ARE CHOLERA AND TYPHOID VACCINES A GOOD INVESTMENT FOR A SLUM IN KOLKATA, INDIA?

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ABSTRACT

JOSEPH COOK: Are Cholera And Typhoid Vaccines A Good Investment For A Slum In Kolkata, India?
(under the direction of Dale Whittington)

Next-generation cholera and typhoid vaccines have the potential to reduce the burden of both diseases in areas where they are endemic. We examine the case for public investments in these vaccines for the Tiljala neighborhood of Kolkata, a low-income, high-incidence slum. We take a social perspective and use three measures of the vaccines' economic benefits: avoided private and public costs of illness (COI); avoided COI plus mortality risk reduction benefits; and private willingness-to-pay (WTP) derived from stated preference studies we conducted in Tiljala in 2004. The study represents a unique opportunity to evaluate vaccine programs with a wealth of new high-quality, site-specific data. We also use incorporate recent epidemiological evidence from Bangladesh on indirect protection from cholera vaccines.

We find that a typhoid vaccination program without user fees would most likely pass a social cost-benefit test. Depending on which ages are targeted, all programs would be either "cost effective" or "very cost effective" using the standard comparisons of cost per DALY avoided with GDP per capita. Because many other health interventions have much lower cost-effectiveness ratios, however, typhoid programs are probably not a wise use of scarce public health resources. At an average total cost per immunized person of ~US$2.0, typhoid programs would absorb a large fraction of existing public sector spending on health in India. We find significant private demand for the vaccines such that the government could design a financially-sustainable program with user fees. We find that a program where adults pay a higher fee to subsidize vaccines for children (who have higher incidence) would avoid more cases and maintain revenue-neutrality.

Because of higher average costs (~US$3.5) and lower incidence, cholera programs are less attractive. A program targeting both groups of children, and perhaps even programs that included adults, would probably pass a cost-benefit test. Cost-effectiveness ratios are worse than for typhoid, so the argument for allocating public subsidies to cholera vaccination is even weaker. A financially-sustainable program with user fees of ~US$3.5 is possible. Although only 16% of the population would be vaccinated, the program (with herd effects) would still avoid 329 cases over 3 years.

DEDICATIONS

To the people in Tiljala who struggle every day to improve their lives

and

To my namesakes, Joseph D. Cook and Herbert H. Hillsey

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LIST OF ABBREVIATIONS

CFR	Case fatality rate
COI	Cost of illness
CV	Contingent valuation
DALY	Disability-adjusted life year
DOMI	Diseases of the Most Impoverished
IVI	International Vaccine Institute
NBREG	Negative binomial regression
ORS	Oral rehydration solution or therapy
NICED	National Institute for Cholera and Enteric Diseases
SP	Stated preference (i.e. CV and SC)
WTP	Willingness-to-pay
VSL	Value of a statistical life

CHAPTER 1

POLICY PROBLEM

1.1 Introduction

In considering whether to implement a vaccination program, a health or finance policymaker is faced with several types of questions. First, there are questions of baseline epidemiology. How serious is the disease – how severe are the symptoms, how long do the symptoms last, and how often do patients die from the disease? How many people contract the disease? How is the disease treated? Does the disease affect the poor more than the rich?

Second, there are questions about the vaccine. How effective is the vaccine in protecting against the disease? How long does protection last? How is the vaccine administered, and how many doses does it require? If some fraction of the population is vaccinated, how much protection does this confer (through herd immunity) to the unvaccinated population?

Third, there are questions of finance. How expensive is the vaccine to produce, distribute, store and administer to recipients? How much is the public health sector spending to treat cases? Could the vaccine reduce the number of cases enough so that the vaccine program cost would be paid for through reductions in this public expenditure?

Fourth, there are questions about the design of the vaccination program. What population should the program target – should it target everyone (mass vaccination), target specific age groups, and/or target specific geographic areas where the incidence of the disease is highest? Should the vaccination program be routine (like the EPI program for infant immunizations) or periodic/ campaigns (like the polio vaccine campaigns)? How will the program reach people – will vaccines be delivered house to house or offered at clinics or outposts? How many outposts should vaccines be offered at, and where should they be located? What percent of the population would take the vaccine

(even if no user fee was charged)? If user fees *were* charged, how many fewer people would choose to be vaccinated?

A fifth group of questions is not commonly raised for vaccines in a rigorous way – is the vaccine a good investment of the government's scarce health resources from a social welfare perspective? Because the earliest vaccines protected children from horrible, life-long illnesses (e.g. polio), there was historically little perceived need from a policy perspective for a careful weighing of the social costs and benefits of a vaccine. The perception remains among many that vaccines are always a good investment of public resources.

Thinking in the abstract, all infectious diseases are not alike. Some have only mild, short-term effects in most people (e.g. colds, flu), while others have very long term effects (e.g. river blindness). Some kill often and quickly (e.g. Ebola, SARS), while others are rarely fatal (e.g. Hepatitis A). Some are easily and cheaply treated (e.g. diarrhea) while others are either very expensive to treat (e.g. anti-retrovirals for HIV) or are generally uncurable (e.g. polio). People surely react to these differences if faced with the choice of how to reduce their chances of contracting different diseases through behavioral changes or other averting expenditures. Surely, then, the government's decisions about how to spend scarce health resources should also reflect these differences. Different vaccines will have different values to society depending on all of the factors mentioned above (incidence, severity, fatality, length of illness).

Despite this, theoretically rigorous economic valuations of vaccine programs have generally been lacking, as I detail in the literature review in Appendix A. This dissertation focuses on answering many of these policy questions -- with particular attention to the last group of economic questions – for cholera and typhoid vaccination programs in Kolkata (Calcutta), India. In particular, I focus on the neighborhood of Tiljala, a very poor slum of approximately 120,000 people with relatively high cholera and typhoid incidence. In the summer of 2004, we asked people in Tiljala and another, more middle-class, neighborhood (Beliaghata) about their willingness-to-pay for cholera and typhoid vaccines. Although I focus on Tiljala, cholera and typhoid fever are of course problems

throughout India and in many other developing countries, and the question of whether to invest in expanding coverage with new-generation vaccines against these diseases is important and timely. The next section will provide an introduction to these diseases.

1.2 Cholera and typhoid fever

Cholera is characterized by intense, watery diarrhea. It is easily treated by quickly re-hydrating the patient with oral rehydration solution (ORS) or IV fluids, and antibiotics are generally unnecessary and ineffective (Schaecter et al. 1998; Todar 2006). Cholera can kill a patient within 24-48 hours through severe dehydration, though in practice cases are rarely fatal as long as patients have access to ORS treatment. Ali *et al* (2002) constructed a spatial map of cholera risks in Bangladesh and observed that the risk of dying from cholera increased with distance from the nearest health clinic. Cholera is caused by a bacterium (*Vibrio cholerae*) that lives in coastal estuarine waters in association with phytoplankton; high temperatures and algal blooms have been associated with its transmission into humans and subsequent outbreaks (Schaecter et al. 1998). Since the bacterium has hosts besides humans, it is impossible to completely eradicate cholera (indeed, there are occasionally very small outbreaks on the US Gulf Coast from eating uncooked fish (Salyers and Whitt 2002)).

A total of 131,943 cholera cases and 2,272 cholera deaths were reported to the World Health Organization (WHO) in 2005 (WHO 2006a), though most experts believe this is an underestimate because of under-reporting and inadequate surveillance. India reported 3,155 cases and 6 deaths. Because clinicians can confuse cholera for intense diarrhea, it is also difficult to estimate the number of cholera cases without culturing stool samples. Very few careful studies have been conducted to document the disease burden of cholera in specific locations, though our colleagues on the DOMI project at the International Vaccine Institute and host country institutions are beginning to publish the first of these (Deen et al. 2006, Sur et al. 2005, Sack et al. 2003).

Typhoid fever is characterized by high fever, chills, headaches and malaise or delirium (Parry et al. 2002). Typhoid fever is also caused by a bacterium (*Salmonella typhii*). Unlike the bacterium

that causes cholera, the typhoid bacterium invades and damages the tissues of the GI tract and then progresses into the bloodstream and on to other organs in the body[1]. Typhoid fever must be treated with antibiotics. With antibiotics, cases last 4-9 days (Parry et al. 2002); without treatment they may last 4 – 8 weeks (Schaecter et al. 1998). Resistance to antibiotics is a growing and important problem (Parry et al. 2002): Griffin (1998) 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 (2004) found that the cost of illness for "slow responders" (those who did not respond quickly to antibiotics) was five times higher than for those who were successfully treated. Humans are the only carriers of *S. typhii*, so eradication of typhoid fever is theoretically possible. Because patients are initially asymptomatic for 7-14 days and remain carriers for several weeks after treatment, and because 1- 4% of carriers can remain asymptomatic for over a year (Parry et al. 2002; "Typhoid Mary" being the most famous example), eradication is unlikely in the near term. There are also other closely related serovars (e.g. *S. paratyphii*) that currently produce milder versions of the illness that might step into the ecological niche left by an eradicated *S. typhii* and perhaps increase in virulence through evolutionary pressure.

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 (Crump et al. 2004). Like cholera, the true totals of both diseases are thought to be higher because of under-reporting and inadequate surveillance (WHO 2004).

1.3 Vaccines

This analysis will focus on next generation whole-cell-killed (WC) cholera vaccines (either with or without a recombinant b-subunit). The best estimates for these vaccines, which are delivered orally in two doses, indicate that they are 50% effective at preventing cholera for a period of three years (Acosta et al. 2004). Older vaccines were also whole-cell killed vaccines but were much less

[1] Rather than damage them, the cholera bacterium simply "tricks" the epithelial cells of the gut lining into pumping massive quantities of fluid into the GI tract, thus spreading the bacteria (Schaecter et al. 1998)

effective, had side effects, and were very painful. These new WC vaccines have not, however, been proven safe in infants (under 1 year). There is another next-generation cholera vaccine -- a live-attenuated vaccine (CVD103-HgR) – but the data on effectiveness and safety is less established than for the next-generation oral whole-cell killed vaccines.

We focus on Vi polysaccharide vaccines against typhoid, which are given as an injection and require only one dose (Acosta 2004). The best estimates indicate these vaccine are 70% effective for a period of three years. They have been proven safe and effective in children older than 2 years of age. Additionally, there is a live oral vaccine (Ty21a), but it is only licensed for children older than 6, requires 4 doses and is much more expensive than Vi polysaccharide vaccine. Newer Vi vaccines which are conjugated to a recombinant ecotoxin protein (Vi-rEPA, or the "Vi conjugate") do, however, have the potential to protect children under 2 (Parry et al. 2002, Guerrant 2001): the Vi antigen attached to a protein induces a much better immune response in infants than the antigen alone. Trials have shown the Vi-rEPA vaccine is safe and effective (almost 90% after 4 years) in children aged 2-5 (Canh et al. 2004, Szu et al. 1994), but no studies have yet tested the vaccine in children under 2.

1.4 Comparing vaccines with water and sanitation improvements

Both diseases can, of course, be controlled with improved housing, water supply, sanitation, and food handling. Indeed, both diseases are nearly unknown in rich countries in Europe and North America. One obvious question is the relative wisdom of investing in longer-term but more capital-intensive improvements in water and sanitation versus short-term investments in vaccines. This question, though important, will not be the focus here for several reasons. First, investments in water and sanitation are a necessary, but probably not sufficient, condition for eliminating cholera and typhoid. Improving water and sanitation alone does not, for example, eliminate diarrhea (see Fewtrell et al. 2005 for a recent review of this literature). Housing conditions, food handling, and health behavior all play key roles in reducing transmission of these diseases. In this sense, a city would

probably need a whole package of infrastructure investments and sustained economic development to eliminate cholera and typhoid. Second, this package of expensive investments is unlikely to occur in the near term in most settings where cholera and typhoid are endemic. While it may be true that water and sanitation investments are the best solution in the long-term, people contract these diseases now, and vaccines have the potential to reduce their risk of getting ill now. It seems unwise and unethical to delay *consideration* of vaccines simply because of the perception that water and sanitation are the "right" or "ultimate" fix.

1.5 Endemic vs. epidemic

The policy context of interest for this dissertation is one where the two diseases are endemic to the area – that is, the diseases are present nearly every year. A disease may be endemic and very prevalent or endemic and not very prevalent. An important implication of this endemicity for cholera and typhoid is that a significant fraction of the population have acquired some immunity through previous infection.

A different but very important policy context is when the disease is epidemic. These "outbreaks" often occur in refugee settings, and the number of cases and the death rates can be far higher[2]. I do not address epidemic cholera and typhoid fever, though many of the tools developed (especially assessing herd immunity) are directly relevant to epidemic situations.

[2] Because of this acquired, or "natural", immunity, incidence rates are generally lower in adults in endemic areas and highest in children who have not acquired some protection through infection. In epidemic situations like refugee camps, however, people may come from non-endemic regions and have no acquired immunity. In these circumstances incidence is similar in all age groups. Similarly, a new serogroup of cholera (O139, as opposed to O1) emerged in southeast Asia in the 1990's, and since adults had no acquired immunity, incidence rates of O139 cholera were observed to be similar across all age groups in Bangladesh (Sack et al. 2003). No O139 cholera was observed in our study area in 2005 (Sur et al. 2005): an important finding since there is currently no vaccine effective against O139 cholera.

1.6 Previous work on the evaluation of typhoid and cholera vaccines

There have been relatively few economic evaluations of cholera or typhoid vaccination programs (see Appendix A for a more complete description of the existing literature). None of the five cholera evaluations published (MacPherson and Tonkin 1992, Cookson et al. 1997, Naficy et al. 1998, Murray et al. 1998, Sack 2003) take a social perspective, and only one (Cookson) used actual, on-site data. No economic evaluations of cholera vaccines have been published for Kolkata or India.

There are even fewer economic evaluations of typhoid vaccination programs (Papadimitropoulos et al. 2004, Bahl et al. 2004, Canh et al. 2006, Poulos et al. 2004). No evaluations have been published for Kolkata, although Poulos et al (2004) examined the economic attractiveness of typhoid fever vaccination programs for a slum in New Delhi. Although the authors adopted a social perspective, the scope of vaccine benefits were limited to avoided costs-of-illness, which the authors remedied with a COI "multiplier".

CHAPTER 2

SITE AND STUDY POPULATION

2.1 Kolkata

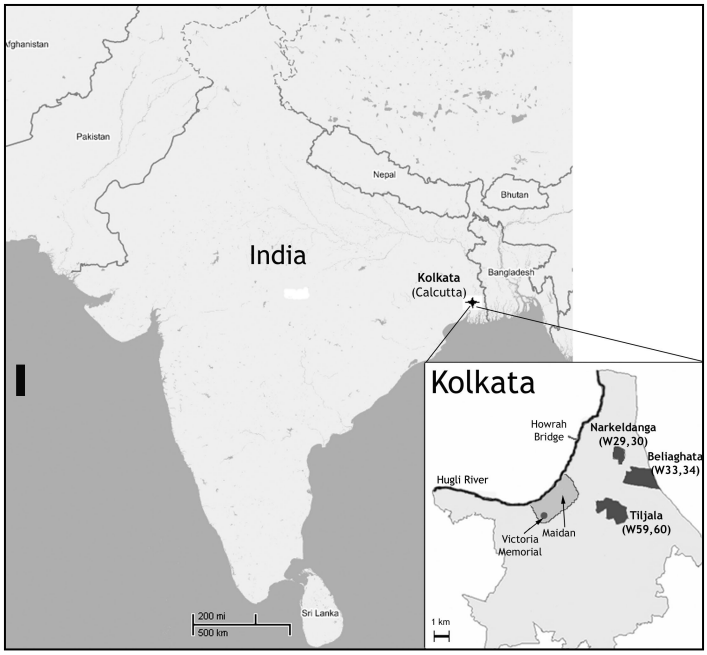
Kolkata (formerly Calcutta) is the third largest city in India, with a population of 4.6 million in the city proper and approximately 13 million in the greater metropolitan area. Of the 4.6 million, about 1.5 million currently reside in slums (both officially recognized and unofficial) (Kundu 2006). Kolkata has three seasons, the cool dry months from November to February, the hot dry period from March to May, and the monsoon season from June to October (Sur et al. 2005). Located in the Ganges-Bramaputra river delta in the state of West Bengal, the city and surrounding region (including Bangladesh) have long been a site of endemic cholera.

2.2 Study Sites in Kolkata

The International Vaccine Institute, in collaboration with the National Institute of Cholera and Enteric Disease (NICED), has conducted a number of studies in Kolkata as part of the Diseases of the Most Impoverished (DOMI) research program. These include cholera and typhoid mass vaccination trials, burden of disease studies, public and private costs of illness (COI) studies, vaccine psycho-behavioral studies, and stated preference (willingness to pay) studies. Each of these studies will be discussed in more detail in Chapter 4. The majority of these studies (vaccine trials, burden of disease, cost of illness and psycho-behavioral studies) were performed in the Narkeldanga neighborhood of Kolkata (Figure 2.1). Narkeldanga includes an area of about 0.7 square kilometers and is mostly composed of "bustees" (i.e. officially recognized slums). NICED and IVI chose Narkeldanga for these studies because they believed it has the highest incidences of typhoid and cholera in Kolkata. The private demand studies were not performed in Narkeldanga, however,

because IVI and NICED did not want to jeopardize vaccine trial participation rates with the information provided in the willingness-to-pay (WTP) studies (hypothetical vaccines with varying user fees).

Figure 2.1 Study site locations



The private demand studies were done in two other Kolkata neighborhoods. The first, Tiljala, is a very poor slum with a population of ~120,000. NICED felt that Tiljala had comparable incidence rates with Narkeldanga. Socioeconomic conditions are also believed to be similar for these two neighborhoods. The second neighborhood, Beliaghata, is a relatively middle-class neighborhood of ~80,000 people with a mix of housing and socioeconomic conditions. We now describe the characteristics of the Narkeldanga and Tiljala in more detail (a description of conditions in Beliaghata can be found in Appendix B). Because we will focus the investment case on the Tiljala neighborhood but use data from the Narkeldanga studies, it is important to establish similarities and differences in the two areas.

2.3 Socioeconomic and environmental conditions

Detailed socioeconomic data are not available from the West Bengal Census at the neighborhood level; however, data exist for Narkeldanga from a census conducted by NICED as well as from a number of socio-economic questions that were included in the cholera and typhoid vaccine WTP studies conducted in 276 Tiljala households. Both areas have poor, very crowded housing conditions with little space between houses (Figure 2.2). Piped water supply in both areas is

intermittent. Data from the WTP study show that most residents in Tiljala get their water from public standpipes, although 11% of households in the sample had private water connections. The vast majority use shared pour-flush toilets, though some households have private flush toilets and others (very few) use open pit latrines. In Narkeldanga, most respondents used either water from private and shared taps or bottled water; about 2% of the population received water from open wells, pumps, or vendors. Although most parts of both neighborhoods have closed sewers, in some parts sewage from toilets flows into open drains outside the houses which can overflow when it rains.

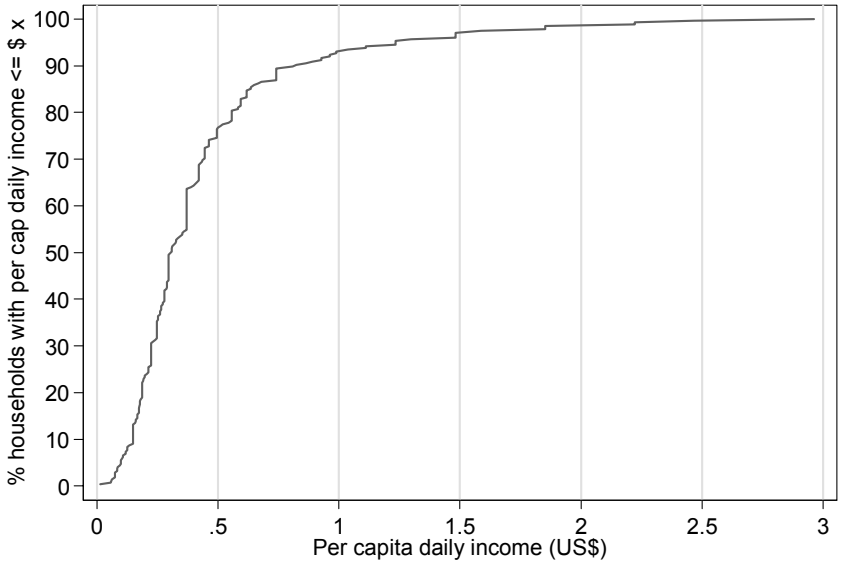
Figure 2.2. Photo of crowded housing conditions in Tiljala, Kolkata

The median monthly household expenditure in Narkeldanga was about US$67 for a median household size of 5 members. This is very comparable to average income estimates based on the Tiljala survey sample, for which average income was US$65 for an average household of 5.4 members –0.6 children less than 6 years of age, 2.0 children age 6 to 18 years, and 2.8 adults – though only households with children under 18 were included in the sample. This makes per capita daily income on the order of US$0.40 in Tiljala. Over 90% of the sample lived on less than US$1 per capita per day, and no one had a per capita income over US$3 per day (Figure 2.3). On the other hand, a

Lorenz curve (Figure 2.4) shows that although absolute incomes are very low throughout the slum, there is still a fair degree of inequality in the distribution of income. The GINI coefficient, one measure of income inequality, is 0.40 in Tijlala, giving it a slightly higher level of inequality than India's nationwide coefficient of 0.33 [3].

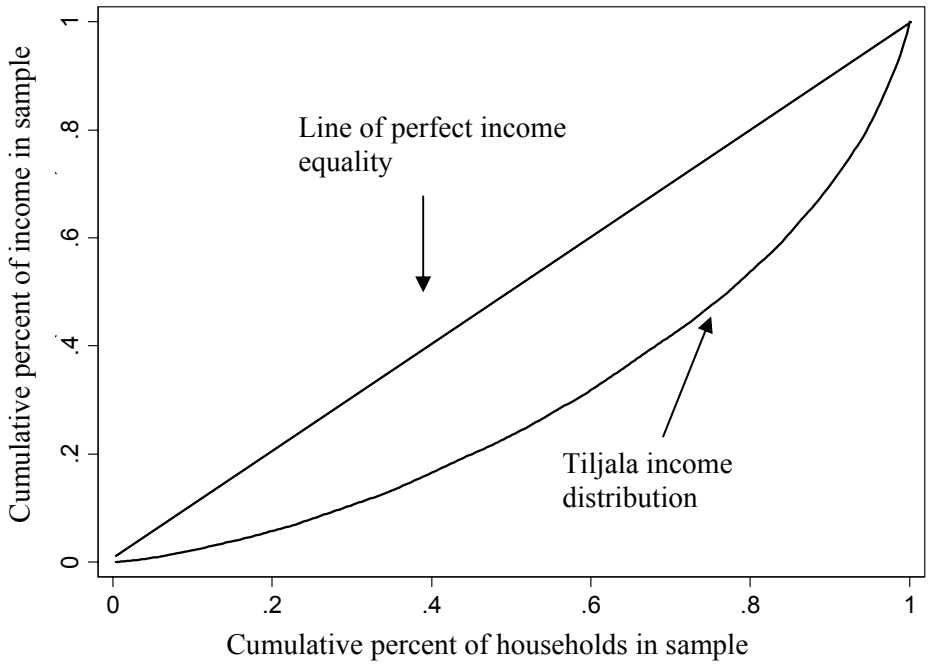
About 40% of sampled respondents from Tiljala had not received any formal education and another 44% had less than 9 years of schooling. In Narkeldanga, Sur et al. (2005) report the literacy rate at 35%. These similarities between neighborhoods suggest that results can reasonably be transferred between the Narkeldanga and Tiljala neighborhoods, confirming the judgment of the NICED staff.

Figure 2.3 Cumulative distribution of per capita daily income in Tiljala (n=275)



[3] UN World Development Report 2006, Table 15, but based on World Bank 2006 data

Figure 2.4 Lorenz curve for Tiljala sample (n=275)



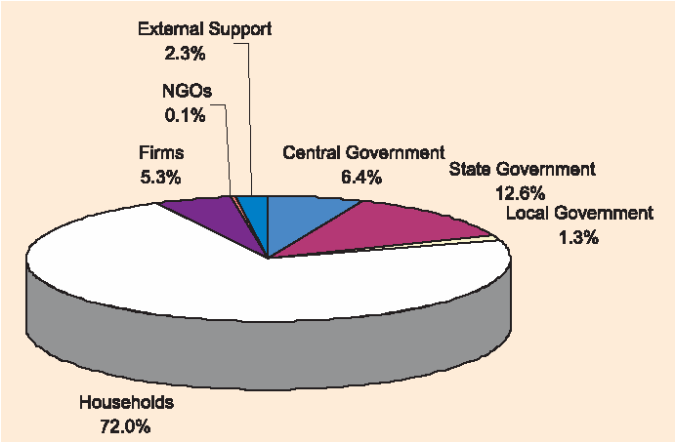
2.4 Health conditions and health spending,

Specific health statistics are not available for Kolkata. However, the West Bengal census reports that the infant mortality rate in 2001 for the urban portion of West Bengal was 42 deaths per 1,000 births (Census 2006). WHO (2006) reports the national average life expectancies at 61 years for males and 63 years for females. Based on a study of 12 slums in Kolkata by health workers, the greatest causes of death for slum residents included diseases of the digestive system (26%), respiratory system (11.4%), cancer (9.7%), and diseases of the circulatory system (9.1%) (Kundu 2006). This suggests that cholera and typhoid might be significant contributors to mortality in Tiljala.

According to the most recently published National Health Accounts data for India (2001-2002), total health spending nationwide was Rs. 1021 per person (Indian MoHFW 2005). At the exchange rate used throughout this dissertation (1US$ = Rs.45), this would make total per capita

health expenditure about US$23[4]. Of this total, though, approximately 77% is private health spending (Figure 2.5), one of the highest percentages of private health spending in the world (Deolalikar et al. 2006).

Figure 2.5 Source of funds for health care in India, 2001-2002



(*Source: India MoHFW, 2005*)

On a per capita basis in 2001-2002, public sector spending was only Rs. 207 (US$4.5). India's public spending on health, at around 1.1% of GDP, is one of the lowest in Asia, and the Indian government is currently considering an initiative (the National Rural Health Mission) to increase public spending on health (Deolalikar et al. 2006). Because the program's focus is on rural states, though, large urban areas like Kolkata are unlikely to see large increases in public health spending in the near future. Also note that state-level spending is double the share of central government spending, and that that external support and NGOs make up a very small fraction of total health spending (although this may have increased somewhat since 2001-2002).

[4] We might also think of adjusting for purchasing power parity (PPP). The PPP conversion in March 2007 (from the IMF's World Economic Outlook Database) is 9.989, making total health spending about US$230. However, throughout the dissertation we do not adjust cost-of-illness, vaccine costs, etc. for PPP, so US$23 is the more relevant number. In any case, relative tradeoffs are what matter; scaling up all costs and benefits with PPP will not change the policy analysis.

2.5 Comparing health interventions

One objective of the Disease Control Priorities Project in Developing Countries ("DCP2") was to help decision-makers prioritize among many health interventions (Jamison et al. 2006). One tool for prioritizing projects is the use of cost-effectiveness measures. These measures are typically provided in the form of ratios of program costs to health outcome achieved. Common health outcomes used are cases avoided, deaths avoided, and life years saved. Two measures – the quality-adjusted life year (QALY) or disability-adjusted life year (DALY) – are composites of mortality and morbidity burdens of disease. Although these measures cannot tell a policymaker if an intervention or program would pass a social cost-benefit test, they can help in comparing projects where there are very restrictive capital budgeting constraints, as is the case in Tiljala. As a first point of reference, interventions are typically considered "highly cost-effective" if the cost per DALY avoided is less than the country's gross national income per capita, about US$620 for India in 2004[5]. They are "cost effective" if the cost per DALY avoided is less than three times per capita gross national income, or US$1860[6].

