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# A Cost–Benefit Analysis of Cholera Vaccination Programs in Beira, Mozambique

Marc Jeuland, Marcelino Lucas, John Clemens, and Dale Whittington

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Economic and epidemiological data collected in Beira, Mozambique, are used to conduct this first social cost–benefit analysis for cholera vaccination in Sub-Saharan Africa. The analysis compares the net economic benefits of three immunization strategies with and without user fees: school-based vaccination for school children only (age 5–14), school-based vaccination for all children (age 1–14), and a mass vaccination campaign for all people older than one year. All options assume the use of a low-cost new-generation oral cholera vaccine. The analysis incorporates the latest knowledge of vaccine effectiveness, including new evidence on the positive externality associated with the resulting herd protection (both protection of unvaccinated individuals and enhanced protection among vaccinated individuals arising from vaccination of a portion of the population), and uses field data for incidence, benefits (private willingness to pay, public cost of illness), and costs (production, shipping, delivery, private travel costs). Taking herd protection into account has important economic implications. For a wide variety of parameters values, vaccination programs in Beira pass a cost–benefit test. Small school-based programs with and without user fees are very likely to provide net benefits. A mass vaccination campaign without user fees would result in the greatest reduction in the disease burden, but the social costs would likely outweigh the benefits, and such a program would require substantial public sector investment. As user fees increase, mass vaccination becomes much more attractive, and the reduction in disease burden remains above 70 percent at relatively low user fees. JEL codes: I1, H23, H4

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Cost–benefit analysis of vaccination programs is now rarely done anywhere in the world. Most health economists have given up on welfare-theoretic economic appraisals of health interventions such as vaccination programs, preferring to present cost-effectiveness calculations that use disability-adjusted life

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45 years (DALYs) or quality-adjusted life years (QALYs) as their measure of health outcomes.

The conventional wisdom based on cost-effectiveness analysis is that cholera vaccination is not “cost effective” compared with other public health interventions and that it is an unlikely candidate to receive scarce public funds, except during cholera outbreaks or in refugee camps (Murray, McFarland, and Waldman 1998; Naficy and others 1998; Jamison and others 2006). The limitations of cost-effectiveness analysis are well known, however. Such analysis cannot provide finance ministries the economic information needed for cross-sectoral comparisons with other public investments, such as education or infrastructure. The cut-off levels used to determine what is a “cost-effective” intervention have no theoretical justification. Nonhealth benefits of policy interventions (such as time savings) are typically ignored, as are private costs (such as queuing and travel costs to obtain health-related goods). Finally, cost-effectiveness analysis does not address the rationale for government involvement. Simply because an intervention is judged to be cost-effective does not mean that there is a good reason why government should be involved in its provision; private markets provide many goods and services that would pass a cost-effectiveness test.

This article uses cost–benefit analysis to show that there is a strong economic case for cholera vaccination in Beira, Mozambique. It also shows that it is both possible and desirable to use standard economic methods to appraise complex health interventions in developing countries and that health economists do not have to rely on cost-effectiveness analysis and its *ad hoc* health outcome measures of DALYs and QALYs.

Section I presents background information on cholera, the new-generation cholera vaccines, and the latest epidemiological evidence for the cholera vaccination externality. Section II describes the analytical framework, including the vaccination program options to be examined and the basis for the herd protection model. Section III develops the cost–benefit model and explains the underlying assumptions. Key results of the model are summarized in section IV. Section V outlines the value of these findings to policymakers.

## I. CHOLERA AND NEW-GENERATION CHOLERA VACCINES

80 Cholera is a serious, persistent disease across large portions of Mozambique. The World Health Organization reported that Mozambique had the world’s highest number of cholera cases (20,080) in 2004, and Mozambique consistently appears among the worst hit countries for other years (WHO 2005). During the most recent outbreak, in 2006, there were at least 5,800 cases nationwide, affecting 22 districts and 4 provinces in the center of the country. The largest city suffering from endemic cholera and high incidence rates is Beira (population of 550,000), where a series of epidemics broke out in 2001–03, with more than 3,800 cases for three years in a row. Most cases occur

90 shortly after seasonal flooding between the end of the rainy season in January  
and February and the advent of the cool, dry season in May and June (Lucas  
and others 2005).

95 Cholera is most commonly transmitted through consumption of contami-  
nated water or through food that has come into contact with such water. Large  
infectious doses are usually required to cause severe cholera. Newly infected  
people pass through an incubating stage averaging 3–4 days, followed by an  
infectious state averaging about 10 days (Barua and Greenough 1992; Sack and  
100 others 2004). Especially in endemic areas, many infected people are asympto-  
matic, due to natural immunity acquired during previous infection or ingestion  
of smaller amounts of contaminated water or food. In symptomatic individuals,  
cholera causes acute dehydration, which can lead to death in the absence of  
prompt treatment with intravenous rehydration therapy. With proper treat-  
ment, case fatality rates from cholera infection are low (typically less than  
1 percent; Ryan 2000). Case fatality rates may reach 20–50 percent in refugee  
camps, after natural disasters, or in other situations where health systems are  
105 unable to deliver treatment promptly and effectively (Naidoo and Patric 2002).

Beira, however, has a dedicated, single-purpose Cholera Treatment Center  
with diagnostic as well as treatment capabilities, all delivered free of charge to  
the sick. Due to mass publicity campaigns, residents know and use the center,  
and the risk of death from cholera is low. Nevertheless, policymakers and resi-  
110 dents remain very concerned about cholera infection. People want to avoid the  
pain and suffering associated with the disease, as well as the (small) risk of  
death and the indirect costs associated with lost time and labor.

New-generation vaccines offer a way of controlling cholera in areas like  
Beira, where modern water and sanitation infrastructure remains largely unaf-  
115 fordable for government and the urban poor. In late 2003, the International  
Vaccine Institute and Médecins sans Frontières conducted a pilot community-  
based cholera vaccination trial in one neighborhood of Beira, using health  
centers and schools as vaccination outposts. The purpose of the trial was to  
test the effectiveness of a two-dose regimen of the Dukoral<sup>TM</sup> oral, killed,  
120 whole-cell vaccine (rBS-WC), given two weeks apart (Lucas and others 2005).<sup>1</sup>  
This work coincided with an epidemiological study of cholera incidence among  
different age groups. The research program in Beira also included parallel econ-  
omic studies measuring the public and private costs of illness associated with  
cholera and private demand for vaccines and private costs (such as travel costs  
125 and time spent traveling to the vaccination clinic or waiting to be seen). The  
results of those studies are reported elsewhere (Lucas and others 2007; Jeuland  
and others 2008). The findings from this suite of epidemiological and economic

130 1. These research activities were conducted through the International Vaccine Institute's Diseases of  
the Most Impoverished program, which works to accelerate the development and introduction of  
new-generation vaccines against cholera, typhoid fever, and shigellosis in developing countries. The  
program involves a number of parallel epidemiological and social science studies, as well as vaccine  
technology transfer activities.

135 research activities, combined with recently published findings on the herd protection effects (when vaccination of a portion of the population confers protection on unvaccinated individuals and enhanced protection of vaccinated individuals) of cholera vaccination from Bangladesh (Ali and others 2005; Longini and others 2007), provide a rich new evidence base that is used in this welfare-theoretic economic appraisal (cost–benefit analysis) of larger-scale vaccination program options in Beira.

140 In the only widely cited cost–benefit analysis of cholera vaccination, Cookson and others (1997) find that cholera vaccination passes a cost–benefit test in the base case for vaccination of a confined population in an outbreak-prone area of northern Argentina. However, the study did not measure demand for the vaccine and instead used avoided cost of illness as a measure of benefits. The main reason that cholera vaccination was found to be an attractive economic proposition was the unusually high avoided cost of illness (\$622 per case<sup>2</sup>) because of high hospitalization rates and costs of cholera, helicopter transport of infected individuals, and extensive medical therapy. Only in very special instances will the use of an avoided cost of illness measure of benefits result in positive net benefits, however, because cholera is relatively easy and inexpensive to treat. The total cost of illness of a cholera episode is generally much lower than the high values reported by Cookson and others (see also Poulos and others 2008).

150 The cost–benefit analysis by Cookson and others (1997) was also conducted before strong evidence was available on the herd protection from cholera vaccination. Ali and others (2005) recently presented evidence of strong indirect herd protection effects from cholera vaccination, which has important implications for cost–benefit analyses. Ali and others reanalyzed incidence data for vaccinated and unvaccinated people from *baris* (neighborhoods) in Matlab, Bangladesh, that had varying levels of vaccination coverage. They showed that cholera incidence in the first year following the vaccination program was highly dependent on coverage rates in the *baris* for members of control groups receiving a placebo rather than the vaccine. Because the cholera vaccine offers less than 100 percent protection, herd protection was also found among vaccine recipients, but the effect was weaker than among nonvaccinated individuals.

## 170 II. ANALYTICAL FRAMEWORK FOR THE COST–BENEFIT ANALYSIS OF CHOLERA VACCINATION PROGRAMS

This section describes the baseline conditions, the three program options, and the approach to modeling herd protection.

175 2. All dollar amounts reported in this article are US dollars.

*The Status Quo, Baseline Conditions*

180 Cost–benefit analyses calculate the costs and benefits of a policy intervention as a change from status quo or baseline conditions. The baseline condition in Beira is that cholera vaccines are not sold on demand—there is no free, competitive market for cholera vaccines.

185 This situation is the norm in developing countries because governments often prohibit importing vaccines for sale by private healthcare providers, a policy endorsed by the international public health community. There are three main reasons why governments in developing countries prevent free market sales of many vaccines. One reason is that governments want to be monopsonists, exerting market power to negotiate low, bulk purchase prices from international vaccine suppliers. In many cases, governments also implement their strategy by securing donor support for vaccine purchases. Another reason is that governments want to ensure that vaccines are safe and effective, and regulatory hurdles to vaccine licensing are often high. A third reason is that governments often have an explicit policy that vaccines must be provided free of charge; charging for vaccines is often illegal.<sup>3</sup>

190 Thus, the analysis compares various government or donor-sponsored vaccination programs with administered prices (including the provision of free vaccines) rather than with prices in a market with private providers. There are two main reasons for this approach. First, government-sponsored vaccination programs with administered prices are the most realistic options in Mozambique and most other developing countries. Neither governments nor donors are contemplating a free market for vaccine provision in Mozambique or elsewhere.

