Academy of Sciences/ Life Sciences*. 1999;322:989-94.
37. Sinha A, Levine O, Knoll MD, Muhib F, Lieu TA. Cost-effectiveness of pneumococcal conjugate vaccination in the prevention of child mortality: an international economic analysis. *The Lancet*. 2007;369:389-95.
38. Podewils L, Antil L, Hummelman E, Bresee J, Parashar UD, Rheingans R. Projected cost-effectiveness of rotavirus vaccination for children in Asia. *Journal of Infectious Diseases*. 2005;192(S1):S133-S45.
39. Lin F-YC, Ho VA, Bay PV, Thuy NTT, Bryla D, Thanh TC, et al. The epidemiology of typhoid fever in the Dong Thap province, Mekong Delta Region of Vietnam. *Am J Tropical Medicine and Hygiene*. 2000;62(5):644-8.
40. Jeuland M, Lucas M, Deen J, Lazaro N, Whittington D. Estimating the private benefits of vaccination against cholera in Beira, Mozambique: A travel cost application. Under review, *Journal of Health Economics*. 2007.
41. MoHFW I. National Health Accounts 2001-2002. New Delhi: India Ministry of Health and Family Welfare; 2005 December 2005.
42. GAVI. Guidelines for preparing proposals for GAVI/Vaccine Fund Investment: GAVI (Global Alliance for Vaccines & Immunization); 2004 May 2004.
43. Lauria DT, Maskery B, Poulos C, Whittington D. An optimization model for use of the Vi polysaccharide vaccine to prevent typhoid in developing countries. 2007.
44. Laxminarayan R, Mills AJ, Breman JG, Measham AR, Alleyne G, Claeson M, et al. Advancement of global health: key messages from the Diseases Control Priorities Project. *Lancet*. 2006;367:1193-208.

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Tables and Figures

Table 1. Site-specific model parameters*

Parameters	Kolkata, India†	Hue, Vietnam	N. Jakarta, Indonesia	Karachi, Pakistan
Population	185,000	282,000	161,000	102,000
Description	2 urban “slums”	City-wide, urban and semi-urban	2 poor urban districts	3 urban squatter settlements
<i>Observed Incidence (cases per 1,000)‡</i>				
2–5yrs	3.4 [1.9–6.3]	n/a	1.5 [0.89–2.5]	5.7 [4.4–7.4]
5–14 yrs	4.9 [4.0–6.7]	0.24 [0.16–0.43]	1.8 [1.5–2.5]	4.1 [3.7–5.2]
15+ yrs	1.2 [0.9–1.6]	n/a	0.5 [0.40–0.66]	n/a
Public cost of illness (2007 US\$), all ages	\$4 [\$2–\$6]	\$33 [\$17–\$68]	\$26 [\$13–\$39]	\$2 [\$1–\$3]
Delivery cost per dose (2007 US\$)	\$0.5 [0.3–2.5]	\$0.5 [0.3–2.5]	\$1.0 [0.6–5.0]	\$0.5 [0.3–2.5]
Acquisition cost per dose (2007 US\$)	\$0.57 [0.4–0.8]	\$0.57 [0.4–0.8]	\$0.57 [0.4–0.8]	\$0.57 [0.4–0.8]
<i>Percent of age group covered if vaccine is free§</i>				
< 5yrs	73% [58–88]	26% [21–31]	59% [47–71]	58% [46–70]
5–14 yrs	69% [65–83]	63% [50–76]	50% [40–60]	48% [38–58]
15+ yrs	62% [50–74]	54% [43–65]	29% [23–35]	n/a

Notes: *Base case value shown, with uncertainty range in brackets. †The neighborhoods are Tiljala and Narkeldanga. ‡Based on blood culture tests, which are known to produce false negatives. True incidence is assumed to be double the observed incidence. §This the percent of people who hear about the program and would take if free. These predicted coverage rates are adjusted for time-to-think, lowering them by ~10–15%. We assume only 80% of the population learns about the program; these percentages are multiplied by 0.8 in the model.