The DCP2 project is essentially a compendium of hundreds of health interventions and the best available range of estimates of their cost-effectiveness. As a second point of reference for our analysis, Table 2.1 presents the per capita costs and cost-effectiveness ratios for a range of health interventions suggested by Deolalikar et al (2006) for India.

[5] Based on the 2004 GDP from IMF's World Economic Outlook database, converted to dollars using the same exchange rate used throughout the dissertation (Rs. 45 =US$1).

[6] These comparisons with per capita GDP (or GNI) began with the World Bank's 1993 report "Investing in Health" and continue to be WHO's standards. See page 108 of WHO's 2002 World Health Report "Reducing risks, promoting healthy life" (http://www.who.int/whr/2002/en/whr02_en.pdf), or

Table 2.1 Per capita cost, and cost-effectiveness ratio, of various health interventions

Objective	Intervention	Per capita cost (US$)	Cost-effective-ness (US$/ DALY)
Maternal mortality	Institutionalization of all births	0.68	707
Infant mortality	Tetanus vaccination incremental to current coverage	< 0.01	< 1
	Institutionalization of all births	1.06	58
Malaria	Arteminisin treatment	0.05	13
HIV/AIDS	Condom promotion targeted at 80% of sex workers from 33% at baseline over 5 years	0.06	3
	Voluntary counseling and testing delivered to a third of sexually active population	0.15	10
	Mother to child transmission intervention via AZT, formula feeding, and no breastfeeding	0.17	130
Tuberculosis	Directly-observed short-course chemotherapy for ss+ patients incremental to current coverage	0.09	16
	Directly-observed short-course chemotherapy for ss- patients incremental to current coverage	0.15	76
Diarrhea	Oral rehydration therapy for every diarrhea episode during first five years of life	0.02	3
Acute lower respiratory infections	Case management of non-severe cases at the community level over first five years of life	0.12	39
	Case management of non-severe cases at the community, facility, and hospital level over first five years of life	2.55	329
Under 5 mortality	Vitamin A supplementation with syrup in area with and without PHC facilities	0.05	8

Source: Deolalikar 2006, from DCP2

2.6 Vaccines in Kolkata

2.6.1 Historical use of TABC vaccines in Kolkata

A combined vaccine against typhoid, paratyphoid A&B and cholera (TABC) was administered free of charge in Kolkata beginning in the 1950s. It was discontinued in the 1980s because of side effects which included pain, swelling, redness, and fever and because recipients were often unable to work for several days after vaccination. In fact, many of our respondents mentioned how painful the TABC shots had been. Among respondents to the CV surveys in Kolkata's

Beliaghata and Tiljala neighborhoods, 8% of household members had received either a previous generation cholera vaccine, a previous generation combined cholera, typhoid, and paratyphoid A and B ("TABC") vaccine, or a new typhoid vaccine. The majority of these (76%) were TABC vaccines, which were discontinued by the early 1980s. Only 1% of respondents reported paying anything for these vaccines.

2.6.2 Current availability of cholera and typhoid vaccines

The typhoid Vi polysaccharide vaccine is currently available for purchase in Kolkata at a few locations, but sales are low because many people do not know that it is available and because of the time, expense, and inconvenience associated with obtaining the vaccine in private physicians' offices. The limited demand is principally for young people in wealthier families who need the vaccine for travel abroad or for school.

There is currently no cholera vaccine available for sale in Kolkata (nor India).

CHAPTER 3

MODELING APPROACH

3.1 Simple model without herd protection

3.1.1 Coverage

We turn now to developing a simple mathematical model of vaccine costs and benefits of a generic vaccination program[7]. For ease of exposition, assume the program targets a population of size *Pop*. This could be either the total population of the area, or the population within a specific age group. We assume that only a fraction *h* of the population hears about the vaccination program. Although this fraction would likely be related to the amount of effort (i.e. costs) expended on information and advertising, we have no information to identify this relationship and we will assume that this fraction is exogenous to the model[8]. The size of the population who hear of the program is therefore $h \cdot Pop$, which we call *N*.

We assume that the government may ask users to share some cost of the program through a user fee *p*. We assume that fee *p* is levied on a per-immunization, not per-dose basis. For example, if an immunization requires four doses, the fee *p* would cover all four doses and would be collected at the first dose. We assume for simplicity that if a person chooses to be immunized he will receive all *d* doses necessary for protection (no partial immunizations[9]).

Vaccine recipients will face other costs in choosing to be vaccinated, both the financial costs of traveling to the clinic (e.g. taxi, bus, etc.) and the economic costs of the time spent traveling and

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[7] This chapter is drawn from a paper in progress on herd protection co-authored with Brian Maskery, Marc Jeuland, Donald Lauria and Dale Whittington.

[8] We will assume that this fraction is 80%.

[9] We use the terms "immunization" and "vaccination" synonymously throughout, and each means that the person has received all *d* doses necessary for protection.

waiting in the clinic (Jeuland et al. 2007). In practice, these costs will vary among the population, based on their location relative to the nearest vaccination clinic and the queues at clinics[10]. For simplicity and because Tiljala is a compact urban slum, we will assume here that the total travel/waiting costs is a constant *t* per dose. The total cost that users face is therefore $(p + (d \cdot t))$.

The proportion of people who choose to be vaccinated will be a decreasing function *P* of the costs that users face. The total number of people vaccinated ("coverage") is:

$$\text{Coverage} = N \cdot P[p + (d \cdot t)] \tag{3.1}$$

The decision-makers in our model do not know about or consider external herd protection effects when making their decision to purchase the vaccine.

3.1.2 Cases and deaths avoided

The population incidence rate is *I*. In the absence of herd protection effects, the effectiveness of the vaccine in preventing cases is assumed to be a constant, *Eff*[11]. This effectiveness is independent of coverage rates, and unvaccinated persons experience no reduction in their chances of contracting the disease, regardless of coverage. The duration of the vaccine's effectiveness (in years) is *Dur*. The total number of cases avoided in the population is:

$$\text{Cases avoided} = \text{Dur} \cdot \text{Eff} \cdot P[p + (d \cdot t)] \cdot N \cdot I \tag{3.2}$$

We assume that some fraction of those who fall ill eventually die from the disease. Multiplying this case fatality rate (*CFR*) by the number of cases avoided gives the number of deaths avoided:

[10] In addition, waiting times might decrease with more vaccination clinics, and increase with additional expenditures on advertising *ceteris paribus*. Wait times may also decrease with increasing user fees, as the fees reduce demand and may reduce queues (the vaccine provider will of course try to match expected demand and staffing levels to minimize unused staff time). Kim (2007) uses more complicated spatial/GIS techniques to model these types of tradeoffs in evaluating optimal locations for vaccination clinics.

[11] Because we assume no partial immunizations (i.e. everyone who chooses to be immunized receives all *d* doses), we can ignore partial protection from receiving less than d doses in the model.

$$\text{Deaths avoided} = CFR \cdot Dur \cdot Eff \cdot P[p + (d \cdot t)] \cdot N \cdot I \quad (3.3)$$

Since *Dur*, *Eff*, *N* and *I* are constants, the number of cases avoided and deaths avoided is proportional to the coverage rate P(•) (for clarity, we suppress notation of the coverage function P). If coverage is a monotonically decreasing function of the costs that users face (as economic theory would suggest), the number of cases avoided decreases with increases in either the user fee, the travel/time costs, or the number of doses needed.

We might be interested in knowing how many cases are expected to continue to occur even in the presence of the vaccination program. There will continue to be cases in three subsets of the population: 1) those who never heard about the program, 2) those who heard about the program but chose not to be vaccinated at fee *p*, and 3) those who chose to be vaccinated but were not protected because the vaccine is not 100% effective (Eq. 3.4). In the absence of herd protection, the only way to eliminate all cases in the population is to achieve 100% coverage with a 100% effective vaccine.

$$\begin{aligned}\text{Remaining cases} = \quad & (Pop - N) \cdot I \quad + \quad Dur \cdot N \cdot [1 - P(\bullet)] \cdot I \\ & + \quad Dur \cdot N \cdot P(\bullet) \cdot I \cdot (1 - Eff)\end{aligned} \quad (3.4)$$

3.1.3 Vaccine costs

The total cost of the vaccination program will be the fixed costs *F* plus variable costs. Variable costs are a function of the total number of doses delivered (*q)*, which is in turn a function of the total coverage and the number of doses *d* required per immunization:

$$\text{Total doses delivered} = q = d \cdot N \cdot P[p + (d \cdot t)] \quad (3.5)$$

We split the variable cost function V(q) into three parts: vaccine production cost, vaccine delivery cost and travel/wait costs. As discussed above, we assume the travel/wait costs are a constant *t* per dose. We also assume that per-unit manufacturing cost is a constant (*Manuf*). This

assumption seems reasonable in the context of evaluating a program of fairly limited size (e.g. one neighborhood). A city-wide, regional or (certainly) national immunization program might have economies of scale in manufacturing so that marginal and average manufacturing costs would vary with the number of vaccines demanded. We will, of course, vary this parameter in the sensitivity analysis, but see no need to complicate the theoretical approach here by modeling a production cost which varies with program size.

We will also model vaccine delivery cost as a constant amount (*Deliv*) per dose. By assuming fixed cost and constant marginal costs, we are by definition assuming that there are economies of scale in vaccination; average costs per dose delivered declines as the number of doses increases. There is evidence for this from trials of the cholera and typhoid vaccines in the Narkeldanga neighborhood (see Chapter 4). A more flexible approach would be to model costs with a two-parameter power function. Although we explore this in Appendix E, our analysis will use a more straightforward constant marginal cost that gives similar results as the power function. Variable costs V(q) are:

$$V(q) = q \cdot [\ \text{Manuf} + \text{Deliv} + t\ ] \qquad (3.6)$$

Substituting (3.5) into (3.6) and adding fixed costs gives the expression for total costs (Eq.3.7). Since the number of doses required per immunization, the fixed costs, and the travel/wait costs are all constants in our model, total costs will be a function of only one varying parameter, the user fee *p*.

$$C(p) = F + [d \cdot N \cdot P[p + (d \cdot t)]] \cdot (\text{Deliv} + \text{Manuf} + t) \qquad (3.7)$$

3.1.4 Benefit measures

We will examine several different measures of economic benefits in assessing whether vaccination programs would pass a social cost-benefit test. The first benefit measure includes the

cost of illness (COI) avoided by preventing a case of the disease. Cost of illness includes both direct and indirect costs, and financial as well as economic costs (discussed in more detail in Chapter 4). We can break down cost-of-illness further into privately-borne COI (*PrivCOI*) and public-sector COI (*PubCOI*). COI incurred in the second and third years of the program is discounted using constant exponential discounting to give a net present value[12]. The benefit of a program using this measure ("COI benefits") is simply the COI avoided multiplied by the number of cases avoided:

$$\textbf{COI benefits} = (\text{PubCOI} + \text{PrivCOI}) \cdot \left[\text{Dur} \cdot \text{Eff} \cdot \text{P}(\bullet) \cdot \text{N} \cdot \text{I}\right] \tag{3.8}$$

The second benefit measure adds the value of mortality risk reductions by multiplying the number of deaths avoided by an estimate of the value of a statistical life (VSL). Adding this mortality risk reduction benefit to the COI benefits gives "COI+VSL benefits"[13]:

$$\begin{aligned}\textbf{COI +VSL benefits} = {} & (\text{PubCOI} + \text{PrivCOI}) \cdot \left[(1\text{-CFR}) \cdot \text{Dur} \cdot \text{Eff} \cdot \text{P}(\bullet) \cdot \text{N} \cdot \text{I}\right] \\ & + \text{VSL} \cdot \left[\text{CFR} \cdot \text{Dur} \cdot \text{Eff} \cdot \text{P}(\bullet) \cdot \text{N} \cdot \text{I}\right]\end{aligned} \tag{3.9}$$

The third benefit measure derives from stated preference studies of what households said they were willing to pay for vaccines. The average willingness-to-pay per vaccinated person (*WTP*) is comprised of per capita expenditures (equal to the fee *p*) plus average per capita consumer surplus (CS, which collapses to $-1/\beta_p$ in our econometric models). For more detail on derivation of the WTP measure, see Appendix C. We multiply this average WTP measure by the number of people who

[12] COI over duration = $\text{COI}_0 + \text{COI}_1/(1+\text{disc}) + \text{COI}_2/(1+\text{disc})^2$ where disc = financial discount rate.

[13] It is possible that this approach double-counts private cost-of-illness. For example, if VSL is estimated by directly asking about WTP for a risk reduction program (i.e. like the stated preference approach used by Maskery et al (2007)), then respondents could be including *ex ante* private COI in their WTP for the risk reduction (see Chapter 4.5).

choose to be immunized at user fee p [14], and add the public sector treatment cost savings (which we assume people did not include in their private valuations) to estimate "WTP benefits":

$$\textbf{WTP benefits} = (p + CS) \cdot \left[P(\bullet) \cdot N\right] + PubCOI \cdot \left[(1\text{-}CFR) \cdot Dur \cdot Eff \cdot P(\bullet) \cdot N \cdot I\right] \quad (3.10)$$

Note that since consumer surplus is a constant ($1/-\beta_p$), total per capita WTP benefits increase linearly with the user fee. Intuitively, as the fee increases, the people remaining in the average (because they still buy a vaccine at the higher fee) are those with higher WTP.

3.1.5 Cost-effectiveness measures

In addition to benefit measures, we also report several different cost-effectiveness ratios. These may be of interest to policymakers in India and elsewhere who are concerned not only with whether a program would pass a social cost-benefit test but how these vaccination programs compare with other possible health interventions (see Chapter 2.5).

$$\text{Cost / Case avoided} = C(p) \;/\; [\, Dur \cdot Eff \cdot P(\bullet) \cdot N \cdot I \,] \quad (3.11)$$

$$\text{Cost / Deaths avoided} = C(p) \;/\; [CFR \cdot Dur \cdot Eff \cdot P(\bullet) \cdot N \cdot I \,] \quad (3.12)$$

We calculate the disability-adjusted life years (DALYs) lost as the sum of life-years-lost due to premature deaths (YLL) plus the life years lost due to disability (YLD) (WHO, 2001). The morbidity effect (YLD) is the product of total time spent ill with the disease (*Length*) and the disease's DALY weight. DALY weights, published by the WHO for a variety of diseases, represent expert judgements by health professionals about the severity of the illness. A weight near one implies

[14] Typhoid immunization requires only one dose, but cholera immunization requires two. We told cholera vaccine respondents that the referendum price covered both doses (see description of scenario at the end of Appendix B)

a very severe disease (either because of intense pain or a large decrease in function), and a weight near zero implies something like the common cold. As is standard in the DALY methodology (Jamison et al 2006), we use local life expectancies to calculate life years lost for each age group (*LE*), and discount life years at 3%. We do not weight cases by the age at which they occur.

$$\text{DALYs avoided per year} = \text{YLL avoided per year} + \text{YLD avoided per year} \quad (3.13)$$

$$\text{YLD avoided per year} = [\ \{(1-\text{CFR}) \cdot \text{Eff} \cdot P(\bullet) \cdot N \cdot I\ \} \cdot \text{Length} \cdot \text{DALY weight}\ ] \quad (3.14)$$

$$\text{YLL avoided per year} = [\{(\text{CFR} \cdot \text{Eff} \cdot P(\bullet) \cdot N \cdot I) / 0.03\} \cdot \{1 - \exp(-0.03 \cdot LE\} \quad (3.15)$$

$$\text{Total DALYs avoided} = \sum_{t=0}^{2} (\text{DALYs avoided in year t}) / (1 + 0.03)^t \quad (3.16)$$

We also present cost-effectiveness ratios with "net public cost" (where public COI has been subtracted out) in the numerator.

$$\text{Net Public Cost / Case avoided} = C(p) - \text{PubCOI} / [\ \text{Dur} \cdot \text{Eff} \cdot P(\bullet) \cdot N \cdot I\ ] \quad (3.17)$$

$$\text{Net Public Cost / Deaths avoided} = C(p) - \text{PubCOI} / [\text{CFR} \cdot \text{Dur} \cdot \text{Eff} \cdot P(\bullet) \cdot N \cdot I\ ] \quad (3.18)$$

$$\text{Net Public Cost / DALYs avoided} = C(p) - \text{PubCOI} / \text{Total DALYs avoided} \quad (3.19)$$

3.1.6 Age groups

We split the population into three age groups: young children who are under 5 but are old enough to safely receive the vaccine (1-yr for cholera, 2-yr for typhoid), school-aged children 5-14yrs , and adults 15 and older. The models above would change only in that we use age-specific

data for incidence rates, private demand and costs-of-illness, but the intuitions from the models would not change.

3.2 Model with indirect (herd) protection

We now move to a model that includes indirect protection due to herd immunity. Herd protection occurs because 1) the vaccine reduces the number of people susceptible to infection and 2) fewer infected individuals will spread the disease among both vaccinated and unvaccinated persons. This may result not only in some degree of protection for unvaccinated individuals but also in higher levels of protective efficacy for the vaccinated. We therefore split the population into vaccinated and unvaccinated subgroups, and re-define the vaccine's effectiveness (the probability of protection from infection) as a function of coverage rates. The function **V**(P(•)) maps coverage rates, which includes the fraction of the population that does not hear about the program, into the probability that a vaccine recipient will be protected. **U**(P(•)) is the probability of protection for the unvaccinated portion of the population. In the presence of herd protection, we replace the term *Eff* in the equations above with these functions **V**(·) and **U**(·), and the number of cases avoided becomes:

$$\begin{aligned} \text{Cases avoided} = \quad & \text{Dur} \cdot V[P(\bullet)] \cdot P(\bullet) \cdot N \cdot I \qquad (\textit{vaccinated}) \\ + \quad & \text{Dur} \cdot U[P(\bullet)] \cdot [\text{Pop} - N + (1 - P(\bullet)) \cdot N] \,] \cdot I \qquad (\textit{unvaccinated}) \end{aligned} \tag{3.20}$$

3.2.1 Benefits per case avoided

The only way that herd protection benefits enter our WTP net benefit measure (see Eq. 3.10) is through additional public COI savings. However, this may greatly underestimate the additional benefits to society of indirect protection. The challenge is: how can we use private benefit estimates from the stated preference surveys (where herd protection was never mentioned) in the context of a model with herd protection effects?

We propose here a single population average benefit measure. We normalize population WTP by the number of cases avoided were the vaccine to work as presented in the CV scenario (i.e.

without mention of external effects[15]). The social benefits of a vaccination program becomes this BPC multiplied by the total number of cases avoided in Eq. (3.20).

$$\textbf{BPC benefits} = \text{BPC} \cdot N \cdot \left[\text{Dur} \cdot V[P(\bullet)] \cdot P(\bullet) \cdot I + \text{Dur} \cdot U[P(\bullet)] \cdot (1 - P(\bullet)) \cdot I\right] \quad (3.21)$$

[15] Even though the scenario made no mention of external effects, it is possible that some respondents were independently aware of the concept of herd protection and that this influenced their responses. However, we have no evidence that any of the respondents were thinking about herd protection: it did not come up in any of the dozens of interviews watched by the author or other supervisory staff, and none of the field enumerators raised the subject with their supervisors.

CHAPTER 4

DATA

4.1 Burden of disease studies

NICED carried out a baseline census of the study population in Narkeldanga in early 2003, followed by a second census one year later (Sur et al. 2005). NICED collected information from households on household expenditures, health related behavior, and age, sex, and educational level of each individual. This census identified 63,239 individuals in the surveillance area. Parallel to the census data collection, NICED established 5 diarrhea clinics that provided free treatment for patients from the census area. The clinics were set up to allow passive surveillance and testing for diseases including cholera and typhoid. Additional surveillance was performed at the city's public children's hospital and infectious diseases hospital. Patients from the surveillance area that presented with symptoms suggesting typhoid or cholera were asked to provide a sample for laboratory confirmation of the disease. While it is likely that this surveillance program did not identify all typhoid and cholera cases, Sur et al. (2005) were confident that they had captured almost all serious cases.

From May 2003 to April 2004, the study detected 3,284 diarrhea episodes, of which 126 (4%) were culture-confirmed cholera. Cholera incidence rates by age group were calculated based on surveillance from November 2003 to October 2004 and are shown in Table 4.1. Young children had the highest incidence of cholera, followed by school-age children, and adults. Of the 126 cholera cases observed in the study, 29 (23%) caused severe dehydration, and 48 (38%) resulted in hospitalization. One cholera patient died. Risk factors for cholera included a household member with cholera during the period of surveillance, young age, and lower educational level.

Table 4.1 Observed annual incidence rates (per 1000) in Narkeldanga, by age group

	Cholera	Typhoid[a]
Young children (under 2 yrs)	7.0	0.9 (1.8)
Young children (2 - 4.9yrs)	7.0	3.4 (6.8)
School-aged children (5 -14.9 yrs)	2.2	5.2 (10.4)
Adults (over 15yrs)	0.9	1.2 (2.4)

[a] Numbers in parenthesis reflect the lack of sensitivity for typhoid blood culture tests

The typhoid incidence rates in Table 4.1 are based on one year of surveillance from November 2003 to October 2004. Blood-culture tests were used to identify the presence of S. typhii, but these tests are known to result in false negatives, underestimating the true incidence[16]. Based on guidance from epidemiologists at IVI, the typhoid incidence rates in Table 4.1 were doubled to account for this lack of sensitivity of the typhoid blood culture test (these adjusted figures are shown in parentheses). The typhoid incidence rates are higher for school-children than for other age groups. Also, after accounting for blood culture sensitivity, typhoid is over twice as common as cholera in adults, by far the largest age group.

4.2 Cost-of-illness studies

Those with positive laboratory test results for cholera, typhoid, or paratyphoid were contacted to participate in private cost of illness (COI) surveys (Sur et al. 2007, Poulos et al. 2007a, Poulos et al. 2007b). These surveys asked the patient (or the caretaker of a child patient) questions on private direct expenditure such as amounts spent on clinic/hospital fees, medicine, diagnostic tests, and overnight stays at public and private treatment facilities, traditional or community healers or self treatment. Additional costs for transportation to and from treatment sites, special non-prescription food and drinks, and under the table payments for expedited treatment were also reported. In addition, the surveys included questions about indirect treatment costs such as patient time lost at work and

[16] The other primary test for typhoid fever is the Widal test, which tests for common typhoid antibodies. The Widal test may result in a number of false positive results because reactions may occur with other types of salmonella and non-salmonella bacteria or because the test picks up antibodies from past infections or the use of a typhoid vaccine (Olopoenia and King 2000). For this reason, the blood culture tests were thought to provide a more representative picture of typhoid incidence.

school due to illness as well as lost time by the patients' caretakers and companions. Surveys were performed at intervals of 7 days and 14 days after initial presentation at the surveillance clinics/hospitals for culture-confirmed cholera patients and at 7 days, 14 days, and 90 days after presentation for typhoid patients. A total of 41 cholera patients and 79 typhoid patients or their caretakers have participated in the study (Poulos et al. 2007a,Poulos et al. 2007b).

The greatest contributors to private COI include treatment costs, transportation and lost productivity of patients (Table 4.2). Average private expenditure per case was higher for typhoid than for cholera. Indirect costs for typhoid may be higher because typhoid symptoms typically take longer to subside. The ranges of uncertainty for private COI given in Table 4.5 represent one standard deviation above and below the mean values reported in Poulos (2007a) and (2007b).

Public COI estimates are based on reported expenditures by public clinics and hospitals (Riewpaiboon 2006; Riewpaiboon 2006). The cholera public COI is estimated based on public expenditure for treating 102 cases at Kolkata's Infectious Diseases and Beliaghata General Hospital, and the typhoid public COI is based on treating 83 cases at the Infectious Diseases and B.C. Roy Hospitals. Note that this is a different samples of patients than the private COI study. The average cost per patient day was estimated based on hospital wage, utilities, and treatment records. The average cost per day was multiplied by the number of days spent at the hospital by each patient. Medicine costs were added separately based on actual use by patients.

Of the 83 typhoid cases in the public COI study, 67 were outpatients. Ten of 77 (13%) cases in children resulted in hospitalization, but all six adult cases in the study were hospitalized. The average cost per hospitalized child case was US$115, and US$2.0 per outpatient child case. The average cost per hospitalized adult was somewhat lower (US$73) because adults stayed fewer days in the hospital than children.

Table 4.2 Mean private and public costs-of-illness (2005 US$)

	Children (under 18)	Adults >18 yrs
Cholera		
Cases	27	14
Number hospitalized	10	6
Private COI per case:		
Direct costs	$ 3.2	$ 2.6
Indirect costs	$ 2.1	$ 3.9
Total private	$ 5.3	$ 6.5
Public COI per case [a]:	$ 15	$ 16
Total COI per case:	**$ 20.3**	**$ 22.5**
Ex ante total COI per year [b]	$0.08	$0.02
Typhoid		
Cases	54	25
Number hospitalized	2	0
Private COI per case:		
Direct costs	$ 6.1	$ 8.6
Indirect costs	$ 2.6	$ 10.1
Total private	$ 8.7	$ 18.7
Public COI per case [a]	$ 11	$7.7
Total COI per case	**$19.7**	**$ 26.4**
Ex ante total COI per year [b]	$0.16	$0.06

[a] Estimated separately based on hospital-based surveillance, not from the sample of patients in the private COI study. Public cost per case is the average of costs for hospitalized and non-hospitalized cases, weighted by the estimated hospitalization rate.

[b] Incidence for all children is calculated by weighting incidence of two age groups by their share of the population; cholera (3.8/1000), typhoid (8.2/1000), after adjusting for blood culture sensitivity for typhoid.

To estimate a public cost per case of typhoid, we average the public costs of hospitalized and outpatient/non-hospitalized cases, weighted by the hospitalization rate. This may overstate public COI somewhat because non-hospitalized cases are not necessarily treated as outpatients at public facilities but may be self-treated, incurring zero public sector cost. Using a hospitalization rate for children of 13%, the average cost is US$16.7 (=$115 * 0.13 + $2.0 * 0.87). The number of hospitalized child cases reported by patients in the private COI study was only 3.7%, however, giving an average public COI of US$6. We split the difference and use a hospitalization rate of 8%, giving an average public COI per child typhoid case of $11. We vary this from US$6 – US$20 in the sensitivity analysis.

All of the six adult patients in the hospital-based public COI study were hospitalized, but none of the 25 adult patients in the surveillance-based private COI study reported being hospitalized. Because there is no observed hospitalization rate, we again use 8% and assume the public cost per outpatient/non-hospitalized case is also US$2, implying a public cost per adult typhoid case of US$7.7 (=$73 * 0.08 + $2.0 * 0.92). We vary this from $4 - $20 in the uncertainty analysis.

All 102 cases in the cholera public COI study were hospitalized. Average treatment costs were very similar for children and adults (US$41 and US$38). We have no information on public COI for outpatient cases, perhaps because it is nonexistent (i.e all cholera treatment at a public hospital or clinic involves an overnight stay). The hospitalization rate among private COI participants was 37% for children and 43% for adults (Poulos et al. 2007b). Assuming that the public cost for non-hospitalized cases is zero, this gives an average public COI of US$15 per child case and US$16 per adult case. We vary both of these parameters between US$10 and US$25 for uncertainty analysis.

Ex-ante costs of illness are calculated by multiplying the total cost of illness per case by the incidence rate. This can be interpreted as the expected public and private cost of illness per year for any person in the population.