200 The second reason is that information on the demand curve for cholera vaccines in a market with many private providers, needed to assess costs and benefits, does not exist. This article relies on private vaccine demand curves estimated with data from stated preference (hypothetical market) surveys that describe an institutional setting in which the government administers a vaccination campaign and charges specific user fees for the vaccines. Demand might be quite different in a private market with multiple providers. Also, vaccine demand will be heavily influenced by social marketing and health promotion campaigns associated with government-sponsored programs, as has been the case in Beira in the past. Private vaccine providers might well launch such campaigns to increase awareness of the benefits of new-generation cholera vaccines,

215 3. It would be a relatively straightforward application of cost-benefit techniques to evaluate the costs and benefits of changing government policy to permit market sales of cholera vaccines. Assessing the costs and benefits of such vaccine “deregulation” requires having a private demand curve for cholera vaccines and evidence on the magnitude of the positive externality associated with herd protection. Then the area under the demand curve would serve as a measure of the direct benefits to individuals vaccinated. Accounting for the positive externality from herd protection would require determining what proportion of people among unvaccinated groups would receive the indirect herd protection and what their willingness to pay would be for this ex ante risk reduction.

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but in the current situation in Beira and elsewhere, people expect to receive this health information from public sector health professionals.

### *Program Options*

This article therefore estimates the costs and benefits of three targeted one-time, government-administered vaccination programs in Beira, compared with the baseline condition in which cholera vaccines are not available to anyone:

- *Option 1*: school-based vaccination of school children (ages 5–14);
- *Option 2*: school-based vaccination of all eligible children (ages 1–14); and
- *Option 3*: community-based vaccination of all eligible people (ages 1 through adult; the vaccine cannot be given to infants younger than age 1).

Costs and benefits of each option are calculated over a range of prospective government-administered user fees.

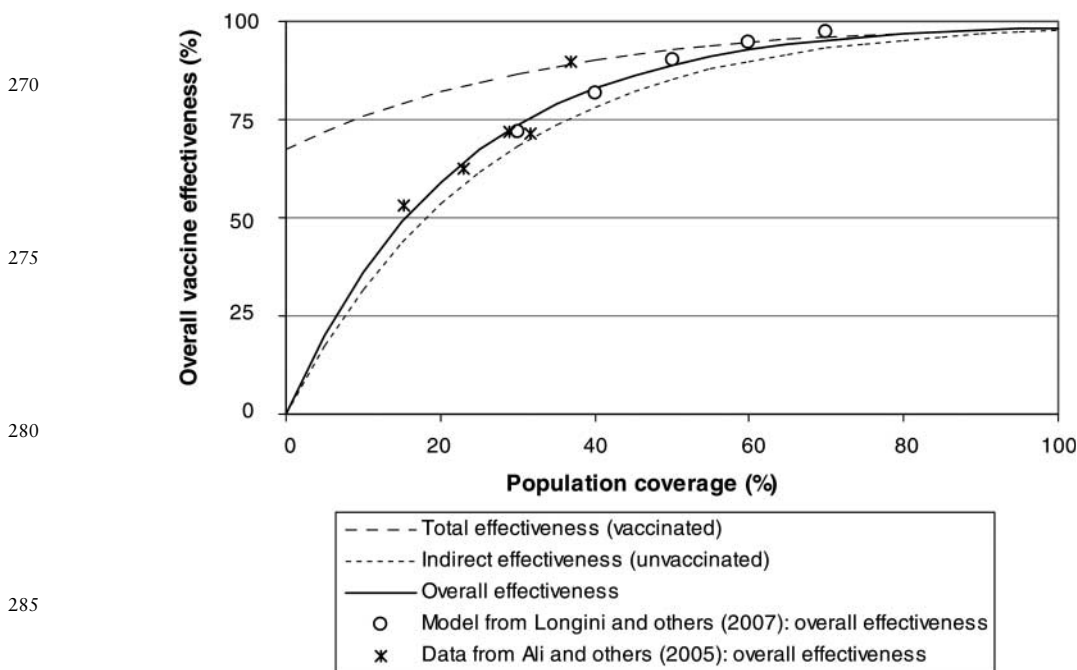
The motivation for targeting different age cohorts is policymakers' interest in designing cholera vaccination programs particularly for children, who are most vulnerable to dying of cholera and have the highest disease incidence. Age-group specifications are based on practical considerations. School-age children are typically easy to reach through targeted school-based immunization (option 1). Option 2 might be more difficult to implement because younger children would have to be brought to the school vaccination site by parents or guardians. Option 3 would require the most extensive planning and awareness-raising efforts in order to encourage adults to bring themselves and children to community vaccination sites.

The analysis assumes that all the vaccination program options would use a whole-cell-type oral cholera vaccine similar to the one now produced in Vietnam that can be purchased for about \$0.50 a dose (The more expensive Dukoral<sup>TM</sup> vaccine manufactured by Crucell in the Netherlands sells for at least \$3–\$4 a dose). A single two-dose vaccine regimen protects against cholera for about three years. The exact level of this effectiveness depends on the proportion of the total population that is vaccinated, because of the herd protection effect.

### *Modeling Herd Protection*

To incorporate the herd protection externality into the cost–benefit calculations, mathematical relationships for both indirect effectiveness ( $\eta_u$ , among the unvaccinated) and total effectiveness ( $\eta_v$ , among the vaccinated) are specified as functions of population coverage using the data in Ali and others (2005). Specifically, two exponential curves are fitted to the data, imposing the constraint that protection among the unvaccinated must be less than or equal to protection among the vaccinated (see appendix A for parameter assumptions

265 FIGURE 1. Model of Overall Cholera Vaccine Effectiveness as a Function of  
 270 Vaccination Coverage Rate in Year 1 in Herd Protection Scenario, and  
 Comparison with Results from Epidemiological Studies



Note: These estimates for effectiveness were adjusted downward by 17 percent in year 3 to represent the vaccine’s waning protection over time

290 Source: Authors’ analysis based on data from a cholera vaccination trials and epidemiological and economic research in Beira, Mozambique; Ali and others (2005); and Longini and others (2007); see text for details

295 and appendix B for a summary of the data and additional details on this mathematical model). When combined into an overall protection curve representing average effectiveness in the general population, these mathematical functions yield effectiveness levels for the first year following vaccination that are very similar to results from epidemiological model simulations conducted by Longini and others (2007) (figure 1).

300 Two limitations of this use of the herd protection data from Matlab, Bangladesh, should be highlighted. First, data are for the year following vaccination only, whereas cholera immunizations provide about three years of protection (Thiem and others 2006; Trach and others 1997). In the cost–benefit calculations, the protective effects for the third year are thus adjusted downward by 17 percent to simulate the typical reduction in field effectiveness of the vaccine over time, estimated in vaccine trials to be from 60 to 50 percent.

305 The second difficulty is the specificity of the herd protection effect to the Matlab setting. Conditions such as population density, in- and out-migration, geography, and natural immunity were somewhat different from those in Beira.

Detailed information on how such factors might influence herd protection was not available, and the effects observed in Matlab were used without modification. As Longini and others (2007) argue, in populations with lower natural immunity than that of Matlab, which experiences a low level of cholera infection year-round, with periodic larger epidemic outbreaks, higher coverage rates would be needed to achieve the observed levels of overall vaccine effectiveness. Nonetheless, it seems reasonable to expect that natural immunity would also be high in Beira, where cholera is also endemic and incidence rates appear to be even higher than in Matlab (Deen and others 2008).

### III. THE COST-BENEFIT MODEL

For the cost-benefit calculations, Beira's population was subdivided into six groups: vaccinated and unvaccinated individuals in three age groups (young children ages 1-4 years, school children ages 5-14, and adults ages 15 and older). The costs and benefits of cholera vaccination for each of these six groups were calculated for each program option. (The calculations included infants younger than age 1 under the assumption that infants received the benefits of herd protection from the vaccinated population even though they were too young to receive the vaccine themselves).

The following equation was used to calculate the net benefits of a specific vaccination program option to the total population of Beira:

$$\begin{aligned}
 \text{Net benefits} &= [\text{Total private benefits} + \text{Total public benefits}] - [\text{Total costs}] \\
 &= [\text{WTP}(\text{vaccinated}) + \text{WTP}(\text{unvaccinated}) + \text{Public COI}] - \\
 &\quad [\text{Total costs}] \\
 &= \sum_{i=1}^3 N_i \cdot \{q_i(p_v) \cdot \text{WTP}_{i,v}(p_v, \eta_v) + [1 - q_i(p_v)] \cdot \\
 &\quad \text{WTP}_{i,u}(p_v, \eta_u) + a_i(q_i(p_v)) \cdot \text{COI}_{1,8} - \sum_i N_i \cdot q_i(p_v) \cdot (c_v + c_{p,i}),
 \end{aligned}$$

(1)

where  $N_i$  is the number of individuals in the population in each of the three age groups  $i$ ;  $q_i(p_v)$  is the percentage of individuals in each age group  $i$  that would choose to be vaccinated with two doses at vaccine user fee (price)  $p_v$ ;  $\text{WTP}_{i,v}(p_v, \eta_v)$  is the average willingness to pay for the vaccine protection for each individual in age group  $i$  as a function of  $p_v$  and *total* effectiveness of the vaccine  $\eta_v$  among the subset of households that choose to have household members in this age group vaccinated;  $\text{WTP}_{i,u}(p_v, \eta_u)$  is the average willingness to pay for the two vaccine doses for each individual in age group  $i$  as a function of  $p_v$  and *indirect* vaccine effectiveness  $\eta_u$ , among the subset of households that do not choose to have household members in this age group vaccinated;  $a_i$  is

TABLE 1. Typology of Costs and Benefits Considered in the Beira Cost–Benefit Analysis Model

Benefit	Cost
<i>Private</i> : Benefits to vaccinated persons	Cost of vaccine production
<i>Externality 1</i> : Cost of illness savings to public health system from reduced cholera cases (not due to herd protection)	Cost of vaccine delivery (shipping, cold chain, wastage, outpost rental, awareness-raising, vaccine administration)
<i>Externality 2</i> : Additional protection of vaccinated persons due to herd effects	Private cost of vaccine acquisition (time spent traveling and queuing)
<i>Externality 3</i> : Protection of unvaccinated persons due to herd effects	
<i>Externality 4</i> : Cost of illness savings to public health system from reduced cholera cases (due to herd protection)	

Source: Authors’ analysis.

the percentage of cases of illness avoided in age group  $i$  due to the vaccination program option;  $COI_{i,\delta}$  is the discounted cost of illness incurred by the government or public health care system per case of illness for a person in age group  $i$ ;  $c_v$  is the total monetary cost of vaccination per person for production, shipping, and delivery of two doses; and  $c_{p,i}$  is the additional private cost of vaccination per person in age group  $i$  due to traveling to outposts and waiting in line to receive the vaccine.