Table 2. Parameters used in all five sites

	All Sites	
Case fatality rate	1%	[0.5%–3%]
Effectiveness of vaccine	65%	[55–75%]
Duration of vaccine	3 years	[2–4 yrs]
DALY weight	0.27	[0.075–0.471]
Length of illness	7 days	[4–21]
Discount rate	3%	

Table 3. Vaccination program outcomes—base case analysis

Parameters	Kolkata, India	Hue, Vietnam	N. Jakarta, Indonesia	Karachi, Pakistan
Option 1 - School-based Program targeting only school-aged children				
Number vaccinations	20,118	29,824	18,974	11,238
Cases avoided over duration	384	28	133	181
Deaths avoided over duration	3.8	0.3	1.3	1.8
YLL avoided over duration	104.3	7.8	36.4	49.4
YLD avoided over duration	1.9	0.1	0.7	0.9
DALYs avoided over duration	106	8	37	50
Public COI avoided	\$1,493	\$1,030	\$3,363	\$352
Total program costs	\$21,526	\$31,912	\$29,790	\$12,025
Average cost per imm. person	\$1.07	\$1.07	\$1.57	\$1.07
Net program costs	\$20,032	\$31,018	\$26,426	\$11,673
Net public cost per case avoided	\$52	\$1,111	\$198	\$64
Net public cost per death avoided	\$5,211	\$111,111	\$19,840	\$6,449
Net public cost per DALY avoided	\$189	\$3,924	\$712	\$232
Option 2—School-based program targeting both school-aged and younger children				
Number vaccinations	25,520		23,306	14,717
Cases avoided over duration	456		158	258
Deaths avoided over duration	4.6		1.6	2.6
YLL avoided over duration	124.2		43.5	71.1
YLD avoided over duration	2.3		0.8	1.3
DALYs avoided over duration	126		44	72
Public COI avoided	\$1,772	<i>N/A</i>	\$3,999	\$502
Total program costs	\$27,306		\$36,590	\$15,747
Average cost per imm. person	\$1.07		\$1.57	\$1.07
Net program costs	\$25,534		\$32,591	\$15,245
Net public cost per case avoided	\$56		\$206	\$59
Net public cost per death avoided	\$5,599		\$20,579	\$5,901
Net public cost per DALY avoided	\$202		\$735	\$211
Option 3 - Community-based program (all ages)				
Number vaccinations	90,945		45,975	
Cases avoided over duration	762		203	
Deaths avoided over duration	7.6		2.0	
YLL avoided over duration	193.8		53.9	
YLD avoided over duration	3.8		1.0	
DALYs avoided over duration	198		55	
Public COI avoided	\$2,961	<i>N/A</i>	\$5,137	<i>N/A</i>
Total program costs	\$97,311		\$72,181	
Average cost per imm. person	\$1.07		\$1.57	
Net public costs	\$94,350		\$67,044	
Net public cost per case avoided	\$124		\$330	
Net public cost per death avoided	\$12,377		\$32,952	
Net public cost per DALY avoided	\$477		\$1,221	
GDP Thresholds (for reference)				
“Cost-effective”	\$2,613	\$2,394	\$5,436	\$2,679
“Very cost-effective”	\$871	\$798	\$1,812	\$893

Table 4. Effect of individual parameter uncertainty on cost-effectiveness ratios (2007US\$ per DALY avoided)*