4.3 Private demand (WTP) studies

Private willingness to pay (WTP) for cholera and typhoid vaccines was estimated via contingent valuation surveys as discussed in Whittington et al.(2007) (included as Appendix B). In total, 559 respondents from Kolkata's Beliaghata neighborhood and another 276 from Tiljala answered questions about their families' past experiences with cholera and typhoid illnesses and vaccines. Respondents were then told about a new hypothetical vaccine against either cholera or typhoid and asked if they would purchase vaccines for themselves or for other members of their family at one of four randomized prices. For cholera, which requires two doses, respondents were told that the price was for the full set of vaccinations, not per dose. The sample was split so that each respondent only answered questions regarding one of the diseases. Survey enumerators recorded how

many vaccines would be purchased at the given price and which family members would receive hypothetical vaccines. The survey sample was split in Beliaghata such that some respondents were given overnight to think about their decision to purchase vaccines ("time to think", or TTT) while other respondents completed the entire interview in one session. All respondents in Tiljala completed the survey in one session.

Respondents in the WTP studies in Beliaghata and Tiljala also answered questions about the severity and likelihood of contracting either cholera or typhoid. About half of respondents reported that they knew of someone that had contracted cholera (47%) or typhoid (53%). In addition, about 40% reported that it was "likely" that they would contract the disease in question in the next five years. A majority (65%) reported that the disease in question was "serious" for adults. In general, it appears that people in Tiljala are familiar with the diseases and their consequences.

The results from the survey were used to estimate the average private benefits (WTP) that accrue to a vaccinated individual of a given age. These were calculated based on estimates from negative binomial (count) models (see Appendix C). WTP estimates in Tiljala were adjusted downward in proportion to the time-to-think effect observed in Beliaghata. Table 4.3 presents average WTP estimates for Tiljala. We present two WTP measures. The first, WTP "per vaccinated person", represents the economic benefits that would accrue to the people who choose to be vaccinated. This is the WTP measure used in calculating WTP benefits in Chapter 3. Table 4.3 presents WTP measures when vaccines are provided for free, but this will increase linearly with higher user fees as only people with higher WTP will choose to be vaccinated (see Appendix C).

The second measure, the WTP "per person", is the average benefits that accrue to any member of the population. This measure reflects the fact that some portion of the population said that they would not take a vaccine with no user charge (in other words, it includes people with zero WTP in calculating the average). The smaller this demand intercept, the larger the difference between the two WTP measures. If 100% of people would take a free vaccine, the WTP "per vaccinated person" and WTP "per person" will be the same.

Table 4.3 Average willingness-to-pay in Tiljala, adjusted for time to think(US$)

	Young children (under 4.9 yrs)	School-aged children (5 -14.9 yrs)	Adults (over 15yrs)
Cholera			
Per vaccinated person	$ 6.3	$ 6.9	$ 2.3
Per person	$ 5.9	$ 4.1	$1.4
Typhoid			
Per vaccinated person	$ 4.2	$ 3.5	$ 2.6
Per person	$ 3.8	$ 2.9	$1.8

High income respondents and younger respondents had higher demand for cholera vaccines relative to others. For typhoid vaccines, high income, more educated, and respondents who were not given time to think had the greatest demand. The TTT-adjusted average willingness to pay per person for cholera vaccines amongst Tiljala residents was highest for young children (US$6), followed by school-age children (US$4), and adults (US$1.4). We believe that these time-to-think estimates are better because they are conservative and because they should be more representative of real-life vaccine purchase decisions (since potential purchasers would likely have time to consider the decision). TTT-adjusted average WTP per person for typhoid vaccines was higher for young children (US$3.8) than for school-age children (US$2.9), or adults (US$1.8).

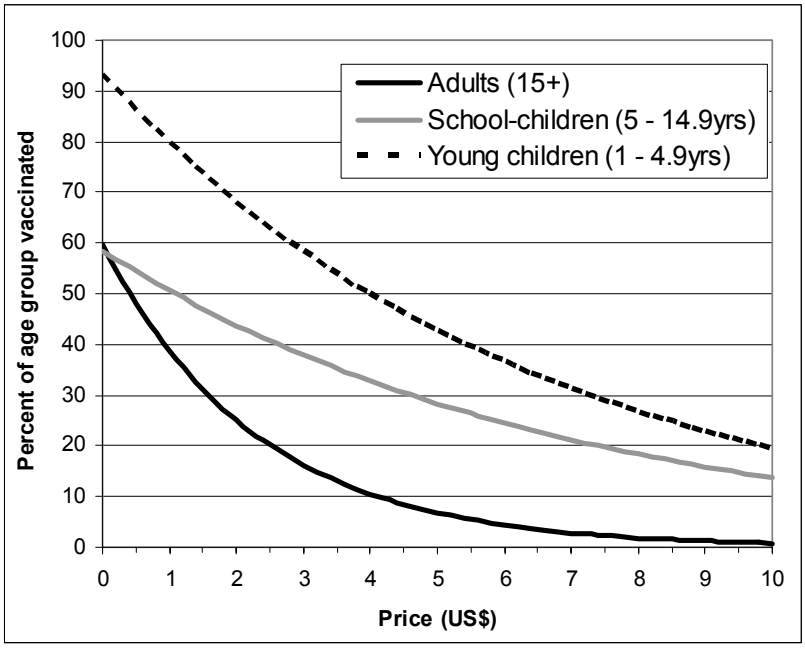
Results from the count models were also used to fit two-parameter exponential demand functions that predict uptake rates by age group as functions of user fee. These predicted fractions are shown in Figures 4.1 and 4.2. One can more easily see the discrepancy in WTP per person compared to WTP per vaccinated person at a price of zero . This difference is larger for adults than for children, because the expected fraction of adults that would receive free vaccines for either cholera or typhoid is much smaller than for children.

The prices at which 50% of each age group would choose to purchase vaccines can be considered the estimated median WTP for that group. This predicted median WTP for cholera vaccines varies from US$0.4 for adults to US$4 for young children. Hence, the median WTP is notably smaller than mean WTP per person, mainly because average WTP estimates are heavily

influenced by small groups of people that have very high WTP. WTP for children is much higher for children than adults because parents were willing to purchase vaccines for their children, especially children under 5, even at the higher referendum prices (see Figures 7 and 8 in Appendix C).

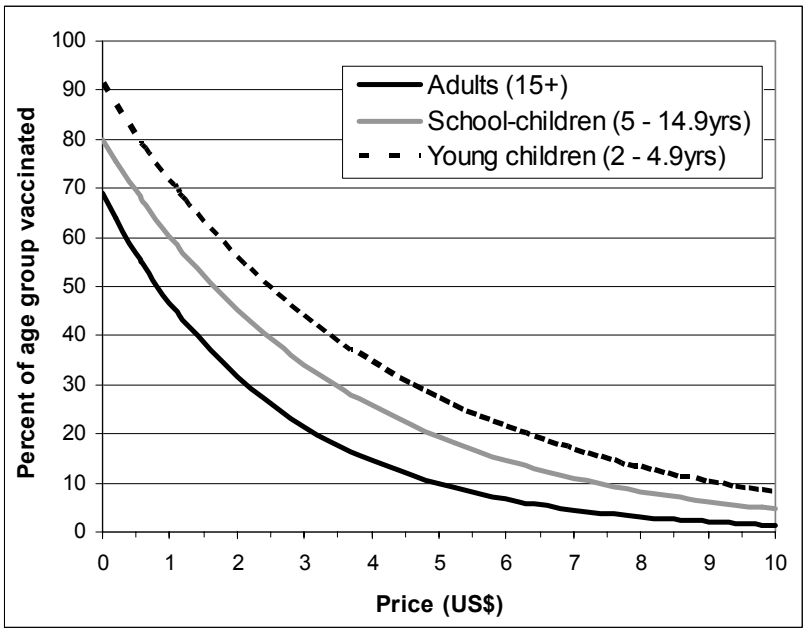
The estimated median WTP for typhoid vaccines varies from $0.80 for adults to US$2.50 for young children. The mean WTP per person is once again higher than the median WTP in the population.

Figure 4.1 Predicted coverage of cholera vaccination in Tiljala, by user charges[a]



[a] adjusted for "time to think" based on average change in slope and intercept observed in Beliaghata TTT experiment.

Figure 4.2 Predicted coverage of typhoid vaccination in Tiljala, by user charges[a]



[a] adjusted for "time to think" based on average change in slope and intercept observed in Beliaghata TTT experiment.

4.4 Vaccine cost

The best source of information on the cost of providing the vaccines in Kolkata comes from two double-blinded, randomized control trials of the cholera and typhoid vaccines in the Narkeldanga neighborhood of Kolkata (NICED 2007a; NICED 2007b). Because these trials included costs related to the fact that they were research projects, however, they may somewhat overestimate costs. Without much more detailed information on expenditures and staff functions, it is not possible to specifically zero-out research-related costs. Rather, we try to fit general cost functions that recognize the fact that the observed data is likely to be inflated (see Appendix E). The resulting estimates are the best available data I have and a reasonable assumption about the fraction of costs that are research-related. They are based on actual vaccine costs in Kolkata in a neighborhood very similar to Tiljala..

The typhoid trial targeted about 61,000 residents of Narkeldanga in the winter of 2004. The trial tested the efficacy of the Vi polysaccharide vaccine (the same vaccine we evaluate here), which requires only one dose. About 6,000 residents were ineligible for vaccination because they were either pregnant or lactating mothers, children under 2, or already had some type of febrile illness. After an information campaign with banners and posters, NICED set up 80 vaccination centers in the area and vaccinated about 38,000 people, or 69% of the target population. In total, the full economic cost of the program was about $3.0 per fully immunized individual (Table 4.4). The typhoid vaccines were donated by Glaxo SmithKline, but NICED estimated the manufacturing cost to be the same as a locally-produced typhoid vaccine in Vietnam (about $0.60 per dose). Assuming that the typhoid vaccine could be locally produced in India, Table 4.4 excludes the cost of shipping the vaccines from GSK in Belgium to Kolkata (this would add an additional $0.31 per dose). Total "delivery" costs – defined as all costs which are not manufacturing – were $2.4 per dose for 38,000 doses. Note that just over 60% of the total delivery costs were for personnel.

NICED (2007a) also estimated a "budgetary" delivery cost of US$0.68 per dose, which excluded the cost of cold chain equipment and rental of vaccination centers (saving US$0.21 and US$0.16 per dose). It also assumed that the vaccines would come in single-dose vials rather than pre-filled syringes (saving about $0.54 per dose) and that "adverse" health events would be handled by existing healthcare facilities and staff rather than program-specific staff (saving US$0.82 per dose). For the social cost-benefit analysis we need the full economic cost (which would include the opportunity cost of cold chain equipment and vaccination centers), but the "budgetary" cost estimate provides a useful lower bound of approximately US$1.3 per immunized individual, including both manufacturing and delivery.

Table 4.4 Summary of cost data from vaccine trials in Narkeldanga, Kolkata (from NICED 2007a,b)

	Typhoid trial	**Cholera trial**
Timeframe	Winter 2004	Summer 2006
Source of vaccines	GSK Belgium (donated)	Shanta Biotechnics (Hyderabad)
Total number of fully immunized people	37,686	67,169
Total number of doses administered [a]	37,686	138,636
Costs in US$, Total (per **dose** administered)		
Vaccine manuf. costs (including wastage)[b]	$23,238 (**$0.62**)	$96,713 (**$0.70**)
Transportation[c]	$2,284 ($0.06)	$5,176 ($0.04)
Syringes and safety boxes	$1,324 ($0.04)	$9,086 ($0.07)
Personnel	$56,041 ($1.49)	$133,044 ($0.96)
Equipment & cold chain	$7,922 ($0.21)	$13,430 ($0.10)
Supplies & Misc	$21,461 ($0.57)	$56,019 ($0.40)
Rental of vaccination centers	$1,778 ($0.05)	$19,042 ($0.14)
TOTAL	$114,048 (**$3.03**)	$332,511 (**$2.40**)
Total less manuf. costs	$90,282 ($2.40)	$235,798 ($1.70)

Notes

[a] Cholera requires two doses and 4,298 recipients (6%) only received one dose. In addition, 416 cholera vaccines and 1038 typhoid vaccines were wasted. These wastages are reflected in the total vaccine costs.
[b] Since the typhoid vaccine was donated, NICED assumed manufacturing costs for a locally-produced typhoid vaccine in Vietnam. [c] Excludes cost of transporting vaccines from Belgium to Kolkata (US$11,504, or US$0.31 per dose administered)

NICED conducted the cholera vaccine trial in the summer of 2006. Although it also targeted the Narkeldanga neighborhood, the cholera trial included an additional ward (KMC Ward 33) and only excluded pregnant women and children under 1 year of age. The target population of 109,000

people was therefore larger than the typhoid trial. The trial examined an oral bivalent killed whole cell cholera vaccine that requires two doses and was produced and donated by Shanta Biotechnics in Hyderabad, India. Using 34 vaccination centers, the program achieved a slightly lower coverage rate – about 61% of the target population (67,000 people) were fully immunized (two doses). 4,300 people received only one dose (about 6% of the 71,000 who received the first dose) and are not considered fully immunized. Vaccine recipients were given small gifts at the clinics for their participation, and refreshments were provided at the clinics[17].

NICED found the total economic cost per fully immunized individual (FIP) to be US$4.98 (Table 4.4 presents costs per dose administered, so the total cost per FIP should be doubled and adjusted to reflect some percentage of people who receive only the first dose). Excluding the manufacturing cost of $0.70 per dose ($1.40 per FIP), the total delivery cost per dose is US$1.70 for about 139,000 doses. The lion's share of delivery costs are again for personnel: the program hired 428 staff members for the campaign, including 49 doctors, 140 nurses, 140 recorders, 40 promoters, 10 community leaders, 36 "traffic controllers", and 12 assistants (NICED 2007b). There was no attempt to estimate the "budgetary" cost of the cholera program. However, using the same assumptions as in the typhoid program (no cold chain or rental cost of vaccination centers and 60% lower personnel costs), we estimate the "budgetary" delivery costs to be on the order of US$0.90 per dose. Again, this provides a lower bound estimate of approximately US$1.60 per dose, including both manufacturing and delivery. The cost per fully immunized person would be US$3.20, or slightly higher as the fraction of partially vaccinated people increases.

Final estimates used in investment cases

We model delivery costs as comprised of a fixed charge of US$10,000 and a constant variable (marginal) cost of US$0.9 per dose delivered (see Appendix E for more details on this assumption). These parameters were based on our best judgment about the fraction of the Kolkata

[17] We don't know the cost of these gifts, so they were not specifically excluded from the cost estimates. Since they would presumably be included in the "Supplies and Misc" category, the cost is no more than $0.40.

trials' delivery costs which were research-related. They imply an average delivery cost of US$1.16 per dose for 38,000 doses, or 52% lower than observed average delivery cost in the Kolkata typhoid trial (US$2.4). For a program delivering 139,000 doses, they imply an average delivery cost of US$0.97, or 43% lower than the average cost observed in the cholera trial (US$1.7). For moderately-sized programs (≥75K doses), they imply an average delivery cost on the order of US$1. Of the 15 vaccine cost studies from low-income countries reviewed by Lauria (2007), two-thirds had average delivery costs below US$1, and the median among the 15 was US$0.68.

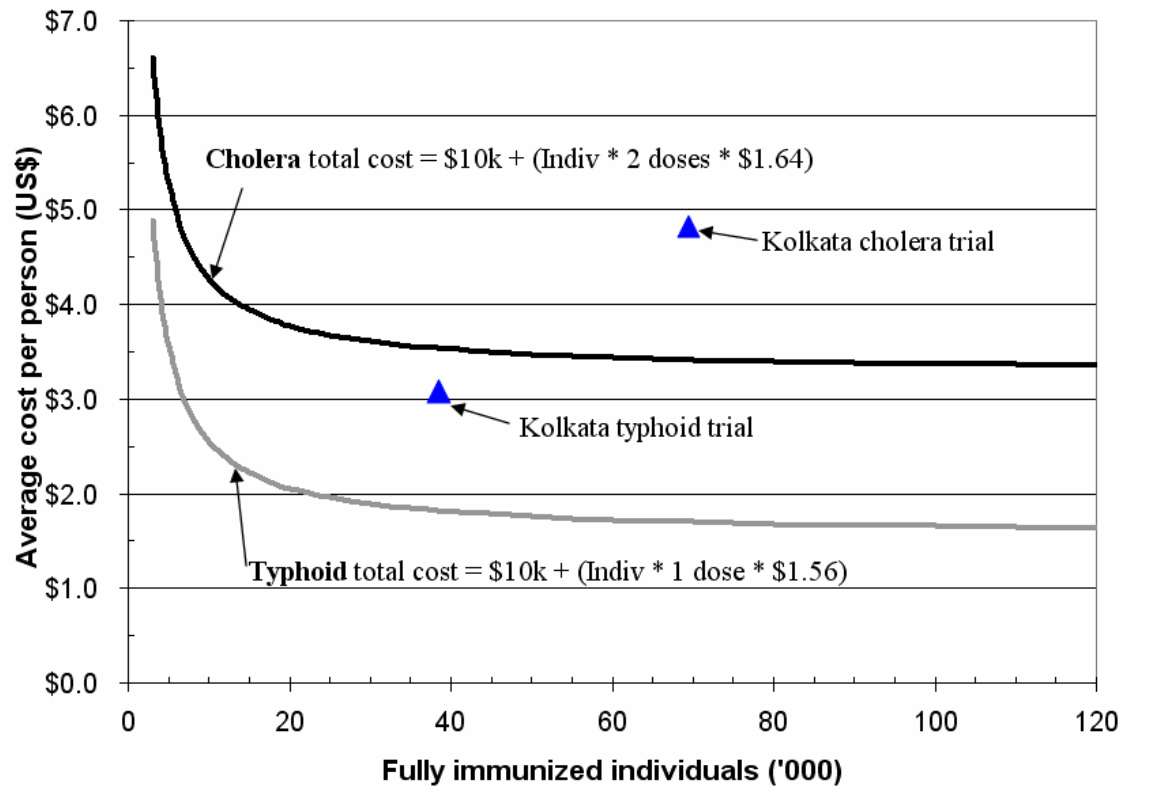
We use the same constant manufacturing cost per dose -- US$0.62 for typhoid and US$0.70 for cholera -- used in NICED (2007a, 2007b), which includes wastage of vaccines. We assume that everyone who receives the first dose of the cholera vaccine receives the second (no partial vaccination).

For our purposes, we model the costs to vaccine recipients of traveling and waiting as follows. For each dose, we assume that every vaccine recipient walks 10 minutes to a nearby clinic (no financial transportation costs), where he or she spends 20 minutes waiting to be vaccinated. We value this time equally for adults and children at one-half the median hourly wage in our Tiljala sample (US$0.15[18]). The economic costs of traveling and waiting to be vaccinated is therefore US$0.04 per dose (0.5hrs * US$0.075/hr).

Figure 4.3 summarizes our best estimates of average total costs. For reference, it also plots the average total costs from the two vaccine trials (blue diamonds). For programs which target over 20,000 people, average total costs per person (for full immunization) are in the range of US$3.2 – $3.7 for cholera and US$1.6 – $2 for typhoid.

[18] Because we asked the occupations and monthly earnings of each household member individually, this represents average hourly wages of the 390 households members who reported income and were not reported as students, housewives, retired or unemployed. It assumes 28 working days per month and 8-hour working days, and as elsewhere assumes 1US$=Rs.45.

Figure 4.3. Final average costs used for investment case



Notes: Constant variable cost per typhoid dose is $0.9 (delivery) + $0.04 (travel/time costs) + $0.62 = $1.56. Constant variable cost per cholera dose is $0.9 + $0.04 + $0.70 (manufacturing) = $1.64.

4.5 Value of statistical life

The value of a statistical life (VSL) is generally estimated one of three ways. The first, called the hedonic wage approach, examines large datasets on wages and job risks (typically in manufacturing jobs) to statistically identify the wage differentials that compensate a worker for higher on-the-job fatality risk. The second approach is a survey-based, stated-preference approach. The survey presents a product or program to respondents which will reduce their risk of dying by some specified amount (e.g. from 5/1000 to 1/1000) and elicits how much the respondent is willing to pay for the program. The VSL implied is the WTP divided by the risk reduction. (If mean WTP for a program that achieved a risk reduction of 4 in 1000 was $500, then the implied VSL would be $125,000.) The third approach examines expenditures on products that reduce risk of dying (i.e.

safer cars, bike helmets, etc.). There is now a large number of all three types of VSL studies in high-income countries, but relatively fewer in low-income countries. We examine four that are particularly relevant for India.

Shanmugam (2001) uses the first approach – examining wage premiums for risky jobs – to estimate VSLs for adults in India. The paper uses survey data on wages of blue-collar workers in factories in one city in 1990 (Madras, in the state of Tamil Nadu). The mortality risk associated with a given factory was based on state government data on on-the-job fatalities, grouped according to an industry classification code. Shanmugam's estimates ranged from Rs.10M – Rs.56M in 2001. Inflating these estimates to the same 2004 terms used throughout the dissertation[19], the estimates range from Rs.11M – Rs.63M, or US$250,000 – US$1.4M.

Simon et al (1999) use a similar approach but do not limit their data to only one geographic area in India. The authors use nationwide data from the Occupational Wage Survey of the Indian Labor Bureau and data on job fatalities, again classified by industry classification code (average risk of dying on the job was approximately 15 per 100,000, compared with 8 per 100,000 in the U.S.). The regressions of fatality risk on wages, controlling for several personal and job characteristics, imply a VSL between Rs.17M – Rs.41M, or US$370,000 – US$920,000, in 2004 terms (Rs.6M – Rs.15M in the 1990 terms presented in Simon et al).

There are, however, concerns with using labor market studies for VSL estimates. The hedonic wage approach assumes that workers are aware of their on-the-job fatality risk. It observes the willingness-to-accept this higher risk for a higher wage, which may be much higher than an analogous willingness-to-pay to reduce risk (Hanemann 1991). It also applies only to working adults, typically to healthy male workers who take risky manufacturing jobs.

Bhattacharya et al. (2007) used the stated preference approach, asking 1200 commuters (pedestrians, cyclists and motorists) in New Delhi about their WTP for several different programs and

[19] Inflated using data from IMF's World Economic Outlook April 2007. http://www.imf.org/external/pubs/ft/weo/2007/01/data/index.aspx

products that would reduce their risk of dying in a traffic-related fatality while commuting to work. They find that WTP increased with the risk reduction, income and existing road traffic fatality risk. Their preferred estimate of VSL is Rs.1.3M in 2007 Rupees, corresponding to about Rs.1.1M, or US$25,000 in 2004 terms.

All of the studies above were concerned with WTP to reduce mortality risk for working adults. Few studies asks parents their WTP to reduce their children's risk of dying (or observe their WTP for risk-reducing products). Maskery et al (2007) presented parents in Matlab, Bangladesh with a generic nutritional health supplement that would reduce their youngest child's risk of dying. They illustrated the risk reductions offered and average baseline risks facing children in the respondents' communities using illustrated risk ladders and extensive training on probabilities. The nutritional supplement offered either a 20% or 60% risk reduction from the stated baseline risk (5 in 1000 per year) over a period of five years. Mean WTP (for a one-month supply of the supplement) was US$1.5, or 2% of average monthly household income in the sample (US$75). Responses were not significantly different between the two levels of risk reduction. WTP was higher for young children (under 5) than for school-aged children (aged 5-17), implying a higher VSL for young children. Although the authors were not able to present age-specific mortality risks to respondents in the scenarios, they note that the actual baseline risk of dying for young children is three times higher than for older children. Using the baseline risk given in the scenario, VSLs for young children are US$120K – $320K and for older children are US$60K - $180K. If, however, respondents' answers reflected reductions from the actual baseline risk facing the two groups of children, the VSL for young children and older children are US$24K - $75K and US$40K - $120K.

Given the available evidence, we choose the most conservative plausible estimates of VSL available. Given that average incomes in Tiljala are very similar to those in the Maskery et al (2007) study in Bangladesh (US$65 in Tiljala, US$75 in Matlab), we feel reasonably confident directly transferring estimates from that study. These are also the only available estimates of the value of mortality risk reductions for children in low income countries. Because the evidence seems weak that

parents have a different WTP to protect children of different ages, we use only one VSL estimate – US$25,000 – for both groups. Estimates for Indian adults in the literature above ranged from US$25,000 to US$1.6M, although the populations in these studies were somewhat wealthier than our Tiljala population. To be conservative, we also use a VSL for adults of US$25,000.

Simply taking the most conservative VSL found in the literature is no guarantee that the true VSL might be still lower. The essential question is whether we believe Indian society is willing to spend $25,000 to prevent the loss of a life in a low-income slum in Kolkata. On the other hand, VSL might higher than $25,000, and indeed all of the evidence above indicates that it is. We therefore assume a lower bound of $20,000 and an upper bound of $50,000 in the uncertainty analysis.

4.6 Other parameters

4.6.1 Case fatality rates

We use a mean case fatality rate for cholera of 0.75%, with lower and upper bounds of 0.15% and 5%. WHO (2006) reported 6 deaths in 3,155 Indian cholera cases, for a CFR of 0.20%. The case fatality rate worldwide (WHO 2006) is 2.3%. Naficy et al (1998) use a CFR of 1% for treated cases and 30% for untreated cases. Murray et al (1998) use 0.7% for children under 5yrs and 0.14% for older children and adults. We choose to use one CFR for all ages rather than distinguish between age groups based on limited data.

We use a mean case fatality rate for typhoid of 1%, with lower and upper bounds of 0.5% to 10%. According to the WHO[20], the CFR for typhoid cases treated with antibiotics is about 1%. CFR without treatment can range from 4% to 10%. The CFR in a January 2005 outbreak in Congo was 0.5% (214 deaths in 42,564 cases)[21]. Crump , Luby and Mintz (2004) use 1% based on "conservative estimates from hospital-based typhoid fever studies, mortality data from countries with reliable

[20] http://www.who.int/topics/typhoid_fever/en/

[21] http://www.who.int/wer/2005/wer8004.pdf

national typhoid fever surveillance systems that employ blood culture confirmation of cases, and expert opinion." Parry et al (2002) also list 1% as a good estimate, though rates of 30-50% have been reported in parts of Papa New Guinea and Indonesia.

4.6.2 Duration of illness

For cholera, we assume the average case lasts two days. Lower and upper bounds for Monte Carlo simulations are one day and 2 weeks, though a cholera case is unlikely to sicken someone for two weeks without some other co-infection. Murray et al (1998) use a duration of 3 days. For typhoid, we assume the average case lasts 1 week, with lower and upper bounds of 4 days to 2 months. Parry et al (2002) 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 where third-line antibiotics are necessary (cephalosporins).

4.6.3 Discount rates

As is standard in WHO DALY methodology, we discount life years saved at a real (net of inflation) rate of 3% and do not vary this parameter. Life years saved in years two and three are also discounted at 3% in the VSL+COI calculation (see Chapter 3). We use a mean financial discount rate of 8%, ranging from 6% - 12% in the Monte Carlo simulations. This applies only to cost of illness avoided in years two and three since the costs of the program all occur in year one and the WTP benefits from the CV survey are already present values.

4.6.4 DALY weights

WHO does not publish DALY weights specifically for cholera or typhoid. For cholera, we use the diarrheal disease weight of 0.11. For typhoid, we use a mean weight of 0.27, which lies

within a range of weights from somewhat similar diseases (malaria, Japanese encephalitis, dengue, upper respiratory infections). The lower bound and upper bounds are those for dengue fever (0.075), and neurological sequelae of malaria (0.471). For both cholera and typhoid, however, the disease weights will have little impact because the time spent ill is relatively short.