The first three terms of equation (1) describe the benefits of the vaccination program option to the population, while the final term corresponds to the costs of implementing the program option.

On the benefit side, the first term includes the direct private and indirect herd protection benefits to vaccinated people. The second and third terms describe two other types of benefits: indirect protection of nonvaccinated people and reduced costs to taxpayers through avoided public health system costs (table 1). If there were no herd protection effect, total benefits would be limited to the private benefits to vaccinated individuals plus the benefits to taxpayers from reduced public treatment costs among those protected by vaccination. Under the assumption that individuals are unaware of the herd protection effect, the private demand for the vaccine remains the same with or without herd protection.

$WTP_{i,v}(p_v, \eta_v)$  is greater than  $p_v$ , and  $WTP_{i,u}(p_v, \eta_u)$  is less than  $p_v$ . As  $p_v$  increases, fewer people are willing and able to purchase vaccines;  $q_i$  thus decreases. At the same time, the private valuation  $WTP_{i,v}$  (per vaccinated individual) increases in  $p_v$  because only people with  $WTP_{i,v}$  greater than  $p_v$  buy the vaccine.  $WTP_{i,u}$  also increases in  $p_v$ , albeit at a slower rate, because raising prices excludes people with increasing private willingness to pay from participation in the vaccination program. For example, charging a price of \$1 for the vaccines excludes some people with nonzero willingness to pay who would not

be excluded by a program without user fees. The result is that average willingness to pay for vaccine protection among the unvaccinated, excluded individuals is higher in the program charging user fees than in the one without them.  $WTP_{i,v}$  and  $WTP_{i,u}$  encompass all the private benefits from vaccination, including private avoided cost of illness and the value of reduced mortality risks, pain and suffering, and lost productivity due to illness.

For public goods and goods not traded in markets (in this case, cholera vaccines), stated preference methods are often used to obtain empirical estimates of average willingness to pay and coverage rates at different prices (Hanemann 1994; Carson, 2000; Whittington and others 2002; Lucas and others 2007). Ideally, such measures would also capture the effect of different vaccine effectiveness levels  $\eta$  on demand. Varying levels of effectiveness would alter the prevalence of the disease, and the health economics literature argues that disease prevalence can have an important impact on demand for preventive goods (Ahituv, Hotz, and Philipson 1996; Philipson 1996; Gersovitz 2000; Gersovitz and Hammer 2003). In other words, the estimates of willingness to pay for a preventive treatment should be prevalence elastic. However, prior work on household demand for cholera vaccines in Beira does not enable estimation of this prevalence elasticity (Lucas and others 2007). Coverage levels were thus assumed to depend only on price:

$$(2) \quad q_i(p_v) = q_{i,0} \cdot \exp(-\beta_{p,i} \cdot p_v),$$

where  $q_{i,0}$  is the percentage of two-dose vaccines that would be acquired for age group  $i$  at a price of zero if everyone was informed of the campaign (obtained using an econometric model predicting demand in age group  $i$  at a price of zero; see Lucas and others 2007); and  $\beta_{p,i}$  is the regression coefficient on price obtained from the models for age group  $i$ .

In practice, equation (2) is written for the  $j$  households in a stated preference sample and includes a set of explanatory variables  $X$  other than price that also influence demand for vaccines. For simplicity, the expression shown in equation (2) is used in the cost–benefit calculations, assuming households to be “average” with respect to these other characteristics. Average willingness to pay per two-dose vaccine regime—among the vaccinated—is then expressed as the average consumer surplus obtained from buying  $q_i$  two-dose vaccinations at price  $p_v$  divided by the number of vaccinations  $q_i$  plus the actual expenditure on each vaccination  $p_v$  (or, alternatively, as the average area under the demand curve for the subset of people with willingness to pay of  $p_v$  or higher:

$$(3) \quad \begin{aligned} WTP_i(p_v) &= CS_i(p_v)/(q_i(p_v)) + p_v \\ &= \frac{\int_{p_v}^{\infty} q_{i,0} \cdot \exp(-\beta_{p,i} \cdot p_v) dp_v}{q_{i,0} \cdot \exp(-\beta_{p,i} \cdot p_v)} + p_v \\ &= (1/\beta_{p,i}) + p_v. \end{aligned}$$

Estimates of willingness to pay calculated using equation (3) thus assume that willingness to pay is independent of vaccination coverage. This willingness to pay measure derived using equation (3) could be used to calculate only  $WTP_{i,v}(p_v, \eta_v)$  in equation (1) because it describes the average willingness to pay among vaccinated people in age group  $i$ , not the willingness to pay for protection among the unvaccinated  $WTP_{i,u}(p_v, \eta_u)$ .

If all residents of Beira are assumed to have nonnegative willingness to pay for cholera vaccines, the average willingness to pay for all people in Beira—not just the vaccinated subsample—should provide insights about  $WTP_{i,u}(p_v, \eta_u)$ . This average willingness to pay measure is simply the area under the private demand curve for the population<sup>4</sup>:

Q1

$$(4) \quad \overline{WTP}_i(p_v) = \int_0^\infty q_{i,0} \cdot \exp(-\beta_{p,i} \cdot p_v) dp_v = \left( \frac{q_{i,0}}{\beta_{p,i}} \right).$$

$WTP_{i,v}(p_v, \eta_u)$  was then calculated as follows:

$$(5) \quad WTP_{i,u}(p_v) = \begin{cases} (\eta_u/0.5) \cdot [\overline{WTP}_i(p_v) - q_i(p_v) \cdot WTP_{i,v}(p_v)], & \forall \eta_u < 0.5 \\ [\overline{WTP}_i(p_v) - q_i(p_v) \cdot WTP_{i,v}(p_v)], & \text{otherwise} \end{cases}$$

Demand among the unvaccinated is assumed to be directly proportional to effectiveness up to the “normal” level of protection cited in the literature on cholera vaccines (50 percent over three years). For example, a person willing to pay \$1 for the vaccine but who would remain unvaccinated at  $p_v = \$1.50$  would also be willing to pay \$0.50 for a vaccine that offered 25 percent

4. It is possible to use respondents’ average willingness to pay for cholera vaccination to estimate the value of a statistical life. This derived estimate of the value of a statistical life can then be compared with estimates in the literature using other methods to check the plausibility of the willingness to pay estimates. In interpreting the following value of a statistical life calculation and comparison, it should be noted that research on the value of a statistical life in developing countries is limited, and estimates may not be directly comparable.

Assume that all private benefits are from reduced private cost of illness and averted mortality. The cost of illness study in Beira found a private cost of illness of \$21.60 for children and \$17.10 for adults (Poulos and others 2008). To calculate the present value of avoided private cost of illness from cholera vaccination, it is assumed that these benefits accrue over three years, that the vaccine is 55 percent effective, and that the real discount rate is 8 percent. The ex ante avoided private cost of illness in each age group is then simply its three-year cost of illness multiplied by the observed annual incidence rate (table 2). The ex ante avoided private costs of illness are \$0.29 for young children ages 1–4 (range of \$0.15–\$0.58); \$0.09 for school children ages 5–14 (\$0.05–\$0.19); and \$0.10 for adults ages 15 and older (\$0.05–\$0.20). These amounts are subtracted from the average willingness to pay for vaccine protection to estimate the ex ante value of the mortality risk reduction from cholera vaccination: \$1.60 for children ages 1–4 (\$1.30–\$1.80); \$1.2 for children ages 5–14 (\$1.10–\$1.30); and \$1.10 for adults ages 15 and older (\$1.00–\$1.20).

Finally, to convert these ex ante values of mortality risk reduction to values of a statistical life, the cholera case fatality rate is assumed to be 1 percent. The resulting values of a statistical life are \$11,000 for children ages 1–4 (\$4,300–\$25,000), \$ 25,000 for school children ages 5–14 (\$11,000–\$54,000),

485 protection through indirect effects. Beyond 50 percent effectiveness, it is assumed that demand will not change with increasing indirect vaccine effectiveness, similar to the behavior of demand among the vaccinated.

490 Equations (3) and (5), for willingness to pay among vaccinated and unvaccinated individuals in age group  $i$ , rely on several restrictive assumptions. First, they assume that respondents have a realistic understanding of vaccine effectiveness based on the language in the contingent valuation survey scenario. To avoid having to explain the concept of vaccine effectiveness in percentage terms to very poor, often illiterate, respondents in the contingent valuation survey in Beira, respondents were told that the hypothetical vaccine would provide “strong protection” in the first year, with declining effectiveness in  
495 years two and three.