<i>Value</i>	Cost <i>(see below)</i>	CFR <i>3%– 0.5%</i>	Duration <i>2yrs– 4yrs</i>	Incidence <i>(see Table1)</i>	Efficacy <i>55%– 75%</i>
Kolkata, India	<i>\$0.7– \$3.3</i>				
Program Option 1	119– 611	64– 371	140– 286	135– 232	162– 225
Program Option 2	127– 652	68– 397	150– 305	136– 263	173– 241
Program Option 3	307– 1,504	161– 937	360– 713	335– 616	412– 567
N. Jakarta, Indonesia	<i>\$1.0– \$5.8</i>				
Program Option 1	421– 2,875	240– 1,399	520– 1,096	488– 885	605– 858
Program Option 2	436– 2,960	248– 1,445	538– 1,130	486– 960	625– 886
Program Option 3	744– 4,763	412– 2,397	907– 1,850	840– 1,578	1,046– 1,460
Karachi, Pakistan	<i>\$0.7– \$3.3</i>				
Program Option 1	149– 730	78– 455	175– 346	184– 262	200– 275
Program Option 2	135– 664	71– 414	159– 315	165– 248	182– 250
Hue, Vietnam	<i>\$0.7– \$3.3</i>				
Program Option 1	2,528– 12,338	1,324– 7,712	2,959– 5,855	2,151– 5,861	3,386– 4,658

Notes: *Program Option 1 targets only school-aged children (5–14.9), Option 2 also includes young children (2–4.9); Option 3 is a community-based program targeting all ages.

Table 5. Results of Monte Carlo analysis on net public cost per DALY avoided (2007US\$)*

	Kolkata, India	Hue, Vietnam	N. Jakarta, Indonesia	Karachi, Pakistan
Option 1 - School-based Program targeting only school-aged children				
Median	196	3,765	847	243
95% confidence interval	65–637	1,195–12,283	249–2,841	83–755
% chance “very cost-effective”	>99%	<1%	89%	99%
Option 2—School-based program targeting both school-aged and younger children				
Median	207		866	222
95% confidence interval	69–665	N/A	257–2,907	76–690
% chance “very cost-effective”	>99%		88%	99%
Option 3—Community-based program (all ages)				
Median	487		1,422	
95% confidence interval	166–1,544	N/A	436–4,646	N/A
% chance “very cost-effective”	83%		65%	

Notes: *Results from 10,000 model runs, triangular distributions for parameters with lower and upper values set to ranges shown in brackets in Table 1 (except for duration).

Table 6. Private cost of illness per typhoid case and private COI avoided for base case programs (2007\$)

	Kolkata, India	Hue, Vietnam	N. Jakarta, Indonesia	Karachi, Pakistan
Private COI per case	11	38	106	53
<i>Private COI avoided over duration (base case)</i>				
Program Option 1	4,107	1,030	13,712	9,317
Program Option 2	4,872	n/a	16,303	13,297
Program Option 3	8,143	n/a	20,945	n/a

Notes: From Poulos et al (2007).

Figure 1. Effect of variation in total vaccination cost per dose on net public cost per DALY avoided for program that targets only children attending school (Option 1).