4.6.5 Knowledge of campaign

Finally, we assume that 80% of the Tiljala population learns about the campaign. This is a fairly ad hoc assumption, but will generally not affect the results since it simply scales the benefits and costs up linearly. This fraction might be more important if there are large economies (or diseconomies of scale) as the number of people vaccinated has a large effect on average costs.

Table 4.5 summarizes the assumptions and data used.

Table 4.5 Parameter assumptions for Tiljala, Kolkata, India (uncertainty range for Monte Carlo analysis in parentheses)

SITE CHARACTERISTICS	**Value (uncert. range)**	
Total population[1,2]	120,000	
Children <1 yr (% of population)	2	
Children 1-4 yrs (% of population)	7	
Children 5-14 yrs (% of population)	20	
Adults 15+ yrs (% of population)	72	
TYPHOID	**Value (uncert. range)**	
Epidemiology		
Incidence per 1000: Children 0-2	0.9	(0.5 – 1.8)
Incidence per 1000: Children 2-4	3.4	(1.7 – 6.8)
Incidence per 1000: Children 5-14	5.2	(2.6 – 10.4)
Incidence per 1000: Adults 15+	1.2	(0.6 – 2.5)
Blood culture sensitivity multiplier	2	
Case fatality rate (%)	1.0%	(0.5% - 10%)
DALY weight	0.27	(0.08 – 0.47)
Average duration of case (days)	7	(4 – 30)
Vaccine Characteristics & Costs		
Effectiveness (%)	70	(60% – 80%)
Duration (Years)	3	
Fixed costs	$10K	($5K – $15K)
Manufacturing cost **per dose**	$0.62	($0.5 – $1.0)
Marginal delivery cost **per dose**	$0.9	($0.5 - $1.5)
Marginal travel/time cost **per dose**	$0.04	($0.01 - $0.10)
Cost-of-illness		
Private COI: Children <15 yrs	$8.6	($0 - $18)
Private COI: Adults >15 yr	$18.7	($0 - $38)
Public COI: Children <15 yrs	$11	($6 - $20)
Public COI: Adults >15 yr	$7.7	($4 - $20)
Demand/Benefit Measures		
Percent who would take if free: Children 1-4	91%	(60% - 100%)
Percent who would take if free: Children 5-14	80%	(60% - 90%)
Percent who would take if free: Adults 15+	69%	(50% - 85%)
Slope of demand curve: Children 2-4	-0.24	(-0.12 to -0.5)
Slope of demand curve: Children 5-14	-0.28	(-0.14 to -0.6)
Slope of demand curve: Children 15+	-0.39	(-0.2 to -0.8)
Per vaccine WTP ($): Children 2-4	$4.2	($2.1 - $6.3)
Per vaccine WTP ($): Children 5-14	$3.6	($1.8 - $5.4)
Per vaccine WTP ($): Adults 15+	$2.6	($1.3 - $3.9)
OTHER PARAMETERS	**Value (uncert. range)**	
Percent of population who hear of program	80%	
Discount rate for life years saved	3%	
Discount rate for COI	8%	(6% - 12%)
VSL ($): Young children (under 5 yrs)	$25,000	($20k - 50k)
VSL ($):School-aged children (5-14yrs)	$25,000	($20k - 50k)
VSL ($): Adults (15+ yrs)	$25,000	($20k - 50k)

CHOLERA	Value (uncert. range)	
Epidemiology		
Incidence per 1000: Children under 5	7.0	(3.5 – 14.0)
Incidence per 1000: Children 5-14	2.2	(1.1 – 4.4)
Incidence per 1000: Adults 15+	0.9	(0.5 – 1.8)
Case fatality rate (%)	0.75%	(0.15% - 5.0%)
DALY weight	0.105	(0.05 – 0.39)
Average duration of case (days)	2	(1 – 14)
Vaccine Characteristics & Costs		
Effectiveness (%)	50%	(40% – 60%)
Duration (Years)	3	
Fixed costs	$10K	($5K – $15K)
Manufacturing cost **per dose**	$0.70	($0.5 – $1.0)
Marginal delivery cost **per dose**	$0.9	($0.5 - $1.5)
Marginal travel/time cost **per dose**	$0.04	($0.01 - $0.10)
Cost-of-illness		
Private COI: Children <15 yrs	$5.3	($0 - $11)
Private COI: Adults >15 yr	$6.5	($0 - $11)
Public COI: Children <15 yrs	$15	($10 - $25)
Public COI: Adults >15 yr	$16	($10 - $25)
Demand/Benefit Measures		
Percent who would take if free: Children 1-4	93%	(60% - 100%)
Percent who would take if free: Children	59%	(40% - 80%)
Percent who would take if free: Adults 15+	60%	(40% - 80%)
Slope of demand curve: Children 1-4	-0.16	(-0.32 to -0.08)
Slope of demand curve: Children 5-14	-0.15	(-0.29 to -0.07)
Slope of demand curve: Adults 15+	-0.44	(-0.88 to -0.22)
Per vaccine WTP ($): Children 1-4	$6.3	($3 - $9)
Per vaccine WTP ($): Children 5-14	$6.9	($3 – $10)
Per vaccine WTP ($): Adults 15+	$2.3	($1 - $3)

4.7 Herd protection effects of cholera vaccines[22]

Based on the results of placebo-controlled vaccine trials, the best estimate of the effectiveness of the oral cholera vaccine is on the order of 50% over 3 years (effectiveness is higher initially but declines over time)(Clemens et al. 1990). The comparison to placebo recipients eliminates problems such as yearly variation in incidence and any potential differences between those who choose to be vaccinated and those who do not. However, by ignoring differences in community level coverage and the potential for herd reductions in placebo recipients, these studies may underestimate the vaccine's ability to reduce cases. In fact, non-placebo controlled trials (generally based on an intent to treat approach) tend to find that the oral cholera vaccine's effectiveness exceeds 50% (Trach et al. 1997; Lucas et al. 2005; Thiem 2006).

Ali et al. (2005) provided the first empirical evidence of the herd protection effects of cholera vaccination by re-examining data from a 1985 individually-randomized control trial in Matlab, Bangladesh. These trials targeted all children between the ages of 2 and 15 years as well as women older than 15 years, but not adult men. Although it was not the original study's intention, vaccine coverage varied significantly geographically in baris[23], from 4% to 65% of the target population. Table 4.6 shows the original data from Ali et al (2005), where coverage rates are grouped into quintiles.

[22] This section is also based on a manuscript in progress with Brian Maskery, Marc Jeuland, Donald Lauria and Dale Whittington

[23] A *bari* is patrilinearly-related cluster of 3-10 households.

Table 4.6 Cholera incidence in Matlab, Bangladesh, by coverage rates[a] (Ali et al 2005)

		Vaccine recipients			*Placebo recipients*		
Level of coverage[a]	Target Population	N	Cases	Incidence (per 1,000)	N	Cases	Incidence (per 1,000)
<28%	24,954	5,627	15	2.67	2,852	20	7.01
28-35%	25,059	8,883	22	2.48	4,429	26	5.87
36-40%	24,583	10,772	17	1.58	5,503	26	4.72
41-50%	24,159	11,513	26	2.26	5,801	27	4.65
>51%	22,394	12,541	16	1.28	6,082	9	1.48
Total	121,149	49,336	96	1.95	24,667	108	4.38

[a] Percent coverage is defined as the fraction of the target population (women and children) who were vaccinated, not the fraction of the entire population (which would include men). The 1986 trial targeted 124,000 people from a total population of 188,000 (i.e. 66%).

This variation allowed the authors to test for herd protection effects. They found an inverse monotonic relationship between coverage rates and incidence rates: incidence among placebo recipients declined as coverage increased ($p=0.02$). This inverse relationship was also observed for children less than two years of age who were not eligible for vaccination (Ali et al. 2007). Herd protection effects are especially important for children less than one year of age because the existing vaccine is not considered safe for that age group and because their cholera incidence and diarrhea mortality rates are especially high (ICDDRB 2005). Ali et al. (2005) also found evidence that incidence declined among vaccinated individuals as vaccine coverage increased, although this relationship was only significant at the 8% level.

We use the incidence data in Table 4.6 to estimate the $V(\cdot)$ and $U(\cdot)$ relationships which map overall population coverage rates into protective probabilities (see Chapter 3). We acknowledge that the approach below is largely a curve-fitting exercise based on a limited amount of available data. However, this functional relationship between coverage and protection levels is a useful approximation until more robust epidemiological models of disease spread and vaccine protection are widely available. In fact, Longini et al (2007) have estimated just such a model and found very similar results to those we report. Ideally, more sophisticated epidemiological models would also incorporate how herd protection effects differ by age group.

We assume that the incidences for vaccinated and unvaccinated populations can be modeled with a set of two differential equations. The first equation predicts incidence among the vaccinated subgroup (*v*) as a function only of coverage (*x*). Unlike Table 4.6, we define coverage here over the entire population of the study area, not only the target population (which was 66% of the whole population). The second equation (for the incidence among the unvaccinated, *u*) is similar but modified so that incidence can never be higher in the vaccinated subgroup than the unvaccinated. The two equations are shown below, where *kv* and *ku* are rate constants.

Incidence among vaccinated: $v = v_o \cdot \exp(-kv \cdot x)$ (4.1)

Incidence among unvaccinated: $u = u_o \cdot \exp(-kv \cdot x) + (Uo - Vo) \cdot \exp(-ku \cdot x)$ (4.2)

The parameters for Equation (4.1) can be estimated with a simple OLS regression of each quintile's percent coverage of the entire population[24] on the log of incidence rates among the vaccinated. The intercept in this regression model (v_o) is 4.5 cases per 1000 ($p = 0.03$) and the rate constant (*kv*) is -0.029 ($p = 0.10$). The R^2 for the regression is 0.65. With the estimated parameters for Eq. (4.1) in hand, we then estimate the parameters of equation (8) with a simple non-linear least squares model. The R^2 for this model is 0.97 and the intercept (u_o) is significant at the 10% level ($p=0.07$), but the rate constant (*ku*) has a p-value of 0.15. Rewriting Eqs. (4.1) and (4.2) with these estimated parameters gives:

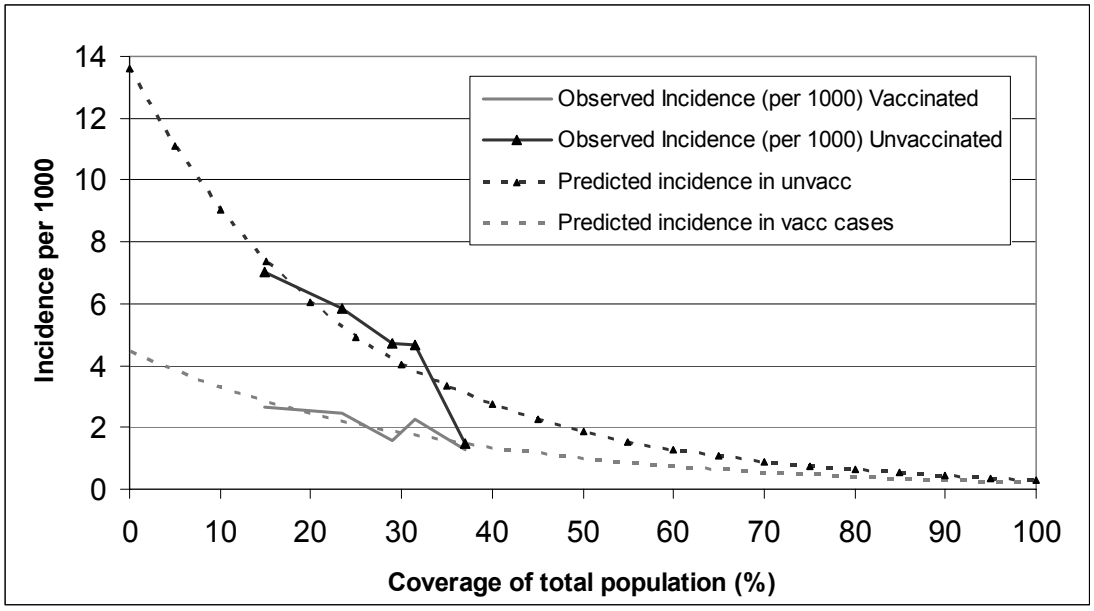
$$v(x) = 4.5 \cdot \exp(-0.03 \cdot x) \quad (4.3)$$

$$u(x) = 4.5 \cdot \exp(-0.03 \cdot x) + (13.6 - 4.5) \cdot \exp(-0.047 \cdot x) \quad (4.4)$$

[24] We take the average number of vaccinated people in each quintile by dividing the total number of vaccinees by the total number of eligible people (Table 4.6). We then adjust this to reflect the percent coverage for the entire population, assuming that the target population is 66% of the entire population. For example, in the first quintile in Table 4.5, 5,627 people were vaccinated from the eligible population of 24,494 (23%). This represents a total population coverage rate of 15% (23% * 0.66). We also fit a model using midpoints of the coverage quintiles but we preferred this approach because it fit the results from Longini et al (2007) better.

Figure 4.4 plots the observed Matlab data against these exponential fits. As coverage increases, the incidence for unvaccinated individuals approaches that for the vaccinated subgroup. As coverage increases from 0 to 100%, the expected annual incidence for the vaccinated subgroup decreases from 4.5 cases per 1,000 persons to near zero cases, while the expected incidence for the unvaccinated subgroup similarly declines from 13.6 cases per 1,000 persons to near zero.

Figure 4.4 Observed incidences in Matlab vs. predictions from exponential fit



Using these exponential functions of incidence as a function of coverage, we can calculate the percentage reduction in incidence for vaccine recipients compared to a baseline of zero coverage (i.e. $u(0) = u_o = 10$ cases per 1,000 persons) with eq. (4.3). The percentage reduction in incidence among the unvaccinated is calculated similarly, in eq. (4.4).

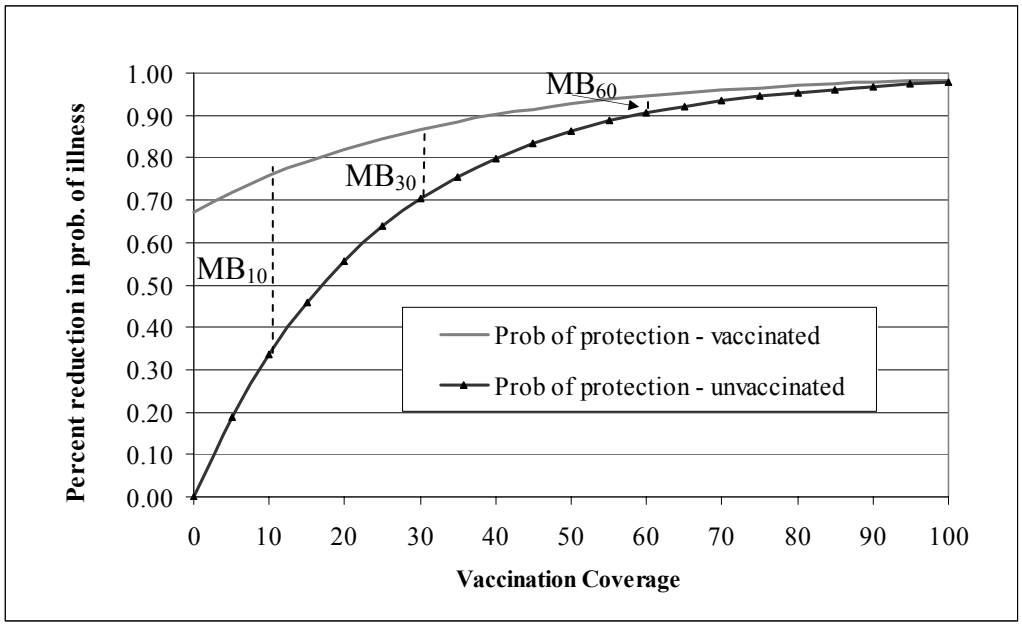
$$V(x) = \frac{U_0 - V(x)}{U_0} = 1 - \frac{V_0}{U_0}\exp(kv \cdot x) \tag{4.5}$$

$$U(x) = \frac{U_0 - U(x)}{U_0} = \left[1 - \frac{V_0}{U_0}\exp(kv \cdot x)\right] - \left[1 - \frac{V_0}{U_0}\exp(ku \cdot x)\right] \tag{4.6}$$

Figure 4.5 plots percent reduction in incidence (i.e. the probability of protection) for both vaccinated and unvaccinated individuals in the population using Eqs (4.5) and (4.6). Note that when coverage is near zero, the vaccine reduces incidence by about 67% (13.6 to 4.5). Thus, the inferred vaccine protection in the absence of herd protection would be about 65%, somewhat higher than the 50% protection level originally reported for the Matlab trial (Clemens et al. 1990).

As shown in Figure 4.5, the marginal change in effectiveness (or probability of protection) resulting from taking the vaccine is dependent on coverage. At low coverage, there is a greater private incentive to be vaccinated because the marginal increase in protection is large. At high coverage rates, though, more of the total protection derives from the indirect effects of herd protection, and the additional protection from taking a vaccine is small. Thus, from a social perspective, the marginal benefit per vaccine distributed decreases monotonically based on our functional forms in equations (4.1) – (4.6) (this is shown in Figure 4.5 as dashed vertical lines showing the marginal benefits of distributing more vaccines at coverage rates of 10%, 30% and 60%). Intuitively, the socially efficient outcome will equate this marginal benefit with the marginal cost of producing the vaccine, which may occur at some coverage rate between 0 and 100%.

Figure 4.5 Effective protection for vaccinated and unvaccinated individuals



CHAPTER 5

RESULTS - TYPHOID VACCINATION PROGRAMS

5.1 Baseline burden of typhoid disease

Applying the incidence rates observed in Narkeldanga to Tiljala, and adjusting these rates for the lack of sensitivity of blood-culture typhoid tests by doubling them, gives the expected annual burden of typhoid fever in Tiljala (Table 5.1). Even though school-aged children make up 20% of the total population, they account for 48% of cases because incidence is so much higher in this age group. We estimate that typhoid fever causes approximately 5 deaths each year in Tiljala, resulting in a loss of 137 life-years. Because an episode of typhoid fever does not last long on average (about one week), the disease's morbidity effects do not add much to the overall DALY burden (i.e. row (4) is not much larger than row (3)). Typhoid fever costs the public sector approximately US$5,000 in treatment costs annually, and costs the patients who contract typhoid about US$6,500 in direct and indirect private costs.

Table 5.1. Baseline annual burden of typhoid fever in Tiljala

		Infants (<2yrs)	Young children (2-4.9yrs)	School-age children (5-14.9yrs)	Adults (15+)	All Ages
(1)	Expected number of cases	9	41	245	212	506
(2)	Expected number of deaths	0.09	0.41	2.45	2.12	5.06
(3)	Expected number of life years lost[a]	3	12	72	51	137
(4)	Expected number of DALYs lost[a]	3	12	73	52	140
(5)	Expected public COI (US$)	$95	$449	$2,692	$1,629	$4,865
(6)	Expected private COI (US$)	$74	$351	$2,105	$3,955	$6,485

[a] Life years discounted at 3%

5.2 Description of the programs analyzed

We will analyze a range of program possibilities for both types of vaccines and use a nomenclature to distinguish these programs. First, a vaccination program may target specific age groups. The letter "Y" will denote a program that targets only young children under 5 yrs old but who are old enough to be safely vaccinated. "S" will denote a program that targets only school-aged children (5-14yrs), and "C" will denote a program that targets both groups of children. We do not analyze programs which target only adults since incidence for both diseases is highest in children and it seems unlikely that programs targeted only to adults would be of interest to policymakers. A program that targets all age groups, including adults, will be denoted with "M" for mass vaccination. Note that for each of these programs, we assume a separate fixed cost charge of US$10,000.

Second, programs may charge different levels of user fees. We will denote the user fee for the program as a super-script on the age group abbreviation. For example, "$\mathbf{C}^{\$1}$" denotes a program that targets both groups of children and charges a user fee of US$1.

5.3 Would a typhoid vaccination program pass a social cost-benefit test?

Table 5.2 shows the likely consequences of a typhoid vaccination program if immunizations were offered with zero user fees (i.e. free of charge). Recall that typhoid vaccines have not been proven safe for infants under 2 years old, so a vaccination program would not reduce cases in this group absent indirect protection through herd effects (which we do not model for typhoid fever). Percentage reductions in disease burden are highest in young children (because they have the highest percent coverage with zero fees), but the absolute number of cases and deaths avoided is highest in school-aged children because of the high incidence in that age group. If the program targeted all age groups (i.e. a mass vaccination program, or "M^0"), we expect that about 67,000 people, or 56% of the entire population would choose to be vaccinated, preventing about 640 cases of typhoid fever and 6 deaths, a 42% decrease overall. This decrease may seem modest, but recall that the vaccine is only

70% effective, that we assume that only 80% of the population hears about the program, and that not everyone will choose to take a vaccine even with zero user fees.

The total program costs for the mass program M^0 would be about $114,000, but the reduction in public COI would bring the net cost of the program for the government to about $109,000. It is clear that the government will not save money with the program: public COI savings are much less than costs for all programs. Because of fixed costs, average costs per person decrease in the programs that vaccinate more people (i.e. average cost is much higher in Y^0 than M^0). The mass program would reduce privately-borne COI by about US$7,400. Much of the COI reductions (public + private) comes from reducing cases among adults and school-children (only 9% of total COI savings in M^0 comes from vaccinating young children). Because 65% of the total program costs come from vaccinating adults, however, a targeted vaccination program towards children would be much less expensive.

Table 5.2 Effects of typhoid program with zero user fees

		Y^0 Young children (2-4.9yrs)	**S^0** School-age children (5-14.9yrs)	**C^0** All eligible children (2-15yrs)	**M^0** Adults plus all eligible children
(1)	Number of vaccinations (%)	4,368 (73%)	15,091 (64%)	19,459 (66%)	66,920 (56%)
(2)	Number of cases	122 → 60	734 → 405	857 → 465	1517 → 881
(3)	Number of deaths	1 → 1	7 → 4	9 → 5	15 → 9
(4)	DALYs	36 → 18	212 → 117	248 → 135	407 → 235
(5)	Reduction in disease burden from baseline %	51%	45%	46%	42%
(6)	Costs of vaccination (US$)[1]	$16,805	$33,512	$40,317	$114,262
(7)	Average cost per person (US$)	$3.85	$2.22	$2.07	$1.71
(8)	Vaccine revenue collected (US$)	$0	$0	$0	$0
(9)	Public sector contribution (Total cost - revenue, US$)	$16,805	$33,512	$40,317	$114,262
(10)	Public COI avoided (US$)	$637	$3,357	$3,994	$5,745
(11)	Private COI avoided (US$)	$498	$2,625	$3,122	$7,376
(12)	Net Public Cost (Total Cost - Revenue - Public COI avoided, US$)	$16,169	$30,155	$36,324	$108,516

Notes: Arrows indicate change from baseline to levels with program. Life years (and DALYs) discounted at 3%, COI discounted at 8%. The rightmost column (mass vaccination) is not the sum of the other three columns because each column is considered a separate program with fixed costs of US$10,000.

To avoid a case of typhoid in the mass program M^0, the government would need to spend about $180 (row 1 in Table 5.3). Adjusting for the savings from public COI avoided, the figure drops to $170 (row 4). The program that targets only school-aged children (S^0)or both groups of children (C^0) have the lowest (most attractive) cost-effectiveness ratios: avoiding a case in program S^0 or C^0 would cost about $100. The ratio is worse (more expensive) if only young children are targeted (Y^0) because of high average costs. The costs per DALY and death avoided follow a similar pattern. Using the standard definition based on GDP per capita (US$620 in India), the costs per DALY avoided for S^0 and C^0 would be considered "highly cost effective". Y^0 and M^0 would be considered "cost-effective" because the ratios are less than three times per capita GDP. The ratios for all Tiljala programs except Y^0 are in the lower (better) half of interventions for South Asia evaluated by the 2nd Disease Control Priorities Project (Jamison et al. 2006, Figure 2.4, pg. 51).

Table 5.3 Cost effectiveness measures for typhoid programs with zero user fees (all costs in US$)

		Y^0 Young children (2-4.9yrs)	**S^0** School-age children (5-14.9yrs)	**C^0** All eligible children (2-15yrs)	**M^0** Adults plus all eligible children
	Total Program Cost				
(1)	Program cost per case avoided	$269	$102	$103	$180
(2)	Program cost per death avoided	$26,942	$10,187	$10,303	$17,951
(3)	Program cost per DALY avoided	$910	$352	$355	$664
	Net public cost (Cost - avoided Public COI)				
(4)	Net public cost per case avoided	$259	$92	$93	$170
(5)	Net public cost per death avoided	$25,922	$9,167	$9,282	$17,048
(6)	Net public cost per DALY avoided	$876	$317	$320	$631

Would these programs pass a social cost-benefit test? Using only a limited definition of social benefits (public and private cost of illness avoided), none of the programs produces positive net benefits (Table 5.4, row 1). If we account for the economic value that society places on reducing deaths from typhoid by multiplying the VSL and the number of deaths avoided, however, the programs look more attractive. All of the programs except Y^0 produce positive net benefits (row 2).

A program to vaccinate all eligible children would produce the largest COI+VSL net benefits, largely because incidence is higher in children than adults.

Table 5.4 Net benefit measures for typhoid programs with zero user fees

		Y^0 Young children (2-4.9yrs)	S^0 School-age children (5-14.9yrs)	C^0 All eligible children (2-15yrs)	M^0 Adults plus all eligible children
	Net benefits				
(1)	COI Net benefits Total COI avoided - Total Costs, US$	($15,671)	($27,530)	($33,201)	($101,140)
(2)	COI + VSL Net benefits (VSL + Public COI avoided + Private COI avoided - Total Costs) (US$)	($1,204)	$48,768	$57,564	$46,492
(3)	WTP Net benefits (WTP benefits + public COI avoided - Total costs)(US$)	$2,177	$24,173	$36,350	$87,556

Finally, respondents in the contingent valuation survey in Tiljala were willing-to-pay significant amounts to receive typhoid vaccines. Households were willing to pay on average US$4.2 to vaccinate a young child, US$3.6 to vaccinate a school-aged child, and US$2.6 to vaccinate an adult. This stated WTP should include not only the value of reducing expected private costs-of-illness but also reductions in mortality risk and pain and suffering. As such, it is the most comprehensive measure of the economic benefits that accrue to residents of Tiljala from a free typhoid vaccination program. Including public COI avoided (which households were unlikely to include their private WTP), we can see that all programs (including Y^0) would produce positive net benefits if the cost of the vaccination program was a fixed charge of US$10,000 plus $1.56 per person vaccinated.

5.4 Sensitivity analyses

We first examine parameters individually to find the "break-even" value that equates benefits and costs. Recall that using the COI net benefits measure, the program did not produce net benefits for any age group. To break even using the COI net benefit measure, incidence or total COI would need to be far higher than observed (Table 5.5). Incidence in young children would have to increase from about 8 per 1000 to 50 per 1000 for Y^0 to break-even, and increase in all age groups five-fold and eight-fold for C^0 and M^0 to break-even. Similarly, the vaccine would have to have a much lower

average cost than we assume to break even using the COI net benefit measure. For the mass program to pass, the government would need to be confident that it could purchase, store and deliver the vaccine for less than US$0.20, which seems very unlikely given that actual costs for the typhoid trial in Kolkata were an order of magnitude higher (~US$3).