Second, because the contingent valuation survey did not allow measurement of the elasticity of demand with respect to effectiveness, demand among the vaccinated was assumed to be fairly unresponsive to rising total vaccine effectiveness,  $\eta_v$ . To the extent that demand would increase in response to the increased benefits from herd protection,  $WTP_{i,v}(p_v, \eta_v)$  may have been underestimated, especially at high coverage (corresponding to a zero or very low price). For the same reasons,  $WTP_{i,u}(p_v, \eta_u)$  may also have been underestimated for high coverage rates. The cost–benefit calculations presented here are thus probably conservative, in that they may underestimate private benefits at high  
500 coverage levels, when herd protection is highest.

Third, it was assumed that respondents were unaware of herd protection effects when answering the contingent valuation survey questions.<sup>5</sup> There was no mention of a possible herd protection effect in the contingent valuation scenario, and it seems unlikely that respondents considered this a possibility.  
510

In equation (1), the third term characterizes the cost savings to the public health system resulting from implementation of the vaccination program option. Because treatment costs in publicly funded health care institutions are not paid by private individuals, the costs would not be captured in the willingness to pay measures of benefits. The percentage of cases of illness avoided,  $a_i$ , in age group  $i$  due to a particular vaccination program option depends on the number of vaccinations,  $q_i$ , and therefore also on  $p_v$ . As  $p_v$  increases and  $q_i$  decreases,  $a_i$  also decreases. Thus higher user charges for vaccines translate into a reduction in public cost of illness savings from vaccination. The number of  
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520 and \$18,000 for adults ages 15 and older (\$8,000–\$38,000). In reality, the cholera case fatality rate is highly uncertain and may be considerably lower than 1 percent, which would mean that these values of a statistical life estimates are too low. These values for households in Beira are comparable to those found in stated preference studies among low-income households in Bangladesh and India (Maskery and others 2008; Bhattacharya, Alberini, and Cropper 2007).

5. Otherwise, they might have been responding strategically to the contingent valuation questions, anticipating that they could receive indirect benefits from vaccination without having to pay anything.

avoided cases in each age group  $a_i$  can then be expressed as:

$$(6) \quad a_i(q_i(p_v)) = I_i \cdot d \cdot [\eta_v(q(p_v)) \cdot q_i(p_v) + \eta_u(q(p_v)) \cdot (1 - q_i(p_v))],$$

where  $\eta_v(\cdot)$  and  $\eta_u(\cdot)$  are again the total and indirect protection levels over a vaccine's duration,  $d$ , among vaccinated and unvaccinated individuals, as functions of the overall coverage level in all three age groups,  $q(p_v)$ , as shown in figure 1, and  $I_i$  is the cholera incidence rate in age group  $i$ .

The final term of equation (1) describes the costs of vaccination. In some situations vaccination costs may exhibit economies of scale due to high fixed set-up costs. It is also possible that in some settings vaccination costs could exhibit diseconomies of scale as it becomes more and more difficult to vaccinate the remaining pool of unvaccinated individuals. The detailed information needed to estimate the costs of vaccination programs in Beira as a function of coverage was not available, so for simplicity, variable vaccination costs were assumed to be independent of coverage level, and no fixed cost for campaign set-up was included.

Finally, other research has shown that the additional private cost of vaccination per person in age group  $i$  arising from traveling to health outposts and waiting in line to receive immunizations is an important determinant of vaccine demand (Jeuland and others 2008). These components of vaccine cost were also assumed to be the same for all three vaccination program options.

### *Parameter Values and Sensitivity Analysis*

The values of the parameters in the cost–benefit model (equation (1)) are summarized in table 2. More discussion of these parameter values and sensitivity ranges, as well as their sources, is provided in appendix A.

To examine the effect of uncertainty in these parameter values on the cost–benefit results, three types of sensitivity analysis were undertaken. The first explored the influence of individual model parameters on total net benefits. The upper and lower bounds for the parameters were chosen to reflect reasonable values based on the evidence in the published literature. When available, 95 percent confidence intervals were used; in other cases, judgment was required in specifying these plausible parameter ranges (see appendix A). The second sensitivity analysis studied the effect of simultaneous changes in several parameters. To investigate such changes, “best” and “worst” case scenarios were specified, corresponding to possible combinations of the extreme parameter values used in the one-way sensitivity analysis, and the net benefits for these extreme scenarios were determined. In the third sensitivity analysis, Monte Carlo simulations were conducted, with parameters assumed to vary randomly between these worst and best case values and with the highest probability outcome corresponding to the base case value specified in table 2.

TABLE 2. Description of Model Parameters, with Ranges of Uncertainty

Parameter	Base case	Sensitivity analysis		Notes/source
		Worst case	Best case	
Population $P$	550,000	550,000	550,000	na
Incidence $I_i$ (cases per 1,000)				Deen and others (2008)
Ages <5	8.8	4.4	17.6	
Ages 5–14	2.9	1.4	5.7	
Ages 15+	3.8	1.9	7.7	
Public cost of illness $COI$ (\$)				Poulos and others (2008)
Ages 1–4	13.0	0	26.0	
Ages 5–14	13.0	0	26.0	
Ages 15+	14.5	0	29.9	
Delivery cost (\$ per dose)	0.5	2.0	0.3	Lauria and Stewart (2008)
Production cost (\$ per dose)	0.6	0.8	0.5	Thiem and others (2006)
Private cost of vaccination $c_p$ (\$ per dose) <sup>a</sup>	0.2	0.4	0.1	Jeuland and others (2008)
Vaccine effectiveness: no herd protection (%)	55	40	70	Thiem and others (2006), Trach and others (1997)
Extent of herd protection effect	Reduced by 17% in year 3	Reduced by 33% in all years	No reduction over time	Adjusted from Ali and others (2005); see Fig. 1
Coverage if vaccine is free $q_{i,0}(\%)$ <sup>b</sup>				Lucas and others (2007): Predicted intercept of demand at price = 0
Ages 1–4	53	40	86	
Ages 5–14	59	44	65	
Ages 15+	61	46	67	
Slope of demand curve $\beta_i^c$				Lucas and others (2007): Predicted slope of demand with respect to price
Ages 1–4	0.28	0.40	0.24	
Ages 5–14	0.47	0.57	0.28	
Ages 15+	0.52	0.62	0.36	

660	655	650	645	640	635	630	625	620
Per capita willingness to pay $\overline{WTP}_i$ (\$)								Average per capita willingness to pay from exponential demand model (equation (3))
Ages 1–4		1.9		1.0		3.6		
Ages 5–14		1.3		0.8		2.3		
Ages 15+		1.2		0.7		1.9		
Per vaccine willingness to pay $WTP_{i,v}$ (\$)								Average willingness to pay per vaccine, from
Ages 1–4		3.6		2.5		4.2		exponential demand model (equation (4))
Ages 5–14		2.2		1.8		3.6		
Ages 15+		1.9		1.6		2.8		
Discount rate $\delta$ (%)		3		10		0		na

na, not applicable.

<sup>a</sup>Estimated from data collected after the mass vaccination campaign in Beira in 2003 and 2004 with no user fees; children are assumed to have half the private costs of adults.

<sup>b</sup>Base case coverage level is estimated based on results obtained in surveys with “time-to-think”; lower bound is 25 percent lower; and upper bound is the no “time-to-think” estimate.

<sup>c</sup>Range obtained from econometric demand models with 95 percent confidence interval on the price coefficient.

*Source:* As shown in table.

## IV. RESULTS

Cost–benefit results are presented for program options 1–3, with and without the herd protection externality, for three levels of user fees (\$0, \$1, and \$2.20). The economic results without user fees are discussed first, followed by the outcomes for programs with user fees.

*Programs with No User Fees*

The greatest reduction in the burden of disease occurs when no user fees are charged, because both vaccination coverage and the number of people protected are highest. For all three program options, herd protection greatly increases the reduction in disease burden, but the economic impact of indirect protection varies across program options (table 3). The economic impact of indirect protection is especially large for the two school-based program options. If herd effects are ignored, the net benefits of both school-based programs are approximately zero (–\$16,000 for option 1 and \$22,000 for option 2); they rise to \$454,000 and \$489,000 when herd protection is incorporated in the analysis.

The effect of herd protection on the community-based option 3 program is much more modest and does not result in positive net benefits (–\$101,000 without herd protection and –\$28,000 with it). With herd protection, the benefit–cost ratios for the three options without user fees are 3.3 for option 1, 2.8 for option 2, and 1.0 for option 3, signifying that the benefits per dollar spent are higher for option 1 than for options 2 and 3, even though the total number of vaccinations and the reduction in disease burden are smallest with option 1.

To examine the sensitivity of these results for programs without user fees to changes in parameter values, the net benefits of the program options were calculated with and without herd protection using one-way sensitivity analysis, the high and low ranges specified in table 2, and the Monte Carlo simulations. Several observations emerge from this sensitivity analysis. First, the worst-case outcomes result in negative net benefits for all programs, irrespective of whether herd protection is included. For example, including herd protection, the net benefits in the worst case are –\$113,000 for option 1, –\$183,000 for option 2, and –\$1.08 million for option 3). However, the Monte Carlo simulations suggest that poor economic outcomes are likely only for the community-based program (85 percent of simulations have negative net benefits), whereas the school-based program options have positive net benefits in 99 percent of the simulations. The worst-case outcomes depend on the convergence of an unlikely set of factors: low herd protection, low demand for vaccines, low cholera incidence and avoided cost of illness savings, high vaccination cost, and high private cost for obtaining vaccines.