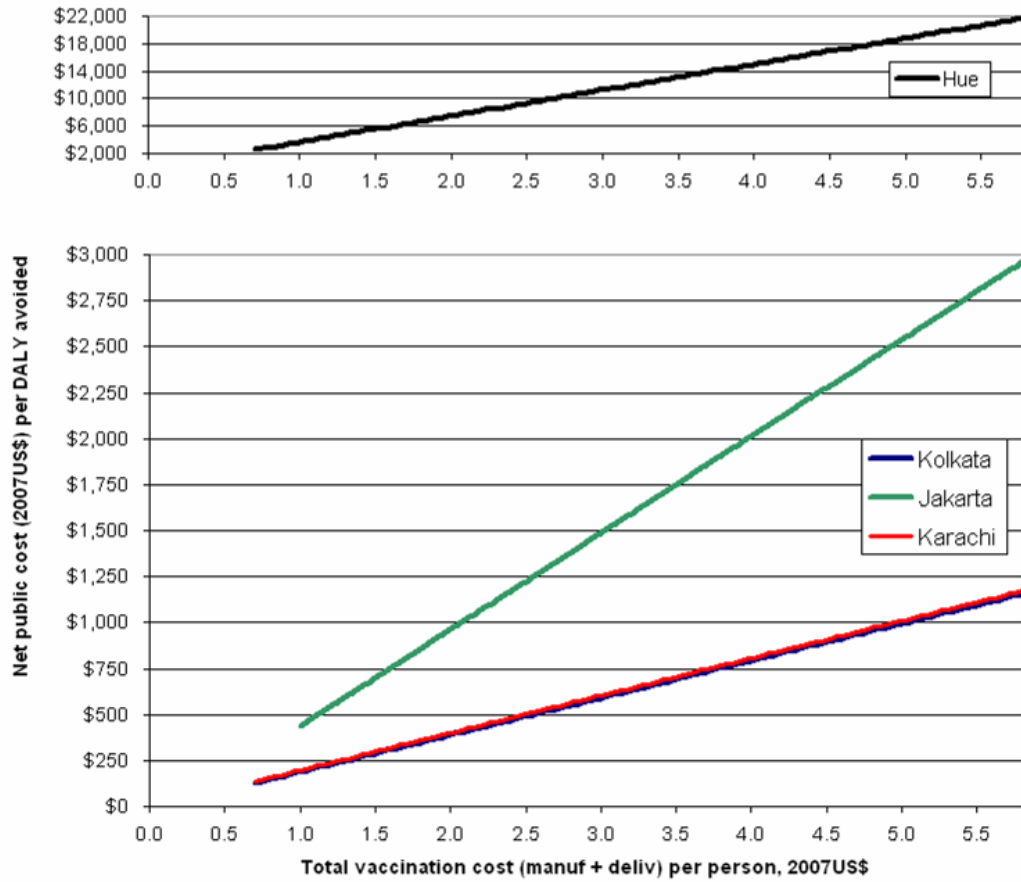


Figure 2. Effect of variation in total vaccination cost per dose on net public cost per DALY avoided for program that targets school-aged and younger children (Option 2).

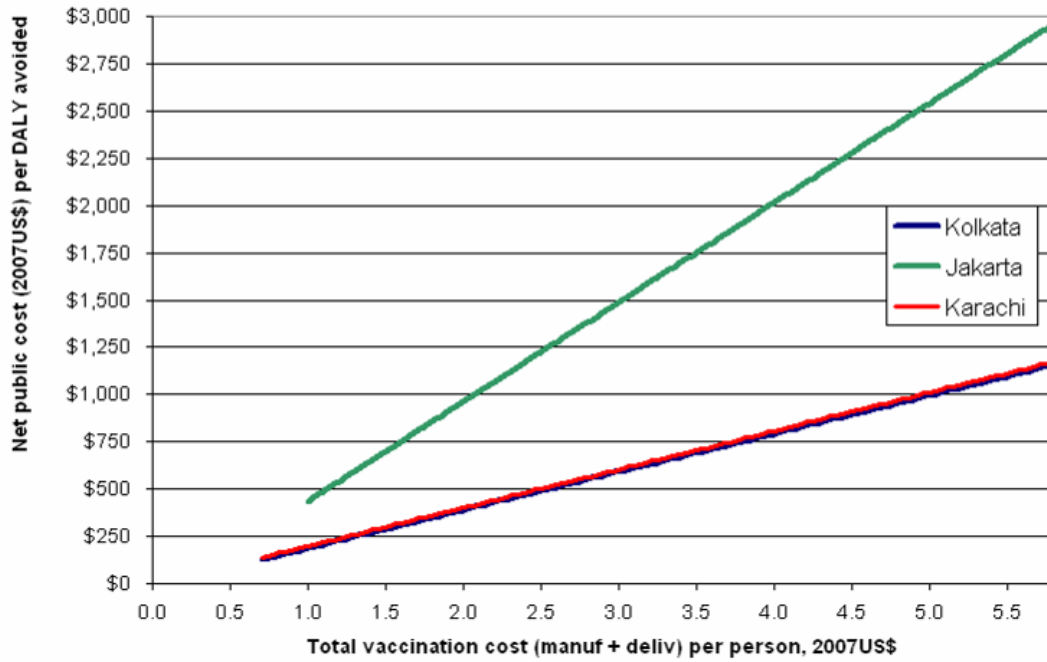


Figure 3. Effect of variation in total vaccination cost per dose on net public cost per DALY avoided for community-based vaccination program that targets both adults and children (Option 3).