Because a free program passed a cost-benefit test for all programs except Y^0 using the VSL net benefit measure, the parameters for incidence or case fatality rate could be 40- 70% of their base case values and the programs would still pass. Similarly, the average vaccine cost could be somewhat higher, or our estimate of VSL somewhat lower, and the programs would still pass. Because Y^0 very nearly breaks even in the base case (see Table 5.4), only small changes in the parameters would make the program pass (i.e. the CFR would only have to increase from 1% to 1.08%). The break-even analysis for the WTP net benefit measure is unsurprising: break-even cost is somewhat higher than our average WTP estimates, and break-even WTP somewhat lower than average vaccine cost (US$1.7 - $2 for all programs except Y^0), because of the expected public COI savings.

Table 5.5. Parameter values at which a vaccination program would produce zero net benefits

Net benefits: COI only	**Y^0** Young children (2-4.9yrs)	**S^0** School-age children (5-14.9yrs)	**C^0** All eligible children (2-15yrs)	**M^0** Adults plus all eligible children
Incidence (per 1000)	50	29	5.6x	8.8x
Total vaccine cost, US$	$0.28	$0.40	$0.37	$0.20
Total (public + private) COI, US$	$290	$110	$5.6x	8.8x
Net benefits: COI + VSL				
Incidence (per 1000)	3.7	2.1	0.41x	0.72x
Case fatality rate (%)	1.08%	0.37%	0.37%	0.69%
Total vaccine cost, US$	$3.9	$5.5	$5.1	$2.4
VSL (US$)	$27,000	$9,000	$9,100	$17,100
Net benefits: WTP + Public COI				
Total vaccine cost, US$	$4.4	$3.8	$3.9	$3.0
Per capita WTP, US$	$3.7	$2.0	0.50x	0.55x

Notes: For programs with multiple age groups, the break-even scalar is shown. A scalar below 1 means that the parameters could decrease and still break even (i.e. 0.66 = 66% less). A scalar of 5.6x means that the relevant parameters would need to increase 560% to break even.

Second, we allow all of the uncertain parameters to vary simultaneously in a Monte Carlo framework. The lower and upper bounds for each parameter are presented in parentheses in Table 4.5. We used Crystal Ball, a plug-in for MS Excel, to run the simulations. The results presented used 10,000 draws from triangular parameter distributions for all variables, with low and high ends of the distribution set to the uncertainty ranges, and the peak of the triangle set to the mean value.

COI net benefits were negative for all programs in all 10,000 model runs (Table 5.6): a typhoid vaccination program in Tiljala would fail a social cost-benefit test if benefits are restricted to avoided treatment costs. However, the model predicts all programs except Y^0 would always produce positive net benefits using the COI+VSL measure, and mean net benefits are quite high. Even Y^0, which did not produce positive net benefits using the base case parameter values (see Table 5.4) produced positive net benefits in 95% of the 10,000 model runs, and on average produced positive net benefits.

Table 5.6 Monte Carlo simulations of typhoid vaccination programs with no user fees

	Y^0 Young children (2-4.9yrs)	**S^0** School-age children (5-14.9yrs)	**C^0** All eligible children (2-15yrs)	**M^0** Adults plus all eligible children
COI Net benefits				
Mean	($15,600)	($27,600)	($33,200)	($106,000)
Std. Dev	$2,350	$4,900	$5,700	$17,800
% positive	0%	0%	0%	0%
VSL + COI Net benefits				
Mean	$59,800	$390,000	$460,000	$704,000
Std. Dev	$53,400	$292,000	$298,000	$375,000
% positive	95%	100%	100%	100%
WTP Net benefits				
Mean	$720	$21,400	$32,000	$76,000
Std. Dev	$4,300	$11,800	$12,700	$32,300
% positive	56%	97%	100%	99%

Using the WTP measure of benefits, the Monte Carlo analysis shows that there is a large probability that all programs except Y^0 would produce positive net benefits. Fifty-six percent of the model runs for Y^0 showed WTP net benefits that were greater than zero, and mean net benefits were

slightly positive. The large discrepancy between mean COI+VSL net benefits and mean WTP net benefits is largely driven by the case fatality rate. The COI+VSL estimates are highly sensitive to this parameter, which we assumed could reach as high as 10%. For M^0, for example, if we change only the case fatality rate from 1% to 2% and keep all other parameters at their mean values, the COI+VSL net benefits jump from $46,000 to $194,000. Increasing the CFR to 3% increases the net benefits to $342,000.

5.5 Typhoid vaccination programs with user fees

If one accepts that the private economic benefits of a typhoid vaccine should include more than treatment costs avoided, it seems likely from the preceding analysis that a typhoid vaccination program that charged no user fees would pass a social cost-benefit test for Tiljala. An investment in a free vaccination program would be welfare-enhancing in that the private benefits that would accrue to the immunized are very likely to exceed the costs of immunizing them.

The program would, however, require that the government commit a substantial amount of financial resources to the program. We expect that a mass vaccination program (M^0) would require an investment of approximately $114,000 every three years, although the government could expect to "get back" approximately 5% of this outlay in reduced public sector treatment costs. A program targeting only children would cost much less – about $40,000 - but would avoid about 250 fewer cases (in adults).

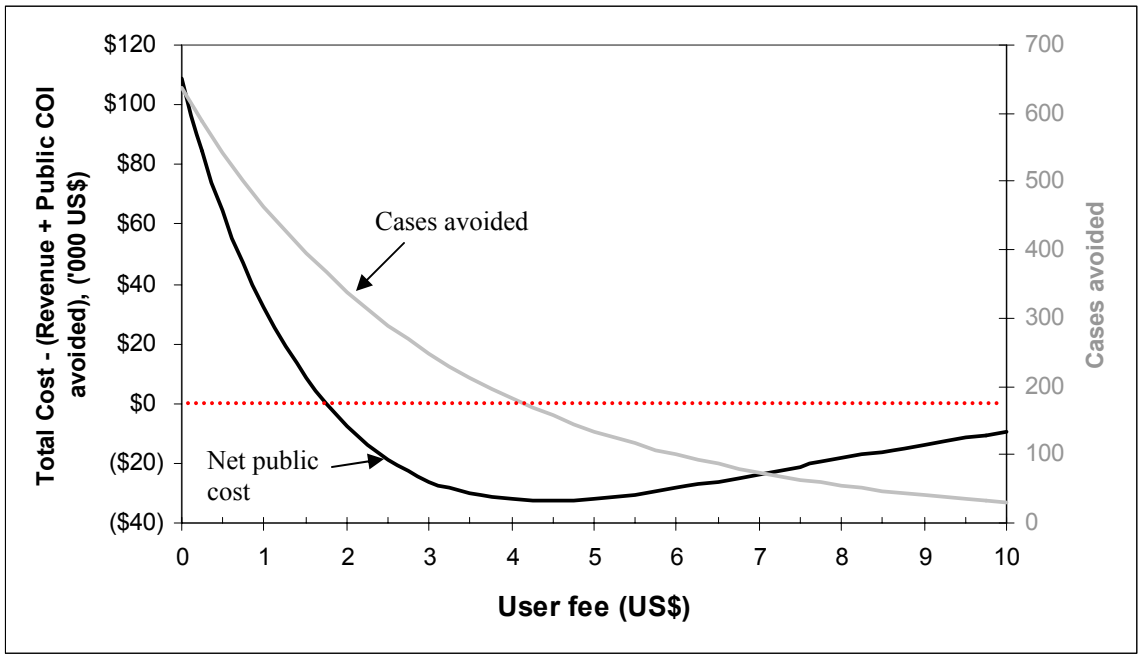
Passing a social cost benefit test is not necessarily sufficient justification to move forward with a program if budgets are highly constrained. As noted in Chapter 2, there are any number of competing health interventions that might appear more attractive to Indian health policymakers or external donors. Suppose that the Indian Ministry of Health or the State of West Bengal decide that a free typhoid vaccination program is not the wisest use of limited health subsidies available (~US$5 per capita). Because typhoid vaccines are not widely available, and because a significant fraction of

the population places an economic value on the vaccine larger than the costs, a program that would make the vaccines available, at a subsidized cost or even at full cost, would be welfare-enhancing.

Before considering specific programs with user fees, it is useful to consider the range of options available for typhoid vaccination programs. We assume that the only policy lever that the government has for these vaccination programs is the user charge levied per vaccinated person. We assume a monotonic relationship between the level of user charges and the cases avoided, so that as user charges increase, fewer people are vaccinated and fewer cases (and deaths) are avoided. Note that, with the exception of WTP, all program benefits (e.g., deaths avoided, DALYs saved, public and private COI avoided) are assumed to be linear functions of the number of cases avoided. On the other hand, as user charges increase, the government's financial contribution to the project decreases.

This tradeoff is illustrated in Figure 5.1. This figure defines the government's financial position as net public costs, or (total costs - revenue collected from vaccine sales - avoided public COI). The net public cost is positive for a program without user charges and reaches zero (i.e. revenue-neutrality, marked with a red dotted line in Figure 5.1) at a user fee of about US$1.75. With this revenue-neutral user fee, the program would avoid 370 typhoid cases. The graph shows the government could prevent about 270 more cases of typhoid over 3 years at a net public cost of $114,000. If the government's objective was to maximize revenue from vaccine sales, a user fee around $4.4 would be optimal; at this point net public revenues reach their maximum. We assume this is not the government's objective, however, and concentrate the policy analysis for user fees between zero and cost-recovery.

Figure 5.1. Program possibility frontier for a mass typhoid vaccine program (**M**)



It may also be useful to view the data in Figure 5.1 from a marginal perspective. Table 5.7 shows the marginal effects of decreasing the user fee by US$0.25 (about Rs.10) starting with the full cost-recovery price of $1.75. By subsidizing the cost of the vaccine US$0.25, the program will prevent an additional 30 cases. The cost of this subsidy to the public sector (net of public COI savings) is about $9,000, or about $300 per additional case avoided. Providing an additional subsidy of US$0.25 (total subsidy = US$0.50) prevents even more cases (32) but costs even more than the first US$0.25 subsidy (the number of vaccines sold is increasing more than proportionally to the change in user fee because of exponential demand). The cost per case avoided ($330 for the second US$0.25 subsidy) is higher because the government is subsidizing even more people who were willing to purchase the vaccine at the higher user fee.

Table 5.7 Marginal effects on cases avoided and public sector cost of reducing subsidy for a mass typhoid vaccination program (M^0)

Moving from fee of $X to $Y	Comes at an addt'l public sector cost of…	But prevents an addt'l _____ cases…	Public sector cost per case
$1.75 → $1.50	$9,000	30	$300
$1.50 → $1.25	$10,700	32	$330
$1.25 → $1.00	$12,700	35	$361
$1.00 → $0.75	$14,900	38	$392
$0.75 → $0.50	$17,500	41	$423
$0.50 → $0.25	$20,400	45	$455
$0.25 → $0	$23,700	49	$488

Finally, Figure 5.2 presents the tradeoff between cases avoided and public sector cost for programs that target only children. Because of the smaller number of vaccinations and fixed costs of $10,000, the revenue-neutral user fee is higher than for the mass program (US$2.30 vs. US$1.75).

Figure 5.2 Program possibility frontier for a typhoid vaccine program that targets only eligible children aged 2-15 yrs (C)

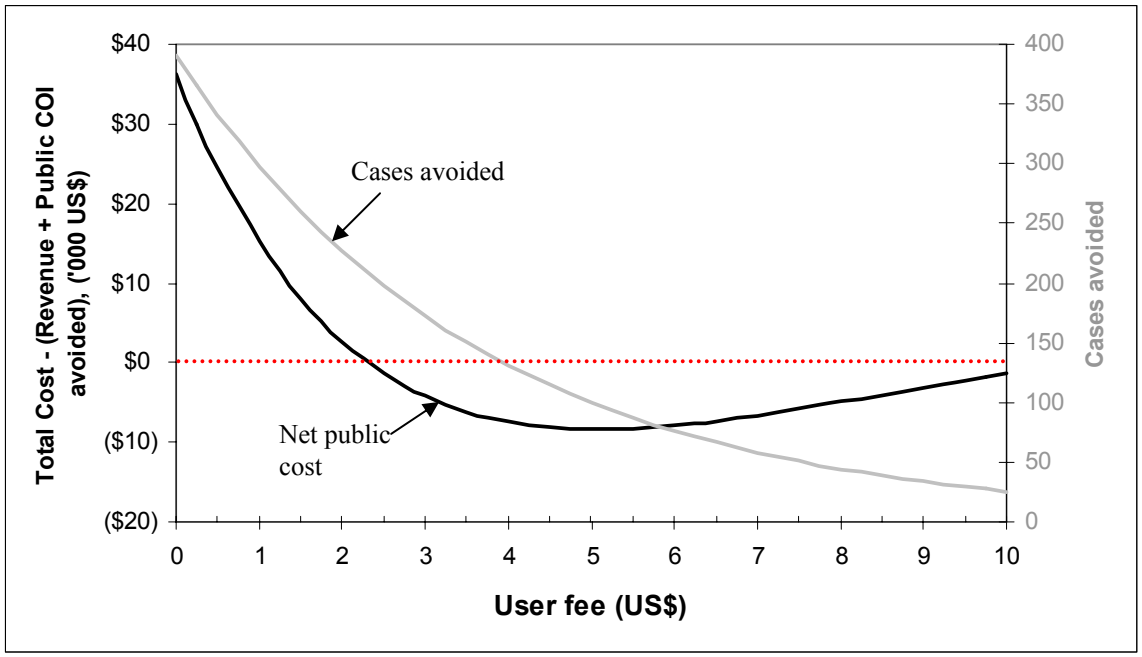
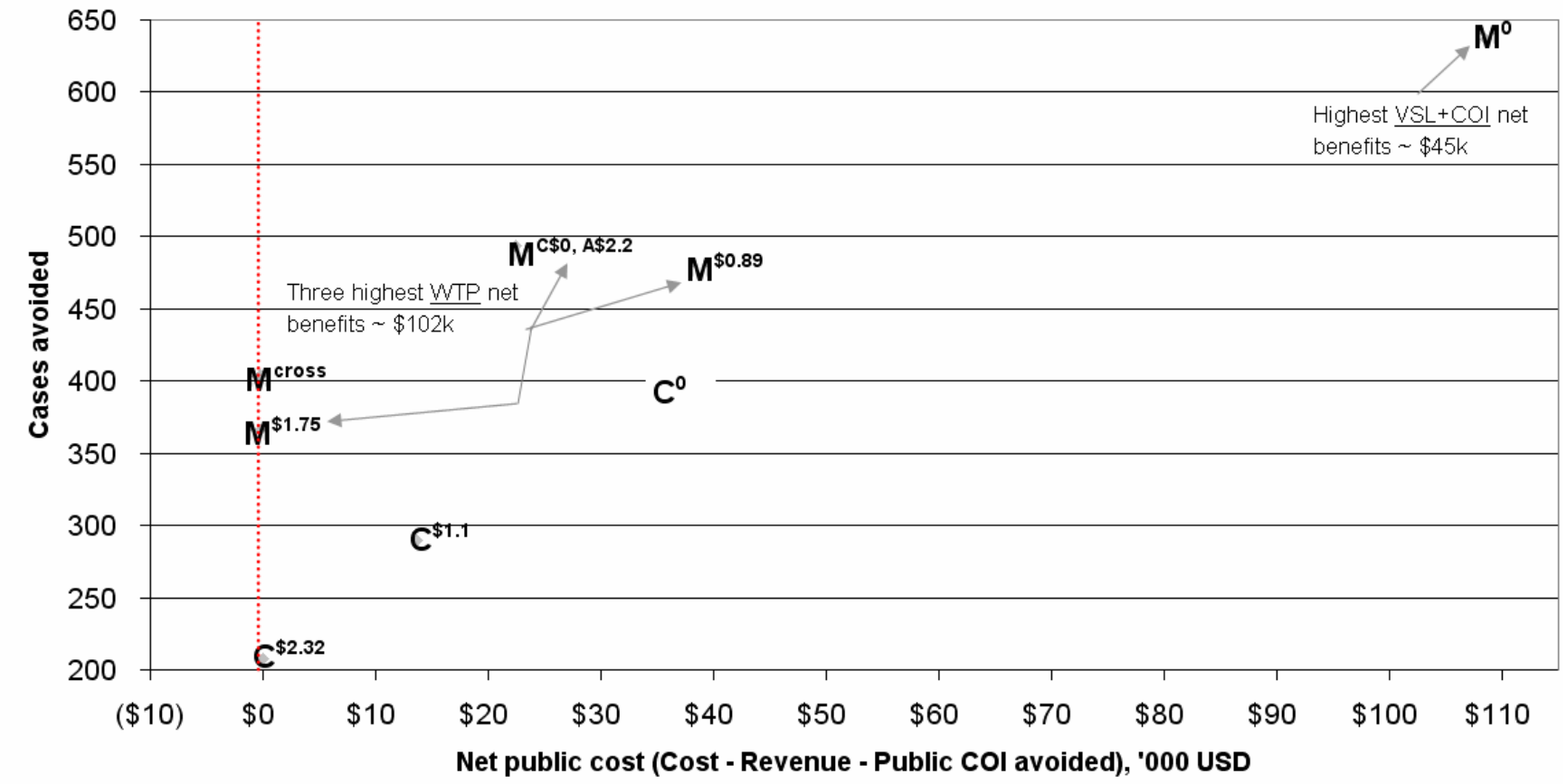


Table 5.8 summarizes the results from several typhoid vaccination programs in Tiljala, and Figure 5.3 similarly displays the tradeoff between cases (and deaths) avoided and net public revenues. We focus only on programs that target all children (C) or adults and children (M). The first two columns show the programs with zero user fee already discussed above (C^0 and M^0). The next two columns ($C^{\$1.1}$ and $M^{\$0.89}$) show the results of programs that would ask users to share the cost of the program equally with the public sector (US$1.1 = Rs. 50, US$0.89 = Rs. 40). These programs still require public subsidies of $14,000 and $38,000 and reduce about 25% fewer cases than the full-subsidy programs. The next program (labeled "$M^{C\$0,A\$2.2}$") would ask adults to pay US$2.2 (Rs.100), but would provide vaccines to children for free. This is not a revenue-neutral program where revenues from adult sales cross-subsidize child vaccines. It does, however, reduce the same number of cases in children as C^0 at less cost because the adult vaccinations drive down the average cost per person. It also has the important advantage that typhoid vaccines are available to adults who are willing and able to pay for them.

Table 5.8 Effects of typhoid vaccination programs with and without user fees

		Subsidized programs					Cost recovery programs		
		C^{0}	**M^{0}**	**$C^{\$1.1}$**	**$M^{\$0.89}$**	**$M^{C\$0,A\$2.2}$**	**$C^{\$2.32}$**	**$M^{\$1.75}$**	**M^{cross}**
(1)	Child user fee	$0	$0	$1.1	$0.89	$0	$2.32	$1.75	$0.65
(2)	Adult user fee	n/a	$0	n/a	$0.89	$2.2	n/a	$1.75	$3.0
(3)	Number of vaccinations	19,460	66,920	14,450	48,830	39,430	10,384	36,100	31,050
(4)	Cases avoided	391	637	290	480	494	208	366	404
(5)	DALYs avoided	114	172	84	130	138	60	100	113
(6)	Costs of vaccination	$40,300	$114,200	$32,500	$86,100	$71,427	$26,200	$66,240	58,370
(7)	Average costs per person	$2.07	$1.71	$2.25	$1.76	$1.81	$2.52	$1.84	$1.88
(8)	Public COI avoided (US$)	$3,990	$5,750	$2,960	$4,370	$4,730	$2,120	$3,360	$3,890
(9)	Total Cost - Revenue - Public COI avoided	**$36,300**	**$108,500**	**$13,700**	**$38,250**	**$22,370**	**($30)**	**($290)**	**($300)**
(10)	Total COI avoided – Total Costs[a]	($33,200)	($101,100)	($27,200)	($76,260)	($61,784)	($22,400)	($58,800)	($50,551)
(11)	Total COI avoided + (VSL * deaths avoided) - Total Costs[a]	**$57,600**	$46,500	$39,900	$35,090	$52,900	$25,730	$26,190	$43,080
(12)	WTP benefits + Public COI avoided – Total costs[a]	$36,400	$87,600	$36,700	**$102,980**	**$102,200**	$33,110	**$102,970**	$97,200

Figure 5.3 Comparison of typhoid vaccination program options for Tiljala



Notes: "M^{cross}" sets child fees at $0.65 and adult fees at $3.

Table 5.9 Net public costs (Cost – Revenue – Public COI avoided) in '000US$ with combinations of child and adult user fees

Adult user fee \ Child user fee	**$0.00**	**$0.10**	**$0.20**	**$0.30**	**$0.40**	**$0.50**	**$0.60**	**$0.70**	**$0.80**	**$0.90**	**$1.00**	**$1.50**	**$2.00**
$0.00	$109	$106	$103	$101	$99	$97	$95	$93	$91	$89	$87	$80	$75
$1.00	$53	$50	$48	$46	$43	$41	$39	$37	$35	$34	$32	$25	$19
$1.50	$37	$34	$32	$29	$27	$25	$23	$21	$19	**$17**	$16	$9	$3
$2.00	$26	$23	$21	$18	$16	$14	$12	$10	$8	$6	$5	($2)	($8)
$2.50	$19	$16	$14	$11	$9	$7	$5	$3	$1	($1)	($2)	($9)	($15)
$3.00	$15	$12	$9	$7	$5	$3	$1	($1)	($3)	($5)	($7)	($14)	($19)
$3.50	$12	$10	$7	$5	$3	$1	($2)	($3)	($5)	($7)	($9)	($16)	($21)
$4.00	$12	$9	$7	$4	$2	($0)	($2)	($4)	($6)	($8)	($9)	($17)	($22)
$4.50	$12	$9	$7	$4	$2	$0	($2)	($4)	($6)	($8)	($9)	($16)	($22)
$5.00	$13	$10	$8	$5	$3	$1	($1)	($3)	($5)	($7)	($8)	($15)	($21)
$5.50	$14	$12	$9	$7	$5	$2	$0	($2)	($3)	($5)	($7)	($14)	($19)
$6.00	$16	$13	$11	$8	$6	$4	$2	$0	($2)	($4)	($5)	($12)	($18)
$6.50	$18	$15	$13	$10	$8	$6	$4	$2	($0)	($2)	($3)	($11)	($16)
$7.00	$19	$17	$14	$12	$10	$8	$5	$4	$2	($0)	($2)	($9)	($14)
$7.50	$21	$18	$16	$14	$11	$9	$7	$5	$3	$2	$0	($7)	($13)
$8.00	$23	$20	$18	$15	$13	$11	$9	$7	$5	$3	$2	($5)	($11)
$8.50	$24	$22	$19	$17	$15	$12	$10	$8	$7	$5	$3	($4)	($9)
$9.00	$26	$23	$21	$18	$16	$14	$12	$10	$8	$6	$5	($3)	($8)
$9.50	$27	$24	$22	$20	$17	$15	$13	$11	$9	$8	$6	($1)	($7)

Notes: Net public costs include public COI savings, although these savings are not readily convertible into cash for funding vaccination programs. Public COI savings were calculated with herd protection effects.

The last three columns of Table 5.8 show three cost recovery (i.e. revenue-neutral) typhoid vaccination programs. The first, which targets only children and would not make vaccinations available to adults, would require a user fee of $2.32, or Rs.105 ($C^{\$2.32}$). At this price, we expect that parents in Tiljala who hear about the program would vaccinate 35% of their children, preventing 208 cases. Because the total number of vaccinations is small (~10,400), the average cost per child is fairly high (US$2.52) because of fixed costs. The next revenue-neutral program would make vaccines available to adults as well as children with a fee of US$1.75, or Rs. 80 ($M^{\$1.75}$). This program is much more attractive than targeting only children, reducing 75% more cases than $C^{\$2.32}$ but still achieving revenue-neutrality.

The last program (M^{cross}) sets adult prices higher than the full cost-recovery price in order to cross-subsidize vaccines for children. Because of the cost of the vaccine and the size of adult demand, it is not possible to fully cross-subsidize vaccines for children: user fees for children must be larger than zero. Table 5.9 reports the net public costs of typhoid vaccination programs for various combinations of adult and child user fees, and shows that child fees must be at least US$0.5. We examined a number of revenue-neutral price combinations from Table 5.9, and found that a child fee of US$0.65 and an adult fee of US$3 reduced the most cases and still maintained revenue-neutrality. Even though fewer people overall are vaccinated in M^{cross} than $M^{\$1.75}$, M^{cross} reduces slightly more cases because more of the vaccinations are in children who have higher incidence.

5.6 Comparison and Discussion

If the decision criteria were simply to maximize the number of cases avoided without a revenue constraint, then a mass program without user fees (M^0) would be optimal. The analysis above suggests that such a program is likely to pass a social cost-benefit test. Because health budgets are so limited, though, financing issues must be considered. If the criterion is to minimize public sector expenditure, then the three revenue-neutral programs ($C^{\$2.32}$, $M^{\$1.75}$, or M^{cross}) would be preferred. If

the objective was to maximize the number of cases avoided subject to a revenue-neutrality constraint, then the cross-subsidy program M^{cross} would be the best option. Another objective might be to maximize social net benefits. Because the VSL+COI net benefits are proportional to the number of cases avoided, M^0 would again be optimal. Three programs produce roughly the same WTP net benefits ($M^{\$0.89}$, $M^{C\$0,A\$2.2}$, and $M^{\$1.75}$), although the revenue requirements varied widely, from revenue-neutral to US$38K.

On balance, a program targeting children, especially school children, looks like a good investment, and a strong argument could be made for providing them with vaccines for free (C^0) because incidence is much higher than in adults. On ethical grounds, however, adults should also have the opportunity to protect themselves from typhoid. The government might do this by encouraging provision in the private market (and providing some support in disseminating information on the benefits and availability of typhoid vaccines). It might also do this by providing typhoid vaccines in public clinics and hospitals at the full cost of providing them. This is precisely what program $M^{C\$0,A\$2.2}$ does, avoiding even more cases than C^0 at a slightly lower net public cost (see Figure 5.3)

We suspect, though, that the health ministry would find investments in any number of other health interventions more appealing, and a revenue-neutral program which cross-subsidized vaccines for children looks best. It is worth noting, however, that savings from public sector treatment costs cannot easily be converted into cash to fund vaccination programs. We have assumed throughout that policymakers would consider public COI savings in their calculation of revenue neutrality. They may not. Furthermore, it is possible that even our most conservative demand estimates from the contingent valuation study are too high, and demand for adults may not materialize. If this were the case, revenues from adults would not be sufficient to cross-subsidize the cost of running the program for children. The financial risk to the government of adult demand not materializing is about US$21,000. To maintain revenue-neutrality, user fees for children would then have to be increased, which might be difficult.

To account for this risk, I would recommend that the government charge adults the *expected* revenue-neutral price of US$3 but charge children a fee somewhat larger than the expected revenue-neutral price of US$0.65 (perhaps US$1.1, or about Rs. 50). After distributing vaccines with this pricing structure for 3 years, the government could assess whether actual demand is similar to that predicted from the CV study and whether public COI savings are as expected. If so, it could then reduce the price for children towards US$0.65. If adult sales were much larger than expected, it might even reduce the price for children lower than US$0.65.

CHAPTER 6

RESULTS – CHOLERA VACCINATION PROGRAMS

6.1 Baseline burden of cholera disease

As in the typhoid case, we apply the incidence rates observed in Narkeldanga to Tiljala, giving the expected annual burden of cholera in Tiljala (Table 6.1). Because cholera incidence rates are highest in young children (see Table 4.1), cases in the two youngest age groups (<5 yrs) account for 37% of all cases even though they are only 9% of the population. Assuming that 0.75% of cholera cases are fatal, we estimate that cholera causes approximately 1.5 deaths each year in Tiljala, resulting in a loss of 42 life-years. An episode of cholera from which an individual recovers is even shorter than typhoid fever, lasting at most a few days. As such, the DALY burden (row 4) again mostly reflects mortality rather than morbidity losses. We estimate that cholera costs the public sector approximately US$7,000 in treatment costs annually, and costs the 205 patients who contract cholera about US$1,200 in direct and indirect private costs.