Second, the parameter uncertainty contributing most to the range of economic outcomes is that associated with the cost of vaccination, for all three

TABLE 3. Outcomes for Targeted Vaccination Programs with and without User Fees, in the Base Case and Sensitivity Scenarios (thousands of 2005 US\$ unless otherwise indicated)

Programs	Option 1 School children (Ages 5–14)		Option 2 All children (Ages 1–14 yrs)		Option 3 All ages (Ages 1+)	
	No herd protection	Herd protection	No herd protection	Herd protection	No herd protection	Herd protection
<i>No user fees</i>						
Number of vaccinations (thousands)	82	82	112	112	322	322
Reduction in disease burden (%)	6	45	13	57	31	87
Public cost of illness savings	5	42	10	53	30	82
Costs <sup>a</sup>	181	181	246	246	708	708
Net public costs <sup>b</sup>	176	139	235	192	679	626
Net benefits	–16	454	22	489	–101	–28
Benefit–cost ratio <sup>c</sup>	0.9	3.3	1.1	2.8	0.9	1.0
Worst case net benefits (benefit–cost ratio)	–262 (0.3)	–113 (0.7)	–339 (0.3)	–183 (0.6)	–1,094 (0.3)	–1,084 (0.3)
Best case net benefits (benefit–cost ratio)	29 (1.3)	959 (10.1)	75 (1.5)	1,189 (9.4)	147 (1.3)	1,218 (3.9)
Probability that net benefits > 0 <sup>d</sup> (%)	15	99 +	29	99 +	6	15
Median of net benefits	–67	350	–58	370	–330	–260
<i>User fee = \$1.00</i>						
Number of vaccinations (thousands)	52	52	74	74	199	199
Relative reduction in disease burden (% of program with no fees)	63	70	69	76	63	87
Public cost of illness savings	3	29	7	40	19	71
Costs <sup>a</sup>	114	114	162	162	437	437
Net public costs <sup>b</sup>	59	33	81	48	220	167
Net benefits	42	375	92	459	144	273
Benefit–cost ratio <sup>c</sup>	1.3	4.0	1.5	3.6	1.3	1.5
Worst case net benefits (benefit–cost ratio)	–113 (0.5)	–18 (0.9)	–150 (0.5)	–41 (0.9)	–472 (0.4)	–424 (0.5)
Best case net benefits (benefit–cost ratio)	51 (1.9)	632 (11.6)	97 (2.1)	847 (11.0)	220 (1.9)	1,306 (6.5)
Probability that net benefits > 0 <sup>d</sup> (%)	55	100	68	100	50	70

(Continued)

TABLE 3. Continued

Programs	Option 1 School children (Ages 5–14)		Option 2 All children (Ages 1–14 yrs)		Option 3 All ages (Ages 1+)	
	No herd protection	Herd protection	No herd protection	Herd protection	No herd protection	Herd protection
Median of net benefits <i>User fee = \$2.20</i>	8	310	38	370	–0.6	120
Number of vaccinations (thousands)	30	30	45	45	112	112
Reduction in disease burden (% of program with no fees)	36	43	45	53	37	65
Public cost of illness savings	2	18	5	28	11	54
Costs <sup>a</sup>	65	65	99	99	247	247
Net public costs <sup>b</sup>	–2	–18	–5	–28	–11	–54
Net benefits	59	277	114	384	222	475
Benefit–cost ratio <sup>c</sup>	1.8	4.9	2.1	4.5	1.8	2.7
Worst case net benefits (benefit–cost ratio)	–36 (0.7)	19 (1.2)	–48 (0.7)	24 (1.1)	–152 (0.6)	–72 (0.8)
Best case net benefits (benefit–cost ratio)	47 (2.6)	362 (13.1)	86 (2.9)	534 (12.8)	193 (2.6)	1,060 (10.0)
Probability that net benefits > 0 <sup>d</sup> (%)	87	100	94	100	86	100
Median of net benefits	38	240	79	330	140	360

<sup>a</sup>Not including private costs of vaccination.

<sup>b</sup>Calculated as the total cost—revenues from vaccine sales—public cost of illness avoided. Some of these net public costs are negative; for example, the programs are cost saving, because revenues and avoided public cost of illness outweigh the costs of vaccination.

<sup>c</sup>The benefit–cost ratio is defined as the ratio of benefits (willingness to pay for protection – avoided public cost of illness) to the cost of acquiring vaccines in the program (whether private or through public subsidy).

<sup>d</sup>Based on the outcomes of 10,000 Monte Carlo trials.

*Source:* Authors' analysis based on data described in the text.

795 programs. Figure 2 presents the results of the one-way sensitivity analyses for these options, accounting for herd protection (the equivalent diagrams ignoring herd protection are available in the online supplement at <http://wber.oxford-journals.org/>). Vaccination cost is particularly important for the community-based program option because it delivers the most vaccines.

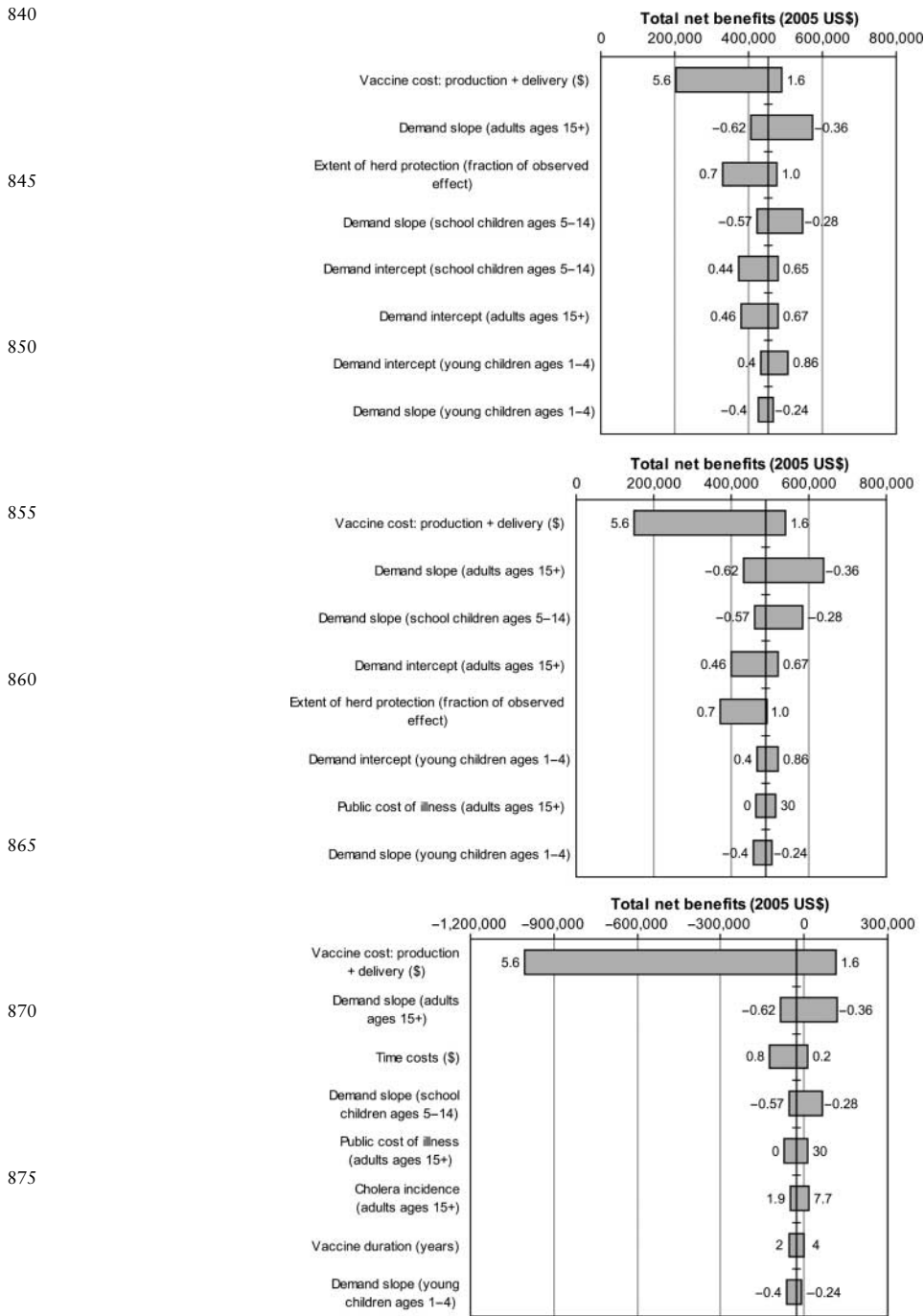
800 Third, as shown in figure 2, the influence of the extent of herd protection decreases as program size increases. For option 1, this parameter is the third most important in influencing the range of final outcomes; for option 2, it is fifth; and for option 3 it is not among the top eight parameters. This results from the interaction between cholera vaccine herd protection and the demand for protection from the disease in the population affected by each program option. In option 3 every individual with nonzero demand for cholera vaccines is assumed to be vaccinated. The remaining unprotected individuals have zero willingness to pay for protection, so that the economic benefits of indirect protection are very low (they include only public cost of illness savings and protection to infants, who cannot be vaccinated). In option 2 all children for whom willingness to pay for protection is nonzero are vaccinated, but adults and infants excluded from the program for whom willingness to pay for protection is nonzero are indirectly protected at a level of more than 40 percent. The per person impact of this externality increases further in program option 1, as another program-excluded group of unvaccinated people (young children) with nonzero average willingness to pay for protection are also protected at no cost (the overall indirect effect is now about 25 percent). The importance of this indirect effect is further shown by the fact that the parameters of the demand function for adults are second in importance in all three programs, even though they are vaccinated only in option 3.

#### 820 *Programs with User Fees*

825 The cost–benefit results for cholera vaccination program options are also calculated at two different user fee levels: a subsidized price of \$1 for the two-dose regime and \$2.20, which corresponds to the full cost of production plus delivery in the base case (see table 3). Based on the demand curve from Lucas and others (2007), slightly fewer than 40 percent of people in Beira are estimated to be willing to pay a price of \$1 for the two-dose cholera vaccine regime in a community-based program; that share drops to about 20 percent at the \$2.20 price. In the base case, net benefits for all three program options are positive for both these user fee levels, even if herd protection is ignored. Overall disease reduction levels drop significantly for the smaller school-based programs. There is a crucial difference between the economics of option 3 and the two school-based programs when herd protection is included. Whereas net benefits of option 3 increase as the user fee increases, net benefits decrease for the two school-based programs.