Table 6.1 Baseline annual burden of cholera in Tiljala

		Infants (<1yrs)	Young children (1-4.9yrs)	School-age children (5-14.9yrs)	Adults (15+)	All Ages
(1)	Expected number of cases	16	59	51	79	205
(2)	Expected number of deaths	0.12	0.44	0.39	0.59	1.54
(3)	Expected number of life years lost[a]	4	13	11	14	42
(4)	Expected number of DALYs lost[a]	4	13	11	14	43
(5)	Expected public COI (US$)	$242	$882	$771	$1,266	$3,161
(6)	Expected private COI (US$)	$85	$312	$272	$514	$1,184

[a] Life years discounted at 3%

6.2 Would a cholera vaccination program pass a social cost-benefit test?

Table 6.2 shows the likely consequences of cholera vaccination programs if immunizations were offered with zero user fees. We use the same nomenclature as in the typhoid analysis to distinguish among programs. Unlike the typhoid case, though, we now present two sets of outcomes – one which includes herd protection effects as described in Chapter 4, and one which does not. These are labeled in Table 6.2 and all subsequent tables as "No Herd / Herd". The first number "No Herd" will include cases avoided, benefits, etc. for the targeted age-group only, but the latter will include effects observed in the non-targeted age groups because of indirect protection. Because cholera vaccines have not been proven safe for infants under 1 year old, the only way to reduce cases in this group is through indirect protection.

If the program targeted all age groups (i.e. a mass vaccination program), we expect that about 59,000 people, or half of the entire population of Tiljala would choose to be vaccinated. Without modeling herd protection, we estimate the program would prevent 159 cases and 1.2 deaths over three years. A higher fraction of young children are vaccinated because they have the highest percent coverage with zero fees, and the absolute numbers of cases (and deaths) avoided are also highest in this age group in the absence of herd protection (66 of the 159 total cases avoided).

Incorporating herd protection, however, increases the total number of cases avoided substantially, from 159 to 547. There is substantial herd protection even for programs that target smaller groups. The program targeting only young children (Y^0), for example, only vaccinates 5% of the total population of Tiljala but confers direct protection to the vaccinated children of 72% and indirect protection of 18% to the other 95% of the population (row 5 of Table 6.2). This effect is a product of the herd immunity relationship we developed (see Chapter 4) which assumes that even at 0% coverage, effectiveness for the vaccinated is 67% rather than 50%[25]. The mass program (M^0),

[25] It may also overstate both the direct and indirect protection from the vaccine because both Ali et al (2004) and Longini et al (2007) analyze only data from the first year after the Matlab trial. Effectiveness declines in the second and third years.

with 49% coverage, provides direct and indirect protection of 92% and 85%, and reduces the overall disease burden in the population by 90%.

If the full cost of producing, storing and delivering both doses of the oral cholera vaccine needed to achieve 50% protection were US$10,000 plus a constant marginal cost of US$1.64 per dose ($3.28 per immunized person), a mass campaign without user fees would cost the public sector approximately US$202,000. The government could expect to recoup about US$2,300 of this cost in reduced public sector spending on treating cholera cases. Although this savings rises to about US$7,800 with herd protection, the government cannot expect to save money through cholera vaccination. As with typhoid, it is also clear from Table 6.2 that sum of private and public COI avoided is insufficient to cover the cost of the program. A cholera vaccination program without user fees is unlikely to pass a social cost-benefit test if we use this limited measure of social benefits.

Table 6.2 Effects of cholera vaccination programs with no user fees

			Y^0 Young children (1-4.9yrs)	S^0 School-age children (5-14.9yrs)	C^0 All eligible children (1-15yrs)	M^0 Adults plus all eligible children
(1)	Number of vaccinations (%)		6,250 (74%)	11,130 (47%)	17,379 (54%)	58,650 (49%)
(2)	Cases avoided	*No Herd / Herd*	66 / 183	36 / 219	102 / 338	159 / 547
(3)	Deaths avoided	*No Herd / Herd*	0.5 / 1.4	0.3 / 1.6	0.8 / 2.5	1.2 / 4.1
(4)	DALYs avoided	*No Herd / Herd*	14 / 38	8 / 44	22 / 69	32 / 110
(5)	Probability of protection with herd immunity for vaccinated (unvaccinated)		72% (18%)	75% (30%)	79% (43%)	92% (85%)
(6)	Percent reduction in all-age disease burden from baseline	*No Herd / Herd*	11% / 30%	6% / 36%	17% / 55%	26% / 89%
(7)	Costs of vaccination (US$)		$30,470	$46,460	$66,940	$202,137
(8)	Average cost per person (US$)		$4.48	$4.17	$3.85	$3.45
(9)	Public COI avoided (US$)	*No Herd / Herd*	$910 / $2,590	$506 / $3,120	$1,420 / $4,800	$2,270 / $7,800
(10)	Private COI avoided (US$)	*No Herd / Herd*	$323 / $950	$179 / $1,160	$502 /$1,775	$845 / $2,900
(11)	Net Public Cost (Total Cost - Revenue - Public COI avoided, US$)	*No Herd / Herd*	$30K / $28K	$46K / $43K	$66K / $62K	$200K / $194K

Notes: Herd protection effects include all age groups, including infants who cannot be safely vaccinated. Life years (and DALYs) discounted at 3%, COI discounted at 8%. The rightmost column (mass vaccination) is not the sum of the other three columns because each column is considered a separate program with fixed costs of US$10,000.

Table 6.3 Cost effectiveness measures for cholera vaccination programs with no user fees

			Y^0 Young children (1-4.9yrs)	S^0 School-age children (5-14.9yrs)	C^0 All eligible children (1-15yrs)	M^0 Adults plus all eligible children
	Total Program Cost					
(1)	Program cost per case avoided	*No Herd / Herd*	$460 / $170	$1,280 / $210	$660 / $200	$1,270 / $370
(2)	Program cost per death avoided	*No Herd / Herd*	$62K / $22K	$170K / $28K	$87K / $26K	$170K / $49K
(3)	Program cost per DALY avoid	*No Herd / Herd*	$2.1K / $0.8K	$6.0K / $1.0K	$3.0K / $1.0K	$6.3K / $1.8K
	Net public cost (Cost - Rev - avoided Public COI)					
(4)	Net public cost per case avoided	*No Herd / Herd*	$450 / $150	$1,260 / $200	$640 / $180	$1,260 / $355
(5)	Net public cost per death avoided	*No Herd / Herd*	$60K / $20K	$168K / $26K	$86K / $25K	$168K / $47K
(6)	Net public cost per DALY avoided	*No Herd / Herd*	$2.1K / $0.7K	$5.9K / $0.9K	$3.0K / $0.9K	$6.2K / $1.8K

Notes: Herd protection effects include all age groups, including infants who cannot be safely vaccinated. Life years (and DALYs) discounted at 3%, COI discounted at 8%.

Table 6.4 Net benefit measures for cholera vaccination programs with no user fees

			Y^0 Young children (1-4.9yrs)	S^0 School-age children (5-14.9yrs)	C^0 All eligible children (1-15yrs)	M^0 Adults plus all eligible children
	Net benefits					
(1)	COI Net benefits (Public COI avoided + Private COI avoided - Total Costs),US$	*No Herd / Herd*	($29K) / ($27k)	($46K) / ($42K)	($65K) / ($60K)	($199K) / ($191K)
(2)	VSL Net benefits (VSL + Public COI avoided + Private COI avoided - Total Costs), US$	*No Herd / Herd*	($18K) / $4.9K	($39K) / ($4.1K)	($47K) / ($1.6K)	($171K) / ($96k)
(3)	WTP Net benefits (WTP benefits + public COI avoided - Total costs), US$	*No Herd*	$9.8K	$31K	$51K	$11K
(4)	BPC Net benefits (BPC benefits + public COI avoided – Total costs), US$	*Herd*	$138k	$155K	$244K	$302K

Notes: Herd protection effects include all age groups, including infants who cannot be safely vaccinated. Life years (and DALYs) discounted at 3%, COI discounted at 8%.

The cost-effectiveness measures presented in Table 6.3 would not seem attractive to many health policymakers. Without herd protection effects, the cost per DALY avoided are US$2100 for the program targeting young children (Y^0), and much higher (US$6000 per DALY) for programs that include adults. None of these would be considered "cost effective" using the cutoff of three times GDP per capita. Incorporating herd protection effects, the cost-effectiveness ratio falls to about US$1,800 per DALY saved for M^0 and US$800 for Y^0. With herd immunity, all programs would be considered "cost effective" using the GDP definition. All ratios improve if public COI savings are included, but are still relatively unattractive from a cost-effectiveness standpoint, even with herd protection (they are in the worst third of interventions in the DCP2, Jamison et al 2006).

All types of programs without user fees fail a benefit-cost test using the COI benefit measure, even with herd protection (Table 6.4). All programs except Y^0 would fail using the VSL + COI measure, although S^0 and C^0 nearly break-even. Using a WTP net benefit measure, all programs would pass, though C^0 has the largest net WTP benefits. WTP net benefits do not change appreciably with herd protection (not shown) because herd protection affects WTP net benefits only through additional public COI savings.

Our fourth benefit measure – benefits per case avoided (BPC) – is a constant benefit per case calculated as the total WTP population divided by the total number of cases avoided if the vaccine worked as described to respondents (50% effective for 3 years without external effects) and the entire population was vaccinated. We estimate this to be on the order of US$907 per case avoided[26]. Adding public COI savings of $15 per case avoided gives a total BPC of approximately US$922. Using this measure, the total social benefits of the mass program are US$922 x 547 cases avoided (with herd protection) ≈ $504,000. Subtracting total costs of the program gives "BPC Net benefits" of $503,000 - $202,000 ≈ $302,000.

[26] This also can be calculated by dividing the population average WTP ($2.3) – not the WTP per vaccinated person – by the risk reduction provided by the vaccine (3 yrs · 50% · incidence of 1.64/1000). BPC = $2.23 / $2.46E^{-03}$ = $907 per case avoided.

6.3 Sensitivity analyses

For any of the programs to break even using the COI net benefit measure (with or without herd protection), incidence or total COI would need to increase by implausible amounts (Table 6.5). Alternatively, average vaccine costs would again have to be an order of magnitude lower: less than $0.60 for both doses with herd immunity (US$0.20 without) for the most attractive program. Even including mortality risk benefits (COI+VSL net benefits), most parameter values would need to change dramatically (two to six times higher) for any of the programs to pass unless herd immunity effects are included. With herd immunity, most programs would produce positive net VSL+COI benefits with only slightly different parameter values. The mass program with adults, however, would still not pass unless costs were approximately half of our best estimates. Using the WTP net benefits measure, total cost could be somewhat higher all programs to still pass.

Table 6.5 Parameter values at which a vaccination program would produce zero net benefits

	Y^0 Young children (2-4.9yrs)	**S^0** School-age children (5-14.9yrs)	**C^0** All eligible children (2-15yrs)	**M^0** Adults plus all eligible children
Net benefits: COI only				
Incidence (scalar)	25x / 8.7x	67x / 11x	35x / 10x	65x / 19x
Total vaccine cost, US$	$0.20 / $0.56	$0.06 / $0.38	$0.12 / $0.38	$0.06 / $0.18
Total (public + private) COI, US$	$500 / 8.7x	$1,400 / 11x	$710 / 10x	65x / 19x
Net benefits: COI + VSL				
Incidence (scalar)	2.4x / 0.86x	6.6x / 1.1x	3.4x / 1.0x	6.6x / 1.9x
Case fatality rate (% of cases)	2.0% / 0.63%	5.4% / 0.83%	2.8% / 0.77%	5.4% / 1.5%
Total vaccine cost, US$	$2.0 / $5.6	$0.64 / $3.8	$1.2 / $3.8	$0.52 / $1.8
VSL (US$)	$64K / $21K	$181K / $28K	$92K / $26K	$180K / $50K
Net benefits: WTP + Public COI				
Total vaccine cost, US$	$6.4 / $6.8	$7.0 / $7.2	$6.8 / $7.0	$3.6 / $3.8
Per capita WTP, US$	0.75x / 0.71x	0.60x / 0.56x	0.56x / 0.53x	0.95x / 0.92x

Notes: For programs with multiple age groups where the parameter has different values in different age groups, the breakeven scalar is shown. A scalar below 1 means that the parameters could decrease and still breakeven (i.e. 0.66 = 66% less). A scalar of 5.6x means that the relevant parameters would need to increase 560% to breakeven. A scalar is also necessary for parameters that differ across age groups when herd immunity is assumed (i.e. even if only young children are targeted for vaccination, the case fatality rate for all age groups will affect benefit measures).

Finally, we allow all of the uncertain parameters to vary simultaneously in a Monte Carlo framework (see the Chapter 5 on typhoid for more details). As with the typhoid case, there is no chance that any of the programs without user fees will pass a social cost-benefit test based only on treatment cost savings. The mean net COI benefits from the programs range from (-US$25K) to (-US$209K), and none of the 10,000 Monte Carlo runs produced net benefits in any of the four programs, with or without herd protection (Table 6.6). Using the VSL+COI net benefits measure, and including herd immunity, however, all programs have a 75% chance or greater that they will produce positive net benefits. Without herd immunity, only Y^0 has better than a 50% chance of passing. Comparing the percent of positive runs for M^0 with and without herd immunity (89% vs. 3%) highlights the large indirect protection effects of a mass program. Again, though, note that the VSL+COI measure is highly sensitive to the case fatality rate. Finally, the probability that S^0 and C^0 will produce net WTP benefits is over 95%, with or without herd immunity. Y^0 has greater than 75% chance with or without herd protection), but only half of the 10,000 simulations were positive for M^0 with herd protection.

Table 6.6. Monte Carlo simulations of typhoid vaccination programs with no user fees, without herd immunity

		Y^0 Young children (2-4.9yrs)	**S^0** School-age children (5-14.9yrs)	**C^0** All eligible children (2-15yrs)	**M^0** Adults plus all eligible children
COI Net benefits					
Mean	*No Herd / Herd*	($28K) / ($25K)	($48K) / ($46K)	($67K) / ($61K)	($209K) / ($200K)
Std dev	*No Herd / Herd*	$3.9K / $4.2K	$7.6K / $7.9K	$9.8K / $10K	$34K / $34K
% positive	*No Herd / Herd*	0% / 0%	0% / 0%	0% / 0%	0% / 0%
VSL + COI Net benefits					
Mean	*No Herd / Herd*	$12K / $108K	($24K) / $45K	($1.9K)/ $163K	($106K) / $165K
Std dev	*No Herd / Herd*	$27K / $84K	$18K / $62K	$33K / $104K	$52K / $145K
% positive	*No Herd / Herd*	59% / 97%	10% / 74%	41% / 98%	3% / 89%
WTP Net benefits					
Mean	*No Herd / Herd*	$7.1K / $9.4K	$29K / $31K	$46K / $50K	($1.6K) / $4.5K
Std dev	*No Herd / Herd*	$8.2K / $8.3K	$18K / $18K	$20K / $20K	$38K / $39K
% positive	*No Herd / Herd*	79% / 86%	96% / 97%	99% / 100%	49% / 55%

In summary, our conclusions about whether a free cholera vaccination program would pass a social cost-benefit test depend critically on whether we incorporate herd immunity effects. Without them, we can be confident only that a program targeting young children would produce net benefits: it passes using either the VSL+COI or the WTP measure, and produces positive net benefits more than 50% of the time when we account for parameter uncertainty. Programs targeting only school children or both groups of children are more difficult to interpret in the absence of herd effects. The VSL+COI measure suggests that both would fail, though C^0 produced positive net benefits in 41% of Monte Carlo runs. On the other hand, our WTP results suggest that any of the three programs targeting children would safely pass, even without herd immunity. Although the program that includes adults produced some positive net WTP benefits with the base case set of parameter values (see Table 6.4), it does not, on average, produce positive net WTP benefits when we incorporate uncertainty, and 51% of model runs produced negative net WTP benefits. It fails badly using either the COI or the VSL+COI measure. After incorporating herd immunity, however, all programs targeting children look to be good investments: they produce positive net benefits using either the COI+VSL or WTP measure. Even the mass program with adults produces average positive net VSL+COI benefits when we account for uncertainty.

6.4 Cholera vaccination programs with user fees

Because the cost of the cholera vaccine is almost twice as much as the typhoid vaccine and has less attractive cost-effectiveness ratios (even with herd immunity), it seems even less likely that a free targeted- or mass-vaccination program would be attractive to Indian health policymakers or donors. As with typhoid, we now examine cases where cholera vaccines would be still made available to people in Tiljala, but with user fees where the level of subsidy varies.

Figure 6.1 Program possibility frontier for a mass cholera vaccine program (M).

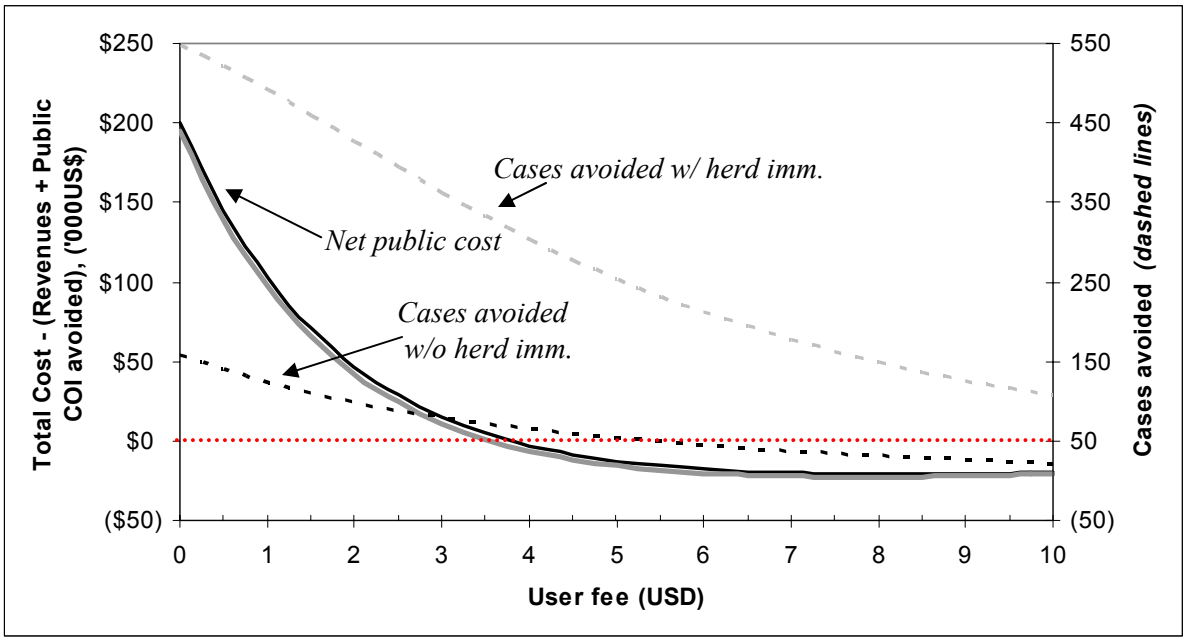


Figure 6.1 again shows the principal tradeoff between public sector cost vs. cholera cases avoided. Note that the net public costs are not much different with herd protection (the solid gray line) or without it (the solid black line) because herd protection only affects net public revenues through avoided public sector treatment costs, which are a small percent of the total costs. With a user fee of US$3.55, a mass program would be revenue-neutral, raising enough revenues to cover program costs[27]. If all users were charged the revenue-neutral price of US$3.55, the program could expect to prevent about 329 cases with herd immunity (71 cases without). As the user fee decreases (moving right to left), the public sector revenues decrease (i.e. expenditures increase) but so do cases avoided. At a user fee of zero, this graph shows the results for M^0 discussed above: the program would cost about $202,000 but prevent 547 cholera with herd protection, 218 more than the revenue-neutral program. As with typhoid, the marginal cost per case avoided increases as user fees approach zero (Table 6.7).

[27] With herd immunity effects. Ignoring herd effects would decrease the public COI savings (from fewer cases avoided), and raise the expected revenue-neutral user fee to US$3.80.

Table 6.7 Marginal reductions in the subsidy level for a mass cholera vaccination program

Moving from fee of $X to $Y	Comes at an addt'l public sector cost of… ('000 US$)	But prevents an addt'l _____ cases (*without / with herd protection*)…	Public sector cost per case (*without / with herd protection*)
$3.55 → $3.30	$4,626 / $4,467	3.7 / 14.8	$1,247 / $302
$3.30 → $3.05	$5,350 / $5,189	4.0 / 15.2	$1,350 / $341
$3.05 → $2.80	$6,180 / $6,017	4.2 / 15.6	$1,458 / $385
$2.80 → $2.55	$7,130 / $6,967	4.5 / 15.9	$1,571 / $437
$2.55 → $2.30	$8,219 / $8,057	4.9 / 16.2	$1,689 / $497
$2.30 → $2.05	$9,466 / $9,307	5.2 / 16.4	$1,812 / $569
$2.05 → $1.80	$10,894 / $10,739	5.6 / 16.4	$1,940 / $654
$1.80 → $1.55	$12,529 / $12,382	6.0 / 16.4	$2,074 / $757
$1.55 → $1.30	$14,401 / $14,263	6.5 / 16.2	$2,212 / $883
$1.30 → $1.05	$16,543 / $16,418	7.0 / 15.8	$2,355 / $1,039
$1.05 → $0.80	$18,994 / $18,885	7.6 / 15.3	$2,503 / $1,234
$0.80 → $0.55	$21,799 / $21,708	8.2 / 14.6	$2,655 / $1,483
$0.55 → $0.30	$25,007 / $24,938	8.9 / 13.8	$2,812 / $1,803
$0.30 → $0	$34,895 / $34,845	11.7 / 15.3	$2,991 / $2,273

Table 6.8 again illustrates the possibilities for cross-subsidizing child vaccinations with adult sales through differential pricing. Given our estimates for the shape of the demand functions, there is no way to subsidize child vaccines below a user fee of about US$3, only US$0.50 less than the full cost-recovery price. Furthermore, even though incidence is higher in children, subsidizing vaccines for children (while still maintaining revenue-neutrality) does not reduce more cases than a program that charges both age groups the same price because of herd immunity effects[28]. For these reasons, we do not examine revenue-neutral cross-subsidy programs.

Also, we do not examine user fee programs that target only children, but assume that cholera vaccines will always be available to adults in Tiljala with a cost-recovery user fee. This is important not only for ethical reasons mentioned in Chapter 5 for typhoid, but also because adult vaccinations induce more herd protection and reduce average costs.

[28] In fact, because adults are a larger fraction of the population than children, the model results indicate that cross-subsidizing vaccines for adults (with higher fees for children) would actually increase the number of cases avoided. This is because the herd immunity effects are not sensitive to the age of the vaccinated person, and reducing fees for adults increases the overall population coverage rate faster than for children, inducing more indirect herd effects. We doubt such a program would be attractive to policy-makers.

Table 6.8. Net public costs ('000US$) of a mass campaign under various combinations of adult and child user fees

Adult user fee \ Child user fee	$0.00	$2.00	$3.00	$3.10	$3.20	$3.30	$3.40	$3.50	$3.60
$0.00	$194	$154	$141	$140	$139	$137	$136	$135	$134
$1.00	$120	$80	$67	$66	$65	$64	$63	$62	$61
$2.00	$82	$42	$29	$28	$27	$26	$25	$24	$23
$3.60	$58	$19	$5	$4	$3	$2	$1	$0	($1)
$3.80	$57	$17	$4	$3	$2	$1	$0	($1)	($2)
$4.00	$56	$16	$3	$2	$1	$0	($1)	($2)	($3)
$4.20	$55	$16	$3	$1	$0	($1)	($2)	($3)	($4)
$4.40	$55	$15	$2	$1	($0)	($1)	($2)	($3)	($4)
$4.60	$54	$14	$1	$0	($1)	($2)	($3)	($4)	($5)
$4.80	$54	$14	$1	$0	($1)	($2)	($3)	($4)	($5)
$5.00	$54	$14	$1	($0)	($1)	($2)	($3)	($4)	($5)
$5.20	$54	$14	$1	($0)	($1)	($2)	($3)	($4)	($5)
$5.40	$53	$14	$1	($0)	($1)	($2)	($3)	($4)	($5)
$5.60	$54	$14	$1	($0)	($1)	($2)	($3)	($4)	($5)
$5.80	$54	$14	$1	($0)	($1)	($2)	($3)	($4)	($5)
$6.00	$54	$14	$1	($0)	($1)	($2)	($3)	($4)	($5)
$7.00	$55	$15	$2	$1	$0	($1)	($2)	($3)	($4)
$8.00	$56	$17	$4	$3	$1	$0	($1)	($2)	($2)

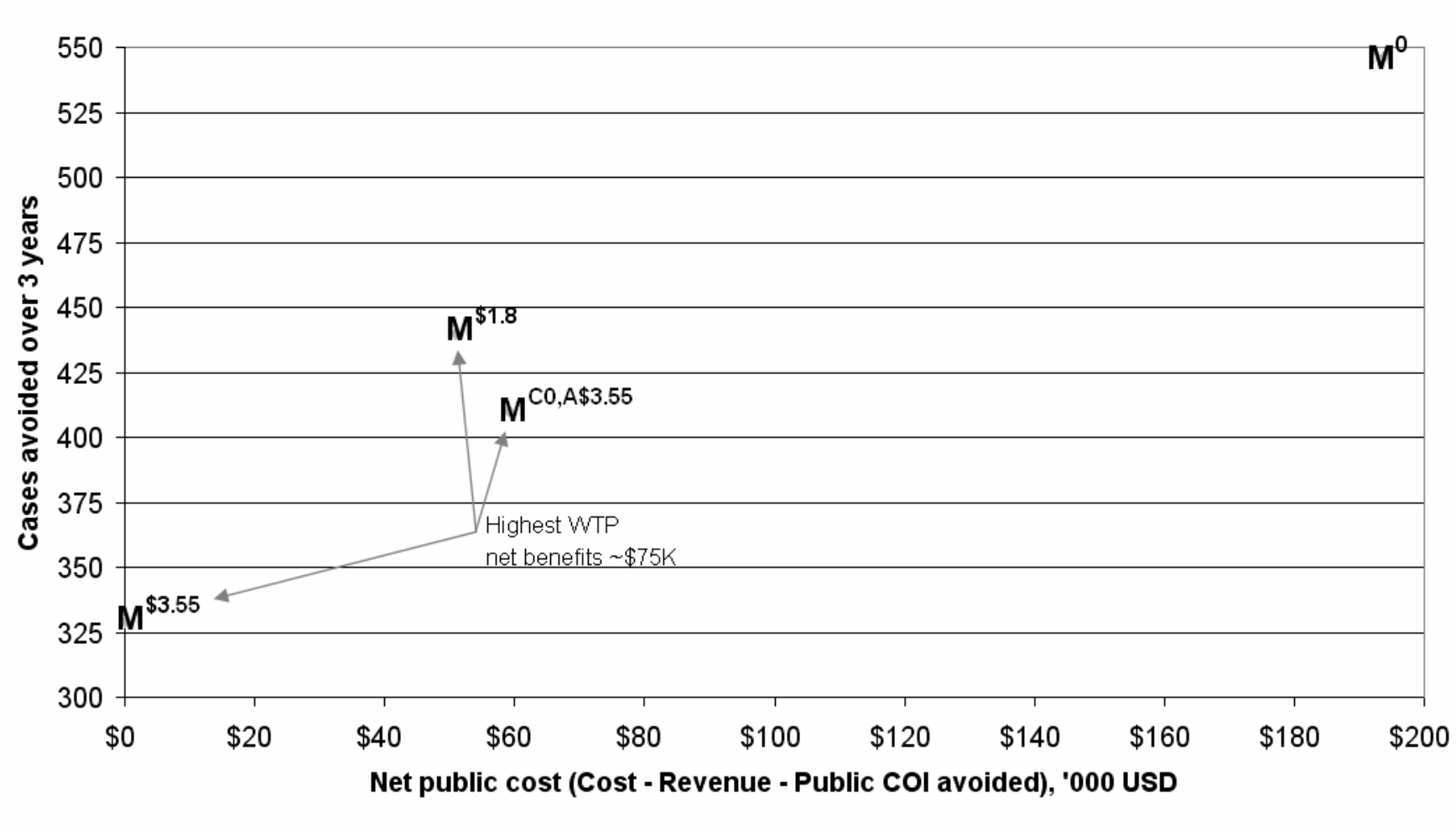
Notes: Net public costs include public COI savings, although these savings are not readily convertible into cash for funding vaccination programs. Public COI savings were calculated with herd protection effects.