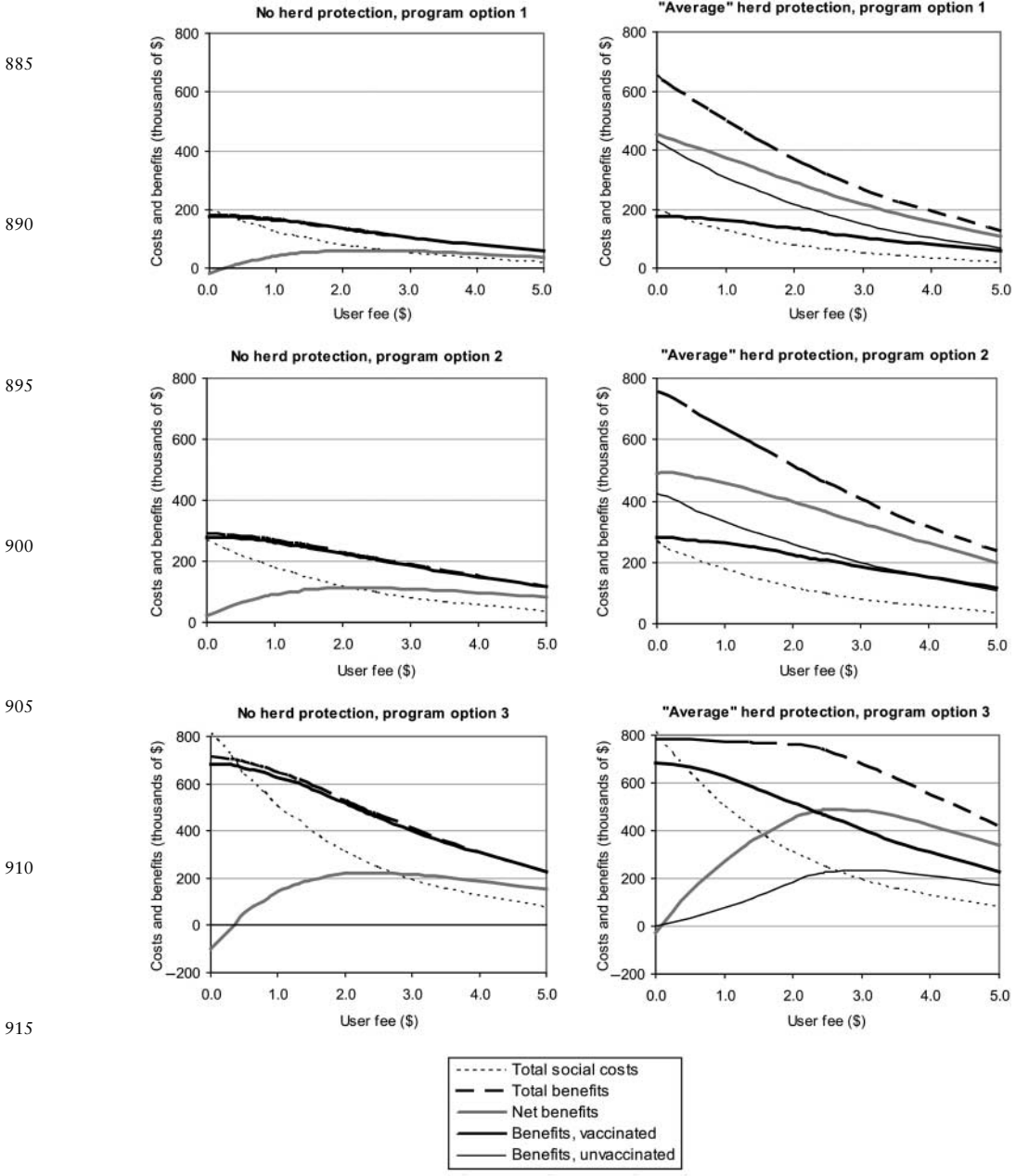
835 Figure 3 shows in more detail how social costs, benefits, and net benefits change over a range of user fees from zero to \$5, assuming base case

FIGURE 2. Tornado Diagrams Showing the Eight Parameters Most Important in Determining Variation in Net Benefit Outcomes, Including Herd Protection for Program Options 1–3



Source: Authors' analysis based on data from a cholera vaccination trials and epidemiological and economic research in Beira, Mozambique; see text for details

FIGURE 3. Total Costs, Benefits, and Net Benefits As a Function of User Fees for All Three Program Options, with and without Herd Protection



Source: Authors' analysis based on data from a cholera vaccination trials and epidemiological and economic research in Beira, Mozambique; see text for details.

925 parameter values, for all three program options, with and without herd pro-  
tection. When herd protection is not included, net benefits are maximized  
930 very close to the full economic cost of vaccination, for all three programs  
(\$2.60, including private costs), because public cost of illness savings are  
relatively small. Also, for option 3, net benefits also peak very close to this  
full economic cost of vaccination (the maximum is at roughly \$2.45). This  
is because benefits to the unvaccinated continue to increase as the user fee  
increases well past the full cost of vaccination, such that total benefits stay  
relatively high even as cost decreases. In contrast, total benefits tend to fall  
935 faster than total costs for the school-based options (note, however, that net  
benefits do increase at first for option 2 up to a user fee of about \$0.15),  
because herd protection in the untargeted population is lost as coverage  
declines. In option 1, for example, only 3 percent of the population are vac-  
cinated when the user fees are \$1 and 2 percent when they are \$2.20, so the  
herd protection is low.

940 Because of the very different sizes, it is easier to compare the three program  
options by examining the benefit–cost ratios, which give an indication of the  
magnitude of benefits of vaccination relative to its costs. These calculations  
show that the smallest program achieves the highest benefit–cost ratios. This  
stems from the fact that the small programs both target people for whom  
945 household demand for cholera vaccines is high and take advantage of the fact  
that marginal herd protection benefits increase most quickly at low coverage  
levels. All school-based programs have a benefit–cost ratio of about 3 or  
higher in the base case, indicating that these programs are economically very  
attractive.

950 The sensitivity analysis of the programs with user fees shows that the impor-  
tance of the cost parameter decreases as the user fee goes up (figure 4).  
Targeting individuals with higher demand for the vaccine begins to offset the  
downside risk associated with cost uncertainty. School-based programs are  
likely to pass a cost–benefit test in Beira even for very pessimistic cost assump-  
955 tions. High vaccination costs would have to be combined with unfavorable  
values of other parameters for school-based programs to fail. For the  
community-based programs, however, the risk is quite high, although it  
decreases quickly as user fees rise because higher user fees ensure that vaccines  
go to the individuals who value them most. At a user fee of \$2.20, option 3 is  
960 very likely to pass an economic test.

In varying multiple model parameters simultaneously, it can be noted that,  
in the worst case, net benefits improve for all program options as the user fee  
increases. Net benefits in the best case all decline as the user fee rises from \$1  
to \$2.20. These results demonstrate that the shape of the net benefits curves for  
965 the three program options shown in figure 3 changes with the values of the par-  
ameters in the cost–benefit model. In the best case, the net benefits curves  
remain similar to those depicted in the case of options 1 and 2 but peak

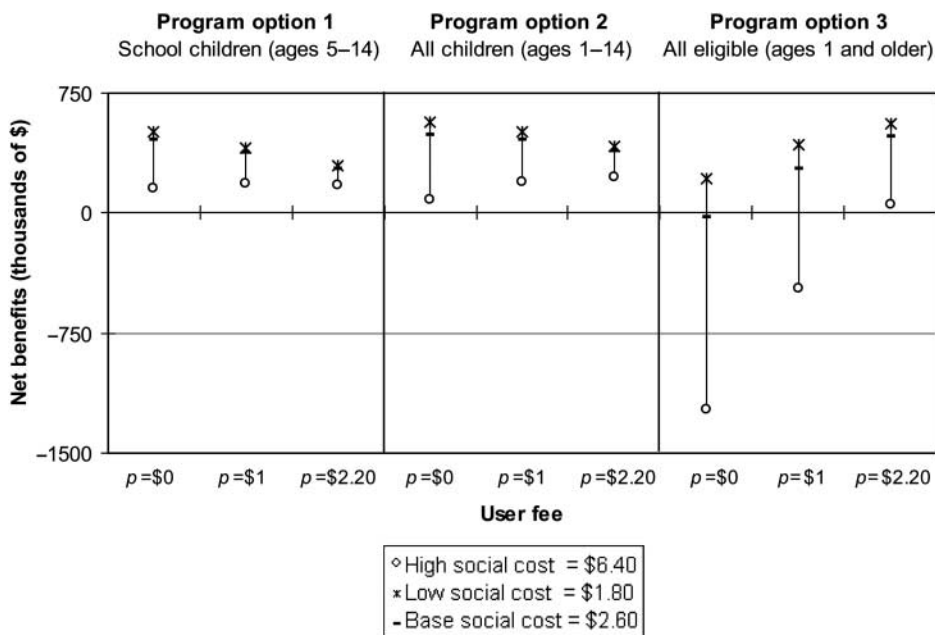
FIGURE 4. Sensitivity of Net Benefits to Total Social Cost of Immunization (Production Plus Delivery Plus Private) of Program Options from Table 3, Including Herd Protection

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Source: Authors' analysis based on data from a cholera vaccination trials and epidemiological and economic research in Beira, Mozambique; see text for details.

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somewhere below \$2.20 for option 3. In the worst case, net benefits peak well above \$1 for all three program options.

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The outcomes for program options 1 and 2 obtained in the Monte Carlo simulations are relatively insensitive to changes in the user fee. More than 99 percent of simulations for both of these school-based options with user fees have positive net benefits, and the median outcomes decline slightly as the user fee rises. For option 3 the percentage of simulations with positive net benefits increases from 15 to 70 percent to 100 percent as the fee increases. Also, inclusion of herd protection greatly reduces the risk of negative economic outcomes associated with all three program options (full cumulative distributions of these Monte Carlo results are available in the online supplement).