We examine several programs in Table 6.9 in addition to M^0. Program ($M^{C\$0,A\$3.55}$) would provide cholera vaccines to children for free but charge adults the full cost of US$3.55 (Rs.160). The second program ($M^{\$1.8}$) would ask both children and adults to pay approximately half the full cost of vaccination. The last program ($M^{\$3.55}$) is revenue-neutral and charges a uniform user fee of US$3.55. All scenarios assume herd protection effects.

Table 6.9 Effects of cholera vaccination programs with and without user fees, assuming herd protection

				Cost recovery program	
		M^{0}	$M^{C\$0,A\$3.55}$	$M^{\$1.8}$	$M^{\$3.55}$
(1)	Child user fee	$0	$0	$1.8	$3.55
(2)	Adult user fee	$0	$3.55	$1.8	$3.55
(3)	Number of vaccinations	58,650	26,034	31,952	18,848
(4)	Cases avoided	547	410	440	329
(5)	DALYs avoided	110	83	89	67
(6)	Costs of vaccination	$202K	$95K	$115K	$65K
(7)	Average costs per person	$3.45	$3.66	$3.59	$3.81
(8)	Public COI avoided (US$)	$7.8K	$5.8K	$6.3K	$4.7K
(9)	Total Cost - Revenue - Public COI avoided	**$194K**	**$59K**	**$51K**	**$0.1K**
(10)	Total COI avoided – Total Costs[a]	($191K)	($87K)	($106K)	($65K)
(11)	Total COI avoided + (VSL * deaths avoided) - Total Costs[a]	($96K)	($16K)	($30K)	($8.0K)
(12)	WTP benefits + Public COI avoided – Total costs[a]	($17K)	$77K	$72K	$75K

Figure 6.2 Comparison of cholera vaccination program options for Tiljala, assuming herd immunity effects



6.5 Comparison and Discussion

Investment in free cholera vaccinations do not seem to be a particularly wise investment for Tiljala. Even in an area with relatively high incidence, there are still only 205 cases each in year in a population of 120,000. At US$3-$4 per person, the vaccine is relatively expensive and not very effective, although incorporating potential indirect protection from herd immunity dramatically increases the number of cases avoided. A mass program without user fees and other subsidized programs would come at a significant public cost. Put another way: if the per capita spending on health in India were doubled in Tiljala, the funding increase would be almost entirely consumed by subsidies for cholera vaccines. Revenue-neutral programs, on the other hand, require user fees set high enough that only about 16% of the population would choose to be vaccinated. Although this would reduce fewer cases than a program without user fees (330 cases vs. 547 cases), the reduction in disease burden (with herd immunity) is still substantial. I feel this would be the best option. The government should provide vaccines at their full cost (no public subsidy), or encourage provision of vaccines through private market channels.

CHAPTER 7

SUMMARY

In evaluating vaccine investments for Tiljala, there are three key questions that summarize our results and conclusions. First, would a program that provided the vaccines for free pass a social cost-benefit test? The answer for typhoid vaccines in Tiljala is yes. We feel confident that programs targeting either all children or even all adults and children would produce positive net benefits. This is true using either the VSL+COI measure or our WTP estimates, in which we have a greater degree of confidence.

The answer for cholera vaccines is more nuanced. Using our WTP estimates, programs targeting school-aged children or all children would pass. Our average estimates of adult WTP are almost exactly equal to the expected full cost of providing the vaccine, so providing free vaccines to adults would just barely pass with the VSL+COI measure. No programs (except Y^0) would produce net COI or VSL+COI benefits, even accounting for herd protection effects. However, if parameter uncertainty is accounted for in a Monte Carlo framework and we include herd effects, there is a high probability that programs targeting school children or all children would pass with this measure. Finally, all programs would pass using our benefits per case avoided (BPC) approach with herd immunity. Because this is a novel approach at valuing the vaccine's benefits to the unvaccinated (and is therefore untested in the literature), we place less emphasis on this approach.

Second, would the vaccination program be a wise use of limited public health resources? The answer for both vaccines is no. Cost-effectiveness ratios for typhoid programs were at best $350 per DALY avoided, and as high as $910 per DALY avoided. Although the programs targeting school children or all children would be considered "highly cost-effective" using a standard comparison with per capita GDP, there are a large number of health investments with much more favorable cost-

effectiveness ratios that should receive higher priority in allocating health subsidies. The ratios for cholera vaccines are even worse, although the three programs targeting children (without user fees) would be "cost effective" using the GDP standard if herd effects are accounted for . Without herd immunity they range from $2,100 to $6,300 per DALY avoided, and even with herd protection they are never below $800 per DALY.

Third, is a financially self-sufficient vaccination program in Tiljala practically possible? We believe the answer is yes based on our private demand studies, though again we have more confidence in a financially self-sufficient typhoid program. Although demand for cholera vaccines for children is higher than demand for typhoid vaccines for children (demand for adults is somewhat similar), the cholera vaccine has a much higher average cost. To achieve revenue-neutrality, the user fee for a cholera vaccine would need to be in the range of US$3.6, driving down demand to where only about 16% of the population would be vaccinated. If this demand does not materialize, the public sector would face a loss of the fixed costs sunk into the program. On the other hand, the cost of providing the cholera vaccine may be lower than observed in the Kolkata cholera vaccine trial, or private demand may be higher than our study indicates, and a financially sustainable program may well be possible.

There are several caveats to the analysis. First, the most important source of uncertainty is in vaccine costs. We feel confident that we've used the best data available to us and adjusted estimates downwards to account for the fact that the vaccine trials in Kolkata included some research-related costs. If the vaccine could be produced and delivered at a lower cost than we assume, however, the programs might be more attractive investments.

Second, our analysis is sensitive to our extrapolation of epidemiological data from the Narkeldanga neighborhood to Tiljala. Incidence may in fact be lower in Tiljala than Narkeldanga, though it may also be higher. This points more generally to a warning to the reader in extrapolating our results and conclusions to other areas in Kolkata or to India as a whole. Incidence is almost certainly lower in most other areas of Kolkata (with the exception of Narkeldanga), though private

demand may be higher because of higher incomes. Similarly, typhoid incidences are likely to lower in most places in India, although our typhoid results could be broadly applicable to other crowded slums in major Indian cities (one would first want to compare typhoid incidence (if available) and average incomes in the slum). Because of the epidemiology of cholera, most Indian cases are localized to just a few endemic areas (namely West Bengal) and would not be applicable to many other urban slums in India.

There are also opportunities for further research. First, we used a static, one-period model. In reality, vaccinations would need to occur every three years to maintain protection. This could be accomplished with a campaign-based approach every three years, or by incorporating programs into routine vaccination schedules (if programs only targeted children). Over time, as the program reduced incidence, one would expect that private demand for the vaccines might also decrease (so called "prevalence elasticity"). For these reasons, a multi-period model would be a useful extension to our approach, although one would need to estimate prevalence elasticity. This is not known for either disease.

Our herd immunity relationships were admittedly curve-fitting exercises, and a second useful extension would be to imbed our demand relationships within a more robust epidemiological model of cholera transmission. This might highlight the benefits of preferential vaccination for certain groups (most likely children) because of their higher disease transmission rates. This preference could be given in targeting free programs, or by finding the optimal public subsidies (to the full cost user fee) which induce the a socially-optimal vaccination mix.

APPENDIX A: Detailed Literature Review

Economic evaluations of vaccine programs

Economic evaluation studies of vaccines are common (see Walker and Fox-Rushby (2000) for a review of vaccine economic evaluations in developing countries). These studies typically limit themselves, however, to fairly simplistic analyses. The simplest studies take the perspective of the public sector or health care provider (for recent examples, see Uzicanin et al (2004), Allsup et al (2004), and Salo et al (2005)). They estimate the public sector treatment costs per case (hospital visits, medical care, drugs, etc.), estimate the disease burden (number of cases) and the potential reduction in cases as a result of vaccination. Comparing this with the estimates of the vaccination program cost, they calculate cost-effectiveness ratios (cost per case avoided, cost per death avoided, or cost per DALY avoided) and determine if the vaccination program is likely to actually produce public sector costs savings.

The next level of complexity attempts a social perspective by including some benefits that accrue to individuals. Here the analyst includes the patient's financial outlays for treatment (direct medical costs) with the public sector treatment costs, and calculates the reductions in these costs as a result of the vaccination program. These may also include economic (non-financial) costs of time spent ill (and not working), the costs of substitute labor (the opportunity cost of the person filling in for the sick person at the sick person's job), or the time costs of caretakers. Time is typically valued at some average wage in the local economy. The private benefits of the vaccine to someone in the general population is therefore a probabilistic one: the total private costs of being ill (the "*ex post*" cost of illness) multiplied by the probability of contracting the disease. (This is sometimes called the "*ex ante*" costs of illness). Recent examples of this type have been conducted for global rotavirus (Podewils et al. 2005), influenza in the US (Pisu et al. 2005), pneumococcal 7-valent vaccine in Spain

(Navas et al. 2005), pertussis in the US (Lee et al. 2005, Hay and Ward 2005)), varicella in France and Germany (Coudeville et al. 2005), and pediatric dengue in Asia (Shepard et al. 2004).

Though an improvement, this latter approach has several flaws. First, it misses at least three benefits that accrue to individuals. For fatal diseases (like cholera and typhoid fever), vaccine also reduce an individual's risk of dying. Vaccines also reduce the pain and suffering caused by contracting the illness, a benefit which is not captured in direct medical expenditures and the time spent ill valued at average wages. Households may also spend money on averting behaviors (i.e. boiling or treating water) which are not captured in cost-of-illness estimates.

Second, this framework is problematic for children. Parents may well value protecting their children from the disease more than themselves (though this is an empirical question and hardly obvious, since parents may find it more important to protect themselves from the potential loss of family income). The productivity approach outlined above would require assigning a wage rate to young children, and in practice the wage rates for children are often presented as some fraction of adult wages. Third, this approach misses larger macroeconomic benefits that may accrue to society as disease incidence falls (for example: increased labor productivity, fewer school days missed for children, increased tourism, etc, see Bloom et al. 2005). Finally, it assumes individuals are risk-neutral expected-utility maximizers. Risk-averse individuals may prefer a vaccine which costs more than the expected cost of contracting the disease. This may be particularly true in developing countries where individuals may lack access to a full range of insurance products.

These studies typically miss two additional benefits of vaccine programs. First, they do not account for antibiotic resistance. As is the case with typhoid fever (see above), resistance increases private and public medical expenditure, increases the number of cases that require expensive hospitalization, and lengthen the duration of illness. As the medical and non-medical cost of cases increases, the benefit of vaccines in preventing cases increases. Vaccines also have the potential to slow the spread of antibiotic resistance by decreasing the number of hosts and possibilities for mutation, though this is also far from obvious. Vaccines may in fact increase the evolutionary

pressure on organisms to mutate to acquire resistance or increase in virulence. Second, most economic evaluations of vaccine programs do not account for the positive externality of vaccination, the so-called "herd immunity" effect. This will be discussed in more detail below.

Stated preference studies (contingent valuation or stated choice) attempt to capture a fuller picture of the private benefits of vaccination by asking respondents hypothetical questions about their willingness-to-pay for a certain vaccine[29]. When respondents answer these questions, the researcher assumes the individual is including not only the benefit of reducing the *ex-ante* costs of illness for herself and her children, but also the reduction in risk of dying and pain and suffering. Stated preference studies are now routinely done in fields of transport, marketing, and the environment (and others), but in the next section I will focus my review on the existing stated preference studies of demand for vaccines.

Stated preference studies on vaccines

Two of the earliest stated preference studies for vaccines asked adult respondents about demand for hypothetical vaccines against HIV/AIDS in Mexico (Whittington et al. 2002) and against malaria in Mozambique (Whittington et al. 2003). Both studies used contingent valuation (the malaria study used a referendum price approach and the HIV study used payment cards[30]) and both asked about demand for the adult respondents themselves, not for family members. Similarly, Bishai

[29] One might prefer, of course, a market study of demand for vaccines where the benefits (in the form of Marshallian consumer surplus) would be directly observable. We know of no published studies on the market demand for vaccines, and such studies are generally infeasible in settings (like ours) where countries have a tradition of providing vaccines for free and there is considerable resistance to user charges.

[30] In a referendum price approach, each subsample is asked about only one price – "if the vaccine cost $X, would you buy it for yourself?", and price responses (and WTP calculations) are built on comparing response probabilities across subsamples. In the payment card approach, a large range of prices is listed on a card that is shown to respondents. Starting with the lowest price, the interviewer asks the respondent if she is completely sure she would pay that amount, completely sure she would NOT pay that amount, or not sure whether or not she would pay. If she is completely sure, the interviewer repeats the question for the next highest price. This continues until the respondent identifies a price which she is not sure she would pay. The interviewer then moves to the highest price (or vice versa if he started with the highest price and moved down) and repeats the exercise. If the respondent is completely sure she would NOT pay, he repeats the question with the next lowest price. This continues until the respondent identifies a price is she not sure she would pay. This approach provides an upper and lower bound on WTP for each respondent and an interval over which the respondent is uncertain.

et al (2004) used a referendum price approach to ask respondents in Uganda about demand for an HIV/AIDS vaccine for themselves.

In contrast, Cropper et al (2004) was the first to elicit household demand for vaccines: the authors asked respondents in Ethiopia about the total number of malaria vaccines they would purchase for their household at a given price. A similar study in Thailand for HIV/AIDS vaccines (Whittington et al. 2006[31]) asked respondents about household demand, but interviewed different members of the household to investigate whether husbands and wives had different preferences for vaccines for themselves and their children.

Only two studies measure private demand for vaccines using a choice modeling, or stated choice, approach. Cook et al (2006) asked 400 respondents in Hue, Vietnam to choose between two vaccine alternatives and an opt-out where the vaccine attributes included disease (cholera or typhoid), effectiveness, duration, and price. Hall et al (2002) were primarily interested in predicting uptake rates of varicella (chickenpox) vaccine among Australian children rather than estimating the private benefits/WTP of vaccination. Using a relatively small sample size (n= 50), they modeled responses with a mixed logit model and found that higher prices, the presence of severe or mild side effects, and lower effectiveness decreased the probability that parents would vaccinate their children. The location of vaccination (school versus at an early childhood clinic) did not influence the probability of vaccination. Interestingly, they also found a lack of free riding on the positive externality of vaccination: parents were in fact *more* likely to immunize their children when most other children had also been vaccinated, perhaps because they believed that not immunizing their child violated some type of social contract. Table 3.2 summarizes all of the studies listed above.

[31] Results of respondent demand only were reported separately in Suraratdecha et al. 2005.

Table 1. Summary of studies measuring private benefits of vaccination using stated preference methods

Authors	*Vaccine*	*Site*	*Respondent or Household demand?*	*Methods Used*
Whittington et al (2002)	HIV/AIDS	Guadalajara, Mexico	Respondent	CV (Payment card)
Hall et al (2002)	Varicella (chickenpox)	Sydney, Australia	Asked respondents about their children	Stated choice/choice modeling
Whittington et al (2003)	Malaria	suburban Mozambique	Respondent	CV (Referendum price)
Cropper et al (2004)	Malaria	rural Ethiopia	Household	CV (Referendum price)
Bishai et al (2004)	HIV/AIDS	Uganda	Respondent	CV (Referendum price)
Suraratdecha et al (2005) and Whittington et al (2006)	HIV/AIDS	Thailand (eight provinces + Bangkok)	Respondent (Suraratdecha et al 2005) and household (Whittington et al 2006)	CV(Referendum price)
Cook et al (2006)	Cholera, typhoid fever	Hue, Vietnam	Respondent	Stated choice/choice modeling
Canh et al (2006)	Typhoid	Hue, Vietnam	Respondent and household	CV (Referendum price)

Review of economic evaluations of cholera vaccines

Five studies have used economic tools to evaluate cholera vaccines; because these are so directly relevant to this proposal I will discuss them in some detail (Table 3.3 summarizes the studies). MacPherson and Tonkin (1992) used a decision analysis framework to evaluate the cost-effectiveness of vaccinating North Americans traveling to cholera endemic areas. They evaluated a whole-cell killed vaccine which was 50% effective (assuming a total cost per fully immunized person[32] of Canadian$28 in 1992), incorporated the possibility of adverse reactions to the vaccine, assumed a traveler had a 1 in 500,000 chance of contracting cholera, and assumed someone sick with cholera had a 1% chance of dying. They did not attempt to quantify the public sector or private/social

[32] Because vaccine costs include the cost to produce, store, transport and deliver the vaccine, and because many vaccines require more than one dose, I will try to consistently use the term "cost per fully immunized person" or "cost per FIP" to denote the full economic costs of providing all of the needed doses of the vaccine to one person.

benefits of a vaccination program, but rather simply presented the cost per case avoided. They found that preventing one case in travelers cost C$28 million, and recommended that travelers not be vaccinated. Citing the outbreak occurring at that time in Peru (with incidence rates of 2 in 100 in some areas), they acknowledged that the vaccine might be cost-effective for some travelers to very high risk epidemic areas (the cost per case avoided dropped to C$2867).

Naficy et al (1998) compared several different strategies for controlling cholera epidemics in a hypothetical refugee camp in sub-Saharan Africa: pre-emptive treatment set up at inception of the camp; reactive treatment set up after an outbreak is identified; pre-emptive vaccination with a whole-cell killed vaccine; reactive vaccination; and various combinations of these four strategies. Again, this study made no attempt to monetize the vaccine's benefits. They find that the most cost-effective strategy (i.e. lowest cost per case avoided or death avoided) is pre-emptive treatment. Adding pre-emptive would only become more cost-effective than treatment alone if the cost per delivered dose fell below US$0.16 per dose (or US$0.32 per full immunized person).

Murray et al (1998) also examined the cost-effectiveness of the whole-cell killed vaccine in a hypothetical refugee population as well as a location with endemic cholera, and compare it with a treatment strategy and a theoretical water and sanitation improvement. They find that combining a treatment strategy with water and sanitation improvements is the most cost-effective strategy. Adding vaccination as a strategy improves the cost-effectiveness only if the vaccine costs less than US$0.38 per dose (US$0.76 per FIP). Similarly, Sack (2001) used a very simple approach and little data to conclude that a whole-cell killed cholera vaccine would be cost-effective if it could be produced for under US$0.40.

Only one study attempted to monetize the benefits of vaccination. Cookson et al (1997) evaluated the possible use of the live oral vaccine (CVD 103-HgR) in Argentina. Although labeled a "cost-benefit" study, the authors' analytical perspective was financial; they included only avoided direct costs incurred by the government as benefits. The authors use estimates of direct medical costs from a 1991 outbreak in Argentina that averaged US$602 per case, and find that a vaccine that was

75% effective for 3 years and cost US$1.50 per FIP would be cost-saving from the government's perspective. There are several reasons that these results may have limited generalizability. First, the public treatment cost estimates seem quite high, even for a middle income country like Argentina. The total costs of US$602 per case were comprised of: direct medical costs of US$228, hospitalization costs were US$113 per case (US$67 per hospitalized day, with an average case requiring 2.9 days of hospitalization), and "managerial costs" (which included bimonthly helicopter trips for medical staff to the remote outbreak site) comprising most of the rest (about US$244 per case). Second, the authors assume unrealistically low vaccination program costs. For example, although "managerial costs" in treating a case which lasted 1.9 days was US$244, the salaries for vaccination staff are assumed to be far lower -- US$15 per day[33]. They assume that staff can record and administer a vaccine every 45 seconds, and cite no basis at all for the vaccine production costs of US$1.25 per dose (recall that the CVD vaccine requires only one dose). Also, the authors assumed the vaccine was 75% effective for 3 years, though the evidence for this seems weak[34]. In summary, although one might point to this study as universal justification for the economic attractiveness of cholera vaccines, there is simply no evidence to suggest that governments in poor countries like India spend anywhere near US$600 on each case of cholera or diarrheal disease, nor any evidence that they could provide a vaccine for $1.50 per fully immunized person.

Before moving on, it is worth noting several things about these studies. First, four of the five studies are hypothetical, using data compiled from other sources and areas to make a generalized case for cholera vaccines. Only the Cookson study evaluates the vaccine in an actual site, using on-site data, though that study is likely to be of little applicability to poorer countries like India, Bangladesh or Mozambique. Second, assumptions about vaccine costs vary dramatically. Third, none account

[33] The total salary bill for vaccination over 3 years is assumed to be US$11,000, though total managerial costs over the three years of outbreaks was US$816,752.

[34] Acosta et al (2004) cite a study showing that the CVD-103HgR vaccine provided very poor protection against cholera, and the study which Cookson et al cite evaluated effectiveness only up to six months. They base the assumption that the vaccine would protect for 3 years on data on infection-derived immunity (i.e. immunity acquired from actually contracting cholera).

for herd immunity effects. Finally, none of these studies take a social perspective. With the exception of Cookson, they find that cholera vaccines are less cost-effective (or not cost-effective at all, measured against an arbitrary cutoff) than treatment, though there is no attempt to quantify the difference in welfare that an individual experiences in contracting cholera with successful treatment versus preventing the case altogether.

Table 2. Summary of cholera economic evaluation studies

Study	Vaccine type	Perspective	Setting	Key assumptions	Conclusions
MacPherson and Tomkin (1992)	Whole-cell killed, 50% effective	Cost-effectiveness	North American travelers	Incidence 1/500K, CFR 1%, Vaccine Cost C$28	C$28 million per case avoided, not recommended for travelers unless incidence increases to 1/200
Cookson et al (1997)	Live CVD 103-HgR, 75% eff for 3 years	Financial	Argentina	Medical costs per case US$602, Incidence 2.5/1000, Vaccine cost US$1.50	Vaccination program would be cost-saving from public sector financial perspective
Naficy et al (1998)	Whole cell killed; 80% eff for first 6 months, 50% 6mos – 2 years	Cost-effectiveness	Hypothetical refugee camp	Vaccine cost $1.00; Pr[outbreak]= 80%; incidence if outbreak = 37/1000	Setting up treatment facilities at inception of camp most cost-effective strategy; could be supplemented with vaccination if cost <US$0.22 per dose
Murray et al (1998)	Whole cell killed; 50% eff for children and 70% eff for adults for 1 yr	Cost-effectiveness	Hypothetical refugee camp and endemic areas	Incidence 8/1000 in outbreak, 0.3 – 3/1000 in endemic; vaccine cost US$6.3 (epidemic) or US$5.2 (endemic) per immunized person; outpatient COI US$4.7 per case; hospital COI $47 per case; W&S improvements US$12 per person per year, reduce cholera	Combining treatment with water and sanitation improvements most cost effective strategy. Add vaccines only if cost per FIP falls below US$0.76
Sack (2001)	Whole cell killed; 75% effective for 3 years adults, 25% for 3 years for children <5	Cost-effectiveness	Hypothetical endemic area	Incidence 4/1000 - 20/1000; varied total vaccine costs between US$0.4 and US$6.4	Vaccines cost-effective in endemic areas only if cost below $0.40 and incidence > 1 /1000

Review of economic evaluations of typhoid vaccines

Relatively fewer studies have examined the economics of typhoid vaccination programs. Papadimitropoulos et al (2004) examined the cost-effectiveness of two types of typhoid vaccines (Ty21a and Vi polysaccharide) for travellers. They found that both vaccines were not cost-effective unless travellers were going to areas with very high incidence rates or expected to be in very close personal contact with locals[35]. Bahl et al (2004) 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, though public share of costs were much higher for preschool children (aged 2-5), largely because these children were more likely to be hospitalized. Patients who do not respond to antibiotics had total costs almost four times higher. Mean annual "ex ante" costs (see above) were on the order of US$0.11- $0.22 for adults but US$3.42 - $5.22 for preschool children, though the study did not attempt to an explicit cost-benefit analysis or make recommendations about specific vaccination programs.

Rather, the authors reported a cost-benefit analysis in a separate paper (Poulos et al. 2004). Under a range of vaccine cost estimates, they find that immunizing preschool children would be cost-saving to the public sector. They also find that immunizing other age groups would probably pass a cost-benefit test if a) "clinical" typhoid cases are included because incidence is likely to be underestimated by blood-culture tests and b) the cost-of-illness estimates are multiplied by a "COI correction factor" to account for the important benefits that accrue to individuals which are not captured in the COI (see above). Finally, the Canh et al (2006) study mentioned above examined the benefits of typhoid vaccines in Hue, Vietnam. The paper reports on a more complete picture of vaccine benefits from a stated preference study and concludes a) that a vaccine which cost less than US$3.75 per FIP would likely pass a cost-benefit test, and b) that there is significant potential for the program to be self-financing through user fees.

[35] In areas with very high incidence rates (200 cases/million travellers), the cost per case avoided was 204 Euros (Ty21a) and 136 Euros (Vi polysaccharide)

Herd immunity

Herd immunity refers to the additional protection from a vaccination program that is conferred to unvaccinated people[36]. Herd immunity can happen for three reasons: it can a) reduce the number of susceptible individuals, b) reduce the prevalence of cases, or c) reduce the infectivity of each case. Because of this positive externality, vaccination programs can reduce or even eradicate (as with smallpox) diseases without vaccinating 100% of the susceptible population. Epidemiologists have historically been interested in determining the "critical threshold" of vaccination coverage rates that will "break the chain of transmission" and cause a disease to decrease in prevalence or even be eradicated (as with smallpox). This critical threshold (p_c) is commonly assumed to be ($1 - 1/R_o$) where R_o is the infectivity or reproductive rate of infection. R_o is in turn a function of the biology of the disease (measles is roughly five times more contagious than smallpox), the population density, the average age at which infection occurs, the birth rate, and sociobehavioral factors of transmission. As is obvious from the equation, the higher the R_o (the more infective a disease is), the higher the coverage rate necessary to eradicate the disease.

Beginning with experimental epidemiology studies on rats in the 1930's, herd immunity has been well-documented in the epidemiology literature. Most of the attention has focused on highly-communicable diseases which are the target of elimination or eradication programs. According to Fine's (1993) review of the literature, there have been studies on critical thresholds for vaccination programs against smallpox, measles (the most studied disease of the group), rubella, mumps, diphtheria, tetanus, poliomyelitis, influenza, malaria and tuberculosis. One interesting study in Japan used a natural experiment to identify herd immunity from influenza: the authors had data on influenza mortality both before and after the country's mandatory vaccination program for schoolchildren (Reichert et al. 2001). They found that vaccinating schoolchildren protected the elderly from influenza; they estimated that every 400 vaccines averted one excess influenza-related

[36] This section draws from Anderson 1990, Anderson and May 1985, Gordis 2000, and Fine 1993

death in the elderly. Another study found 42% fewer respiratory illnesses in the members of households with a flu-vaccinated child than in household members without a flu-vaccinated child (Hurwitz et al. 2000).