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## V. DISCUSSION

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Based on the results presented in this article, cholera vaccination appears to be an economically attractive health policy intervention in Beira over a wide range of program options and user fees when the herd protection externality is considered and if the costs of vaccination are about \$2.20 per fully vaccinated

individual. The analysis shows that accounting for herd protection dramatically improves the economic viability of prospective cholera vaccination programs. If the benefits of herd protection are not included in the cost–benefit analysis, there are many plausible combinations of parameters for all three program options without user fees for which the cost–benefit model yields negative net benefits, even in a high-incidence location like Beira. In the base case, when herd protection is not included, school-based programs without user fees may still be attractive from an economic perspective.

Accounting for herd protection also improves the cost-effectiveness of cholera vaccination programs in Beira. However, when herd protection is incorporated in a cost-effectiveness model, cost-effectiveness measures such as costs per DALY avoided become a function of vaccination coverage. In this case, there is no obvious objective function for a cost-effectiveness analysis. Maximizing the number of DALYs avoided results in very high costs per marginal DALY avoided. There is no economic rationale for choosing a coverage level that minimizes the costs per DALY avoided. This could result in a very low coverage level; expanding coverage might still save DALYs at very little cost.

Although school- and community-based program options without user fees are likely to pass a cost–benefit test if herd protection is considered, these program options remain expensive from a public financing perspective. Public cost of illness savings are only about 10–20 percent of the cost of implementing these programs and thus do not provide much help in lowering this budgetary impact of the vaccination program. In addition, the extent to which public cost of illness savings can be converted to cash is questionable in Beira, where cholera cases are almost exclusively treated in the Cholera Treatment Center. Given the short-lived protection afforded by the cholera vaccine, it would not be advisable to close the treatment center unless a long-term program is implemented. Moreover, a large portion of the public costs in the Cholera Treatment Center are fixed in the short term, such as overhead costs and medical staff salaries.

Programs with user fees offer two principal advantages: they focus the vaccination effort on individuals who value the vaccines the most, and they reduce the public sector financing burden of vaccination. The first advantage of user fees, which targets vaccination to those who place higher values on protection from cholera, is especially important for the community-based programs. The analysis shows that mass vaccination programs with low user fees (\$1 per two-dose regimen) are much more likely to pass a cost–benefit test than those without user fees.

The second benefit of user fees is that revenues from the vaccination program would lessen the financial burden on the public sector or reduce reliance on cash investments from the donor community (Lauria and others 2009). When public financing relies on government revenues raised through distortionary taxes, reducing government expenses (and therefore taxes) by \$1

per vaccinated individual will provide more than \$1 of welfare gain. On the other hand, the opportunity cost of vaccination programs financed by donor grants may be very low. Still, cholera vaccination is effective for only about three years, and grants are unlikely to provide a long-term solution for financing the recurrent costs of ongoing vaccination programs. Relatively low user fees of \$1 (perhaps less) could help to offset some of the costs of implementing a vaccination program and still allow important herd protection benefits.

The evidence on cholera disease dynamics suggests that significant herd protection can result from a relatively small number of immunizations, particularly in endemic areas where there is some natural immunity among the population. This fact has economic as well as epidemiological consequences. Even if the very poor are unable to purchase vaccines, they can still reap the benefits of the herd protection externality. In effect, if a government-sponsored program offered cholera vaccines at subsidized prices, the government (through the subsidy) and people with willingness to pay higher than the user fee would be providing free cholera protection to the unvaccinated members of the community through the herd protection externality. In some locations, it may be possible to set user charges at a level to recover the costs of a vaccination program while still retaining sufficient demand for vaccination at that price so that population coverage would ensure that most unvaccinated individuals were protected as well through indirect herd protection.

In other locations, the herd protection externality resulting from a given user charge will not be sufficiently large to appreciably reduce the risk of cholera infection among the unvaccinated members of the population. If many people in the general population are very poor, there may be insufficient private demand to achieve high levels of herd protection. The spatial distribution of the herd protection externality is also important and likely to be highly site specific. To the extent that coverage rates are lower in poor neighborhoods, the herd protection externality among the poor might be lower than expected, with a smaller effect on disease prevalence. In such cases this distributional concern could justify increased subsidies to poor households.

Policymakers can use information on the net benefits of cholera vaccination program options, such as that presented in this article, in a variety of ways. Economists would argue for allocating public sector funds to projects with the highest net benefit per budgetary unit up to the point where such monies were exhausted, thus maximizing the total net benefits from the portfolio of public expenditures. Some might use cost–benefit analysis as a screening test for eliminating bad projects that result in negative net benefits, followed by selection among remaining projects based on distributional, public health, or other criteria. Cost–benefit analyses also might serve to eliminate programs with large budget requirements or high risks. For example, in Beira today, community-based vaccination without user fees could be judged to be both expensive and risky and thus unworthy of consideration for public sector funding. However, even though school-based programs with low user fees have the highest net

benefits, some policymakers might prefer school-based programs with no user fees because they do provide positive net benefits. Avoiding user fees for school-based programs might be deemed more politically acceptable, would create a positive herd protection externality, and would not impose a heavy financial burden on the public sector.

#### SUPPLEMENTARY MATERIAL

A supplemental appendix to this article is available at <http://wber.oxfordjournals.org/>.

#### APPENDIX A. PARAMETER ASSUMPTIONS

This appendix discusses in more detail the parameters (table 2) that go into the calculation of costs and benefits (equation (1)).

##### *Vaccine Effectiveness and Duration*

Estimates of cholera vaccine efficacy,  $\eta$ , in the absence of herd protection come from case-control studies conducted in conjunction with vaccine trials of the whole-cell vaccine produced in Vietnam (Trach and others 1997; Thiem and others 2006). Trach and others found estimated first-year efficacy, or protection among the vaccine recipients in the first year following vaccination, to be 66 percent (46–79 percent at a 95 percent confidence interval), declining to 46 percent over three years. Thiem and others found effectiveness over a longer period of 3–5 years to be 50 percent, which included very low protection after year 3 (9–63 percent at a 95 percent confidence interval). Based on this evidence, the vaccine is assumed to afford recipients 55 percent protection (range 40–70 percent) over duration  $d$  of three years (sensitivity range 2–4 years). To simplify discounting of public cost of illness savings,  $d$  is assumed to be integer valued, with the probability of two- and four-year duration each being equal to half the probability of three-year protection.

##### *Incidence*

The incidence data  $I_i$  for the model were drawn from a recent diseases of the most impoverished (DOMI) project compilation of multiyear disease incidence from the population-based surveillance study in Beira (Deen and others 2008). Incidence rates were found to be highest among children ages 2–5 (8.8 cases per 1,000 people). Incidence was next highest for adults, probably because of the vulnerability of the elderly (3.8 cases per 1,000 people). Incidence rates are very difficult to measure, because they vary considerably over time and are typically measured through passive surveillance studies. The DOMI data were derived from passive surveillance and therefore probably underestimate the true incidence of cholera over the study period (January–December 2004). Deen and others did not estimate confidence intervals, so a wide range of variation

1145 TABLE A-1. Cost of Illness for Cholera in Beira, Mozambique (January–  
December 2004)

Cost component	Children (under age 18)	Adults (ages 18 and older)	Overall
Private			
1150 Direct <sup>a</sup>	3.9	5.0	4.6
Indirect <sup>b</sup>	17.7	12.1	14.1
Public	26.0	29.9	28.4
Total	47.6	47.0	47.2

Note: Based on 50 cases (19 among children under age 18), in 2005 US\$.

1155 <sup>a</sup>Includes treatment costs (diagnostic tests, medicine, examination, and bed charges); transportation costs; expenses on nonmedical items used to aid treatment; lodging for accompanying persons; and other payments made due to the case of illness.

<sup>b</sup>Includes the patient’s lost income and productivity, net cost of substitute labor, and cost of caretakers’ and other people’s time due to the case of illness.

Source: Poulos and others (2008).

1160 of incidence was adopted in the sensitivity analysis here, from half to twice the measured rates.

### Cost of Illness

1165 The DOMI project’s economic studies provided data on the public cost of illness, COI<sub>i</sub>, associated with cholera in Beira for the three age groups (Poulos and others 2008). This public cost of illness includes the cost of outpatient visits or hospitalization, medicines provided free of charge (or at subsidized prices) to patients undergoing cholera treatment, and any diagnostic tests provided to patients (subsidized or free). The data are unpublished and are summarized below (table A-1). It may be incorrect to assume that the full public cost of illness of cases of cholera prevented can be avoided through vaccination, because health facilities such as the Cholera Treatment Center in Beira may not be easily convertible to other uses. Therefore, the savings per case in public cost of illness avoided is estimated to range from zero to the full public cost of illness measured by Poulos and others for each age group (with a 50 percent savings for avoided cases in the base case). A 3 percent annual discount rate is applied for avoided cost of illness (range of 1–10 percent).

### Willingness to Pay and Coverage

1180 The stated preference study from Beira provides econometric estimates of coverage levels at a price of zero  $q_{i,0}$ , the price parameter  $\beta_p$  (Lucas and others 2007). The base case used the demand and coverage estimates favored by Lucas and others, adjusted for the effect of time to think. This adjustment reflected the fact that respondents in Beira who were given the opportunity to consider the vaccine scenario overnight expressed lower willingness to pay and more certainty about their responses. The sensitivity analysis used the 95 percent confidence interval estimate of the value of the price coefficient  $\beta_p$

1190 from Lucas and others and allowed the zero-price coverage rates,  $q_{i,0}$ , to vary  
 1195 from a further 25 percent reduction up to the “no-time-to-think” estimates  
 derived from the data collected in the same survey. Ranges of willingness to  
 pay among covered individuals ( $WTP_i$ ) and on average ( $\overline{WTP}_i$ ) consistent with  
 these estimates were then derived for the different age groups, using equations  
 (3) and (4).

### *Vaccine Cost*

1200 The cost of cholera vaccination programs consists of the cost of acquiring the  
 vaccine from the manufacturer, the cost of delivering and administering the  
 vaccine to the target population, and the private time and travel costs incurred  
 by individuals wishing to be vaccinated. These costs depend on a number of  
 factors for which there is little published information. A few years ago, the  
 selling price of the whole-cell vaccine in Vietnam was about \$0.40 (6,327  
 Vietnamese dong) per dose (Thiem and others 2006). In India, preliminary esti-  
 mates of production cost associated with the DOMI study are \$0.66 per dose.  
 1205 This analysis assumes that the government of Mozambique could purchase  
 such a low-cost whole-cell vaccine at \$0.50 per dose. Price lists from the  
 United Nations Children’s Fund indicate that the cost of shipping vaccines  
 from the manufacturer were about 15 percent of total vaccine cost (UNICEF  
 2003). Wastage is assumed to be about 10 percent. Thus, total vaccine cost,  
 1210 including shipping and wastage, is roughly \$0.60 per dose in the base case  
 (range: \$0.5–\$0.8 per dose, or \$1.00–\$1.60 per person for two doses).

1215 With the exception of the experimental trial conducted in Beira in 2003–04,  
 which offers a partial accounting of program costs, there appear to be no pub-  
 lished estimates of delivery cost specific to cholera vaccines. The delivery cost  
 estimates used here thus rely on data collected during typhoid vaccination dem-  
 onstration projects in the DOMI study sites and a recent review and analysis of  
 22 studies of the costs of vaccine projects in low- and middle-income countries  
 (Lauria and Stewart 2008). Vaccine delivery costs varied widely, even among  
 similar programs (such as vaccination programs under the Expanded Program  
 of Immunization). The median delivery cost per dose (after removing four out-  
 1220 liers) was \$0.80 (mean \$1.10), with estimates ranging from \$0.10 to \$5.70 per  
 dose. Median delivery costs for the low-income countries were roughly \$0.50  
 per dose. These estimates are lower than those reported from the DOMI cost  
 studies for typhoid Vi polysaccharide vaccine (\$0.75 on average); however, it is  
 1225 plausible that delivery costs for oral vaccines would be less than for injectable  
 ones such as the typhoid vaccine, because of lower personnel costs and greater  
 efficiency of the vaccination process.

1230 Following a commonly used convention in the cost-effectiveness literature  
 (see Sinha and others 2007 for a recent example), it is assumed that delivery  
 costs can be captured in a constant marginal cost per vaccinated individual cal-  
 culation and that the marginal delivery cost per dose is the same for a school-  
 based program (options 1 and 2) as for a community-based program (option

3). It is possible that average delivery costs are lower for school-based programs than for mass programs (because health staff time might be used more efficiently and because less social marketing might be needed), but the body of evidence was not strong enough to warrant the use of different delivery costs for the program options. This study thus adopted Lauria and Stewart’s (2008) estimate of \$0.50 per dose for delivery costs and set the range for the uncertainty analysis according to the 12.5–87.5 percent confidence interval of the 16 studies for the low-income countries they review (\$0.30–\$2 per dose).

Another component of the study in Beira found that the average time cost associated with queuing for participants in the Beira trial was \$0.20 per dose (Jeuland and others 2008). This expense was added to the total costs in calculating net social benefits, and a range of \$0.10–\$0.40 was set. For children, time costs are assumed to be half the value for adults (\$0.10 per dose, with a range of \$0.05–\$0.2).

#### APPENDIX B. THE HERD PROTECTION MODEL

Ali and others (2005) recently presented intriguing evidence of indirect herd protection from cholera vaccination, evidence that Longini and others (2007) used in further epidemiological models. Their conclusions are based on a reanalysis of first-year incidence data among vaccinated and unvaccinated people from *baris* with different levels of coverage in Matlab, Bangladesh. For simplicity and use in the cost-effectiveness models, their data were interpreted and applied (table B-1, columns 1, 3, and 4), as explained below. The average coverage rates shown were calculated based on their data (column 2).

The data presented a problem, however, because they apply only to first-year herd protection effects. Because oral cholera vaccine efficacy declines over time, use of the data for longer-term cost-effectiveness and policy analysis requires adjustments so as not to overstate the health benefits of vaccination.

TABLE B-1 Incidence among Vaccinated and Unvaccinated Individuals in *Baris* with Different Levels of Coverage, in Matlab, Bangladesh

(1)	(2)	(3)	(4)
Coverage level (%)	Average coverage in group (%)	Incidence among vaccinated individuals (cases per 1,000 people)	Incidence among unvaccinated individuals (cases per 1,000 people)
<28	23	2.67	7.01
28–35	35	2.48	5.87
36–40	44	1.58	4.72
42–50	48	2.26	4.65
>51	56	1.28	1.48

Source: Ali and others (2005).

*Herd Protection as an Exponential Function of Coverage*

The incidences for vaccinated and unvaccinated populations are modeled with a set of two differential equations. The first predicts incidence among the vaccinated ( $V$ ) as a function of coverage ( $x$ ) only. The second, for the incidence among the unvaccinated ( $U$ ), is similar but specifies that incidence can never be higher among the vaccinated subgroup than among the unvaccinated:

$$(B-1) \quad I_{x,v} = I_{0,v} \cdot \exp(-k_v x),$$

$$(B-2) \quad I_{x,u} = I_{0,u} \cdot \exp(-k_v x) + (I_{0,u} - I_{0,v}) \cdot \exp(-k_u x)$$

where  $k_v$  and  $k_u$  are rate constants. The parameters for equation (B-1) can be estimated with a simple ordinary least squares regression of the coverage data in table B-1 on the log of incidence rates among the vaccinated. The intercept ( $I_{0,v}$ ) is 4.5 cases per 1,000 ( $p = 0.02$ ) and the rate constant ( $k_v$ ) is  $-0.02$  ( $p = 0.09$ ).  $I_{0,v}$  would be the incidence for a hypothetical vaccinated individual if no vaccines were given to the population—that is, if there were no herd protection at all. As shown, incidence  $I_{x,v}$  declines at a decreasing rate as coverage rates increase. The  $R^2$  for the regression is 0.66, which is similar to the  $R^2$  for a linear model (0.69).

Given the estimated parameters for  $I_{0,v}$ , the parameters of equation (6) for avoided cases are then estimated with a simple nonlinear least squares model. The  $R^2$  for this model is 0.97 (higher than the 0.86 obtained for a linear model), and the intercept ( $I_{0,u}$ ) is significant at the 10 percent level ( $p = 0.07$ ), though the rate constant ( $k_u$ ) has a  $p$ -value of 0.14.  $I_{0,u}$  is the baseline incidence among the unvaccinated—it represents incidence among unvaccinated individuals given a coverage level of zero. Without loss of generality, equation (B-2) can be rewritten as:

$$(B-3) \quad I_{x,u} = I_{0,u} \cdot \exp(-\tilde{k}_u x).$$

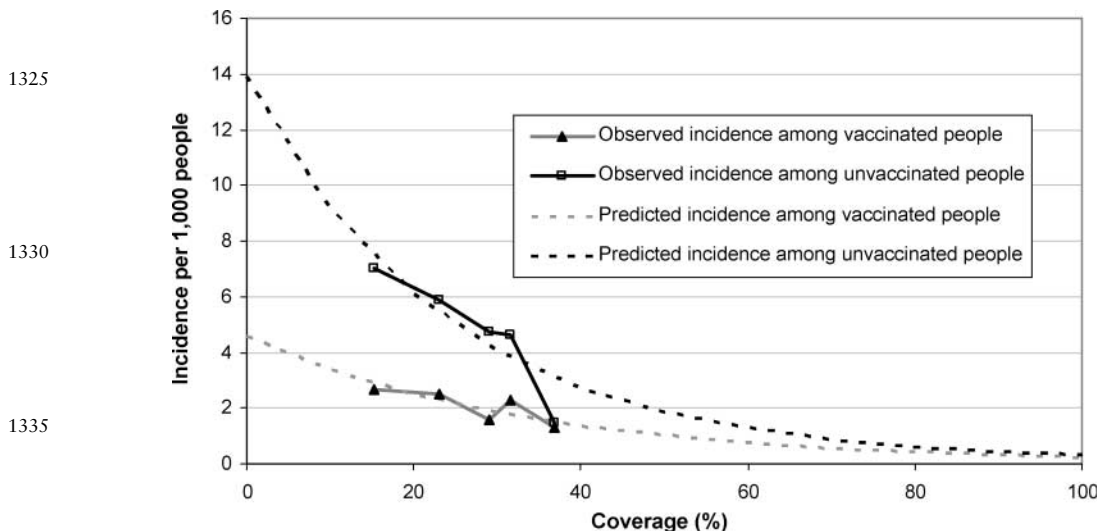
Figure B-1 plots the observed Matlab data against the exponential fits. As coverage increases, the incidence for unvaccinated individuals approaches that for the vaccinated subgroup.

The herd protection among the vaccinated ( $\eta_{x,v}$ ) and the unvaccinated ( $\eta_{x,u}$ ) can be expressed as the difference between the baseline incidence ( $I_{0,u}$ ) and the incidence in the group in question, as shown in equations (B-4) and (B-5):

$$(B-4) \quad \eta_{x,v} = \frac{I_{0,u} - I_{0,v} \cdot \exp(-k_v x)}{I_{0,u}} = 1 - \frac{I_{0,v}}{I_{0,u}} \cdot \exp(-k_v x),$$

$$(B-5) \quad \eta_{x,u} = \frac{I_{0,u} - I_{0,u} \cdot \exp(-\tilde{k}_u x)}{I_{0,u}} = 1 - \exp(-\tilde{k}_u x).$$

FIGURE B-1. Observed Incidences in Matlab, Bangladesh, and Predictions from Exponential Fit



Source: Authors' analysis based on data from Ali and others (2005)

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