The Ali et al (2005) study discussed in main body of the dissertation is the only study in the epidemiological literature on herd immunity with respect to cholera or typhoid vaccines.

Economic evaluations which account for herd immunity

Because so much of the focus on herd immunity has been in designing eradication programs and finding critical thresholds for eradicable diseases, relatively little attention has been paid to the topic in the economic evaluation literature. Caro (2005) evaluated the cost-effectiveness of pertussis vaccines in the U.S. and incorporated herd immunity by modeling an additional decrease in the number of cases as the results of the program. The authors admitted that they had little conclusive epidemiological evidence for herd immunity in pertussis, and decided on an additional 20% reduction in cases as professional judgement. They found this assumed level of herd immunity and the true incidence of pertussis were the most important determinants of uncertainty in the cost-effectiveness of the vaccine. Similarly, Tormans et al (1998) and Edmunds et al (2002) varied the degree of herd immunity for evaluation of pertussis vaccine programs since the parameter was unknown. The Edmunds et al (2002) study was a cost-effectiveness analysis and the Tormans et al (1998) study was a "cost-benefit" which included only reductions in work days lost as indirect economic benefits of vaccination. McIntosh et al (2005) use published herd immunity effects for PCV (pneumococcal conjugate vaccine) in a cost-effectiveness analysis of a childhood vaccination program in the UK. They assume the program would reduce cases in unvaccinated adults by 1% - 23% and, unsurprisingly, find that the inclusion of herd immunity effects improved the ratio of cost per life year gained by almost a factor of five.

APPENDIX B: Kolkata CV manuscript

Private Demand for Cholera and Typhoid vaccines in Kolkata, India

(Submitted, *World Bank Economic Review)*

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Abstract

We asked 835 randomly-selected respondents from two socioeconomically-different neighborhoods in Kolkata (Calcutta), India about their interest in purchasing cholera and typhoid vaccines for themselves and for their household members in the summer of 2004. Using the contingent valuation method, we find that the private economic benefits of providing a free cholera vaccine to an average adult respondent in Kolkata are probably on the order of US$2 – 3; the benefits of a free typhoid vaccine are only slightly less. Five to twelve percent of respondents reported that they would not take a cholera or typhoid vaccine even if it were free. Our results point to the possibility that modest user charges for cholera and typhoid vaccines in Kolkata could recover part of the costs of any future mass vaccination or targeted vaccination program.

Introduction

Cholera and typhoid fever continue to pose a significant disease burden on populations in developing countries. A total of 101,383 cholera cases and 2,345 cholera deaths were reported to the World Health Organization (WHO) in 2004; the true total is thought to be higher because of underreporting (WHO, 2004). 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 (Crump et al., 2004). Though both diseases can be controlled with improved housing, water supply, sanitation, and food handling, in many typhoid- and cholera-endemic areas these investments are expensive and unlikely to occur in the near term. Next-generation vaccines against cholera and typhoid are safe and effective (Acosta et al., 2004) and could be useful short-term public health tools in reducing incidence rates among endemic populations as well as preventing large outbreaks.

Cholera and typhoid fever impose both a private economic burden on patients (treatment costs, lost productivity, pain and suffering, risk of death) and on the public health system. By reducing the number of cases of these diseases, vaccination campaigns have the potential to deliver significant economic benefits (which may or may not be larger than the program's costs). Because health budgets are severely limited in the countries where cholera and typhoid are most common, however, it may be impossible to provide these vaccines free of charge over the long term. Assessments of private demand for these vaccines can help governments design financially sustainable vaccination programs.

The International Vaccine Institute, with support from the Bill and Melinda Gates Foundation, launched the Diseases of the Most Impoverished Program (DOMI) in 2000 to accelerate the development and introduction of new-generation vaccines against cholera, typhoid fever, and shigellosis. The program involves a number of activities, including epidemiological studies, vaccine technology transfer, and sociobehavioral studies. We report here on one in a series of DOMI-led studies of private demand for cholera and typhoid vaccines in developing countries. Similar studies

have been carried out in Hue, Vietnam (Canh et al., 2006; Cook et al. 2006); Jakarta, Indonesia; Lingchuan county, China; Matlab, Bangladesh; Karachi, Pakistan; and Beira, Mozambique.

In the summer of 2004 we interviewed 835 randomly selected individuals in two different neighborhoods in Kolkata, India. We asked them how many cholera or typhoid vaccines they would buy (for themselves and for their household members) if the vaccines were available for purchase at a specified price. This approach, called contingent valuation (CV), has been widely used in the environmental field for goods that are not sold in a marketplace (Carson, 2000; Hanemann, 1994; Whittington, 2002). It has also been used in the health field for goods or services that are not widely available, including insecticide-treated bednets (Onwujekwe et al 2002, Onwujekwe and Nwagbo 2002, Onwujekwe et al 2005), community-based health insurance (Dong et al 2003), health care quality improvements (Protiere et al 2004) and vaccines (Whittington et al., 2002; Whittington et al., 2003; Cropper et al., 2004; Suraratdecha et al., 2005).

Our objective in the study reported here was to obtain the best estimates of private demand for cholera and typhoid vaccines for both children and adults in a low-income slum and a middle-class neighborhood in Kolkata. To accomplish this, we investigated who wanted cholera and typhoid vaccines in these areas and who did not. We also examined how giving respondents "time to think" about their responses affected the demand for cholera and typhoid vaccines. In this paper we report the results for respondents' demand for typhoid and cholera vaccines for themselves.

Background

Kolkata (formerly Calcutta) is the third largest city in India, with a population of approximately 13 million. Located in the Ganges-Bramaputra river delta in the state of West Bengal, the city and surrounding region (including Bangladesh) have long been a site of endemic cholera. A passive surveillance survey conducted in 2004 (Sur et al. 2006a) found the overall annual incidence of cholera in Narkeldanga, a low-income slum in Kolkata, to be 2.2 cases per 1,000 people, with

incidence among young children considerably higher. Though the overall incidence of typhoid fever is similar (approximately 2.0 cases per 1,000), it is more common in older children and teenagers.

A combined vaccine against typhoid, paratyphoid A&B and cholera (TABC) was administered free of charge in Kolkata beginning in the 1950s. It was discontinued in the 1980s because of side effects which included pain, swelling, redness, and fever and because recipients were often unable to work for several days after vaccination. In fact, numerous respondents in our study mentioned how painful the TABC shots had been. There is currently no cholera vaccine available for sale in Kolkata (nor India). The typhoid Vi polysaccharide vaccine is currently available for purchase in Kolkata at a few locations, but sales are low because many people do not know that it is available and because of the time, expense, and inconvenience associated with obtaining the vaccine in private physicians' offices. The limited demand is principally for young people in wealthier families who need the vaccine for travel abroad or for school.

Among our respondents, 8% of household members had received either the old cholera vaccine, the TABC vaccine, or a new typhoid vaccine. The majority of these (76%) were TABC vaccines. Only 1% of respondents reported paying anything for these vaccines. Our respondents were knowledgeable about vaccines: 97% had heard of vaccines, 88% remembered receiving some type of vaccine (not necessarily cholera or typhoid vaccine), and approximately 85% understood the purpose of vaccination.

A Review of the Contingent Valuation Method: Controversies and Best Practices

Reasonable people have good cause to be suspicious of the results from contingent valuation surveys. These studies ask respondents hypothetical questions about their preferences over different hypothetical states of the world, and from its inception the CV methodology has been subject to critical studies that showed errors or inconsistencies in the way people answer such hypothetical questions [see Diamond and Hausman (1994) for an early review of critiques, or Venkatachalam (2004) for a well-organized literature review of the CV method and its flaws]. Since CV was first

used to value environmental goods not traded in markets, much of the debate in the literature has occurred among environmental economists. However, critiques among health economists are increasing as the method gains in popularity for measuring the value of goods and services in the health sector (Ryan and Amaya-Amaya 2005, Lloyd 2003, Shiell and Gold 2003, Cookson 2003). Indeed, Hanley et al (2002) suggest that lessons can be learned from the debates among environmental economists (Portney 1994) in order to inform the parallel debate now occurring in health economics and policy.

Some of the principle concerns with CV (and indeed all "stated preference" methods) include: embedding and scope effects (Kahneman and Knetsch 1992), the difference between willingness-to-pay and willingness-to-accept measures of value (Hanemann 1991), the "reliability" of welfare estimates over time (the so-called test-retest studies; Kealy et al. 1990, Reiling et al. 1990, Carson et al. 1997), ordering or sequencing effects (Diamond and Hausman 1994), the influence of information treatments on WTP (Bergstom et al 1990, Protiere et al. 2004), strategic bias (Mitchell and Carson 1989), and the elicitation method (Venkatachalam,2004).

Arguably the most important question about CV, however, is whether the hypothetical responses are correlated with actual, observed behavior; or to put it less kindly, do CV studies tell us anything useful and reliable about people in the "real world"? Numerous studies have found evidence of "hypothetical bias," in which hypothetical WTP exceeds "actual" WTP, (Bishop and Heberlein,1979, Harrison, 2006). The underlying problem is that most CV studies lack the ability to test whether respondents behave as they say they will in the hypothetical scenario, precisely because the good and services being studied are not available in a market. In one of the rare studies in which hypothetical and real behavior are compared in the field, Griffin et al (1995) found that responses to a CV survey conducted in 1988 (in which respondents were asked whether they would connect to a village water system in Kerala, India) did a good job of predicting actual connections to the water system when it was built (residents were re-interviewed in 1991). Another line of evidence comes from studies which compare WTP derived from CV (or other stated preference methods) with WTP

derived from revealed preference methods, typically travel cost studies of recreation demand. Carson's (1996) meta-analysis of 83 of these paired studies found that estimates were in fact highly correlated: the mean ratio of CV estimates to revealed preference estimates was 0.89 with a rank correlation coefficient of 0.78. A final line of evidence comes from so-called field or experimental studies, recently reviewed by Harrison (2006). Although these studies consistently find robust evidence of hypothetical bias, they also find that the bias can be reduced or eliminated by using "best" practices (discussed below) or perhaps controlled statistically (Hofler and List 2004).

The purpose of our study was not to provide a novel experimental test of any of the CV critiques outlined above. Because the cholera and typhoid vaccines are not widely available in Kolkata, we are unable at this stage to test directly whether hypothetical responses match real behavior. Instead, we take the approach of the vast majority of CV studies by following a set of guidelines for what constitutes "best practice" in CV to maximize internal and external validity. Although such advice is constantly evolving, the interested reader should begin with the guidelines of the NOAA panel (Arrow et al. 1993). Unfortunately, because some CV researchers seem to be unfamiliar with this literature, far too many poor-quality CV studies have been conducted (see Whittington (2002) for a review of common mistakes made in studies in developing countries).

We take "best practice" to mean the following: 1) carefully-trained enumerators who conduct face-to-face interviews[37]; 2) a survey instrument and scenario that is carefully-worded and pre-tested to ensure that the good or service in question is well-understood (see (*Manuscript*) Appendix 1 for our CV scenario); 3) a reminder for the respondent to consider his/her budget constraint and other types of competing expenditures; 4) a "cheap talk" passage (Cummings and Taylor 1999); and 5) a dichotomous-choice (i.e. yes/no) valuation question for a specific price, rather than an open-ended elicitation method (i.e. how much would you pay?). We also gave half of our respondents "time to think" which we believe provides more conservative and realistic estimates of WTP (see below). Finally, we test for the internal validity of responses. We first test whether the price offered to

[37] Training for our study lasted approximately three weeks, including pretesting of the questionnaire

respondents has a negative and statistically-significant on the probability of their agreeing to purchase the vaccine. Because vaccines are normal goods, we also test whether respondents with higher incomes are more likely to report purchasing a vaccine.

Research design and field work

Description of study sites

To assess demand for cholera and typhoid vaccines among both lower- and middle-income residents, we surveyed households in two neighborhoods in Kolkata. Tiljala is a densely-crowded, mostly low-income, predominantly Muslim slum. Beliaghata is a predominantly Hindu area with more diverse living conditions and incomes. Though Beliaghata contains many middle-class families living in apartment buildings that are in relatively good condition, it also has several small slums with living conditions similar to those in Tiljala. Most residents of both areas (in our sample) get their water from communal taps (around 70%), but slightly more households in Beliaghata have private water connections in their homes (19%) than in Tiljala (11%). The vast majority of residents in both areas use shared flush toilets (over 90%), though again private flush toilets are more common in Beliaghata. In some parts of Tiljala, sewage from toilets flows into open drains outside the houses. Though rare, open pit latrines are still used in both areas.

Sampling

Kolkata is a large and ethnically diverse city, with many Urdu-speaking Muslims and Hindi-speaking immigrants as well as native Bengalis. Because it was not practical to translate and implement our survey into more than one local language, we restricted our sample to Bengali speakers, though not necessarily to people who spoke Bengali as their mother tongue. Project staff who pre-interviewed households were carefully trained to evaluate how well a potential respondent could speak and understand Bengali before scheduling an interview. Interviewers were also

instructed to stop any interview if a respondent appeared unable to understand what was being discussed because of language problems.

We used different sampling protocols to select survey participants in Beliaghata and in Tiljala. In Beliaghata, we selected respondents using a stratified two-stage simple random sampling procedure (SRS). As the sampling frame, we used the most recent voter list from the National Election Commission of India, which offers the most complete and accurate listing of households and individuals in Beliaghata. The area is divided into two administrative units (wards); we sampled each proportionately to its population.

Because the Beliaghata voter list contained no household information, we selected individuals as proxies for households in the first sampling stage. Because we used individuals as proxies for households, a few households were selected more than once (e.g., we drew both the father's name and the grandmother's name from the voter list). In those cases, we interviewed the same household only once. In the second stage, a member of the project staff pre-interviewed each selected household to see if it fit three criteria. The first criterion was that the household contained children less than 18 years old. If this criterion was met, project staff then asked to speak to either the mother or father of those children. The gender of the parent to be interviewed was randomly selected *before* the household visit, though we oversampled for males because their refusal rates tended to be higher. The second criterion was that the selected parent understand the Bengali language well enough to be interviewed. Because of difficulty in interviewing older respondents, the third criterion was that the selected parent be less than 65 years of age

In Tiljala, a complete household census was compiled in 2003 by the National Institute of Cholera and Enteric Diseases. This allowed us to create a sample frame that included only households with children under the age of 18. Using this sample frame, we drew a two-stage simple random sample, first selecting households and then selecting the gender of the parent. As in Beliaghata, project staff pre-interviewed the selected households to confirm the presence of children

and to ensure that the selected parent could understand Bengali adequately and was younger than age 65.

Of the 1471 households drawn from the voting list in Beliaghata, 666 were located and met our eligibility criteria. Of these, 12% refused to be interviewed. In Tiljala, we drew 506 households from the NICED census and ultimately interviewed 276. The refusal rate of eligible households in Tiljala was 6%.

Research design

Each respondent was asked about their willingness to purchase only one type of vaccine (cholera or typhoid) at a single, specific price. Both the type of vaccine offered and the price (one of four fixed amounts) were randomly preassigned to respondents. Our total sample size of 835 respondents was determined by overall resource and time constraints, and we used standard rules of thumb to determine the sample size within each design cell ($n \approx 35$) needed for a reasonable degree of statistical power. Choosing the prices shown to respondents is a critical step in the design of a credible CV study. Ideally referendum prices would cover the entire domain of the demand function so that WTP (the area under this demand curve) is well-defined. We carefully examined the results of three separate pretests of approx. 55 respondents each, and found that demand dropped off quickly at "low" prices (below Rs. 50). Because resource constraints limited our research design to only four prices, we decided to use three prices in the lower domain of the demand function (Rs. 10, Rs. 25 and Rs. 50) and to set the fourth price (Rs. 500) high enough to "choke off" demand.

We did not vary the immunological attributes of the vaccines offered to respondents; in all cases we used the best available estimates of their effectiveness and duration: oral cholera vaccine, 50% effective for 3 years; and Vi polysaccharide typhoid vaccine, 70% effective for 3 years (Acosta et al., 2004).

Half of the respondents in Beliaghata were given overnight to think about their responses. Previous studies have found that giving respondents "time to think" (TTT) lowers average

willingness-to-pay (WTP) measures in comparison to results from the standard practice of interviewing a respondent in a single sitting (Whittington et al. 1992, Lauria et al. 1999, Cook et al., 2006). Allowing time to think about their answers may give respondents a chance to consider household budget constraints more carefully, to discuss choices with family members and friends, or to answer questions confidentially. The remaining half of the Beliaghata respondents were not given the TTT protocol; they completed the interview in one session ("no time to think", or NTTT). Informed consent was obtained from all respondents.

Although we would have wished to give respondents in the Tiljala area time to think, we were unable to do so for practically and logistical reasons. Conducting interviews in Tiljala was more difficult than in Beliaghata because of the difficulty in locating houses in such a densely-populated slum and because of safety concerns that prevented our interviewers from working into the evening. Also, TTT interviews require at least two visits to each household, and we did not have the resources to devote to conducting these multiple interviews in Tiljala.

Survey instrument

The research team spent considerable time and effort developing and pretesting the interview questionnaire. The final version was divided into four main sections. The first section elicited the respondents' perceptions and attitudes toward either cholera or typhoid fever (depending on which type of vaccine they had been preassigned), the respondent's knowledge and experience with vaccines generally, and the household's history with the disease. The second section included information for the respondent on how cholera and typhoid fever are transmitted, as well as the symptoms and likely duration of both diseases (see (*manuscript*) Appendix 1 to review the complete CV scenario).

There were three reasons that we decided not to provide respondents with numerical probabilities of their becoming ill with the disease. First, these probabilities are not known with a great degree of certainty and may vary widely from person-to-person based on their health behaviors.

Researchers have an ethical responsibility not to mislead respondents with false certainty about their chances of becoming ill. This type of information could possibly cause respondents to change health or averting behavior and increase their chances of falling ill. Second, because many respondents had low levels of education, we felt that explaining very small probabilities such as 2 in 1000) would have been time consuming. Finally, it seems unlikely that a real vaccine program would be preceded by an information campaign that would describe numerical probabilities of illness to encourage participation. Rather a campaign would remind people about the causes and consequences of the diseases and describe how the vaccine might protect them, just as we do in the scenario. In this respect, the *perceived* incidence of the diseases is probably more important in predicting demand, regardless of the accuracy of this perception. We collect information on this perception by asking how likely the respondent thinks it is that they will contract cholera or typhoid in the next five years.

The second section also explained the concept of vaccine effectiveness (following a protocol adapted from Suraratdecha et al., 2005) and posed a series of short questions to test whether the respondent understood the concept. If the respondent did not understand, the enumerator repeated the explanation and repeated the test for understanding the concept of vaccine effectiveness. Respondents who failed the effectiveness test twice still completed the rest of the questionnaire, though we control for this fact in the statistical analysis.

The third section of the questionnaire, a contingent valuation (CV) scenario, included three tasks designed to elicit information about willingness to pay (WTP). The first was a single-bounded, discrete-choice question: "Would you buy this (cholera or typhoid) vaccine for yourself if it costs *$x*?" The second was the question "How many such vaccines would you be interested in purchasing for members of your household (at this same price)?"

We also asked respondents who said that they would not buy the vaccine for themselves at the specified price if they would take the vaccine if it were provided free. For those that would take the free vaccine, we then asked whether they would pay any positive price for the vaccine.

Respondents who would not take a free vaccine or would not pay any positive price for it (we will refer to these respondents as "out of the market") did not complete the next, third, task.

In the third task the respondent completed what we term a "sliding scale" payment card exercise (see Whittington at el. 2002, for a similar application). Using a price chart and the analogy of a stoplight, we asked the respondent to indicate the highest price that he (or she) was *completely sure he would pay* for the vaccine for himself (a "green light = go" price) and the lowest price he was *completely sure he would not pay* (a "red light = stop" price). In this procedure, the interviewer began by indicating on the scale a very high price (Rs. 5000) that we were confident all respondents would not be willing to pay: this price was "red = stop". The interviewer then indicated lower and lower prices on the scale until the respondent said the price was "yellow (proceed with caution)": he was no longer *certain* he would *not* pay that price for the vaccine for himself. The interviewer then stated a price of zero (free): this price was "green = go". The interviewer then listed higher and higher prices on the scale until the respondent again indicated the price was "yellow": he was no longer *certain* he would pay that price for the vaccine. In this way we were able to map out an interval of WTP (between a lower bound and an upper bound) for each respondent.

The fourth and final section of the questionnaire collected socioeconomic information about the household.

Results

Profile of sample respondents

Table 1 present summary statistics for our samples in Beliaghata and Tiljala. Respondents in Tiljala had lower incomes and had fewer years of education than respondents in Beliaghata. Still, the mean monthly per capita self-reported income in Beliaghata was only Rs. 1250, or about US$1 per day. Although average household size was similar in both areas (5 members), households in our Tiljala sample had fewer adults and more school-aged (6–12 years) children.

Both cholera and typhoid were familiar to respondents in Tijala and Beliaghata. Over 40% of respondents reported knowing someone (either inside or outside the household) who had contracted the diseases. The fraction was somewhat higher for both diseases among Tiljala respondents. Similarly, nearly twice as many Tiljala respondents felt that the diseases were "common" or "very common" in their neighborhoods.

We also asked respondents "how likely is it that you will get [cholera or typhoid] in the next five years"? The results suggest that people may over-estimate these probabilities. If the observed cholera incidence is approximately 2 cases per 1000 adults per year, then the actual 5-year probability of contracting cholera is around 1%. Still, 40% of Beliaghata respondents and 42% of Tiljala respondents thought it was "somewhat likely" or "very likely" they would get cholera in the next five years. The responses are similar for respondents who were asked about their probability of contracting typhoid. Finally, approximately 60% of respondents felt that a case of cholera [typhoid] was "serious" or "very serious" for adults.

Only 9 of the 835 total respondents from both areas did not believe the contingent valuation scenario, i.e., they did not believe the vaccine was safe or that it could prevent the disease. In our test to gauge whether the concept of vaccine effectiveness had been understood, 75% of Beliaghata respondents and 63% of Tiljala respondents correctly answered the questions the first time; 10% of the Beliaghata respondents and 19% of Tiljala respondents answered these questions incorrectly even after the enumerator had reread the passage explaining effectiveness.

Who would not take a free vaccine or would not pay anything for one?

About 10% of all respondents stated that they would <u>not</u> be willing to take the vaccine even if it were provided to them for free, and an additional 5% to 12% said that they would accept a free vaccination but would not pay any positive price for it. These out-of-the-market respondents were older, had lower incomes, and more frequently reported never boiling their water (one measure of

risky health behavior). Overall, 19% of respondents who were offered a cholera vaccine were out of the market, as were 14% of respondents who were offered a typhoid vaccine.

We estimated a probit regression model to investigate which socioeconomic or behavioral factors could predict whether a respondent was out of the market[38]. Four of the factors mentioned above (higher age, lower income, never boiling drinking water, and being offered a cholera vaccine) were statistically significant at the 5% level. Neither the respondent's education nor failure to pass the effectiveness test questions was a significant indicator of who was out of the market. Other variables which were not significant predictors of being out-of-market include water and sanitation conditions, cholera or typhoid vaccination history, neighborhood (Tiljala vs. Beliaghata), the referendum price offered, nor whether the respondent was given time to think. Experience with the disease (knowing someone who had contracted it) was only a weak predictor and had an unexpected (negative) sign.

Responses to the valuation question

Table 2 presents the raw responses to our first WTP question: would the respondent purchase the vaccine for himself or herself if it cost the amount specified? The table includes the 138 respondents who were out of the market but excludes the 9 respondents who had rejected the contingent valuation scenario altogether. Without relying on any statistical assumptions or using covariates, one can easily see that the percentage of respondents who said they would purchase the vaccine for themselves decreases as price increases. This is the first, and perhaps most important, test of the internal validity of the contingent valuation experiment, and is some indication that respondents took the exercise seriously. These data also suggest that demand for both cholera and typhoid vaccines is higher in Beliaghata than in Tiljala and is lower for respondents who were given time to think.

[38] Full regression results are not included in this paper, but are available from the authors upon request.

We calculated respondents' average WTP for the vaccines using the Turnbull lower-bound and Kristrom midpoint nonparametric estimators, which do not rely on statistical assumptions about how WTP is distributed (Haab & McConnell 2002; Kristrom 1990). Both ignore potentially important covariates such as income but provide a useful point of comparison with parametric WTP estimates. The conservative Turnbull lower-bound estimator yields a mean WTP for cholera vaccine of about Rs. 110 (US$2.5) in Beliaghata and Rs. 57 (US$1.3) in Tiljala (Table 3). Turnbull mean WTP values for a typhoid vaccine are similar: Rs. 72 – 128 in Beliaghata and Rs. 70 in Tiljala. These amounts represent the private economic benefits that would accrue to the average respondent (not to society generally) if given a cholera or typhoid vaccine for free. The Kristrom midpoint estimator is less conservative than the Turnbull; WTP estimates are generally about twice the Turnbull estimates for our data. These estimates of average WTP values are heavily influenced by those respondents who agreed to buy the vaccine at the highest price. For example, in the Turnbull calculation the benefits that accrue to the 18% of the respondents who said yes to the highest price for a cholera vaccine in Beliaghata (NTTT) make up 77% of the total average WTP benefits (Rs. 114).

Multivariate models of respondent demand

We estimated a multivariate probit model to investigate the determinants of respondent vaccine demand (Table 4). Because covariates may affect demand for cholera vaccines differently than they affect demand for typhoid vaccines, we ran probit models separately on the subsample of 415 respondents who were asked about a cholera vaccine and the subsample of 411 respondents who were asked about a typhoid vaccine.[39]

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[39] We did run a probit regression on pooled data, combining respondents who were asked about a typhoid vaccine and respondents who were asked about a cholera vaccine. We tracked which vaccine they were offered with a dummy variable for cholera (= 1 if cholera vaccine, = 0 if typhoid vaccine). The coefficient was negative and significant, perhaps indicating a preference for typhoid vaccines. Because a single respondent in the CV survey was not offered both cholera and typhoid vaccines simultaneously, however, and because the attributes of the vaccines did not vary, direct comparisons of demand between the two diseases should be made with caution. If demand is higher for the typhoid vaccine, it may be because respondents are more interested in

As expected, a respondent who was offered a higher vaccine price was less likely to agree to purchase either type of vaccine. Respondents were somewhat more sensitive to the price of typhoid vaccines than cholera vaccines. Furthermore, respondents with higher per capita incomes were more likely to purchase either type of vaccine. Because economic theory provides clear guidance on the effect of income, this is a second critical check on the internal validity of contingent valuation responses.

Respondents who were given overnight to think about their answers were less likely to purchase a typhoid vaccine. Time to think did not have a statistically significant effect on demand for cholera vaccines, although the sign of the coefficient was consistent with the results for typhoid vaccines. Time to think may not only reduce demand but may also increase the certainty that respondents feel about their answers to the question of whether they would buy the vaccine for themselves. Among respondents who were offered a cholera vaccine, 86% of TTT respondents felt "very certain" about their response, compared to 68% of NTTT respondents. A simple *t*-test of sample means shows that the difference between these two percentages is statistically significant at the 1% level. The difference in certainty among respondents who were offered a typhoid vaccine was not significant.

Other potentially important socioeconomic characteristics are education, gender, age and household size. A respondent with a primary or secondary school education was more likely to buy a typhoid vaccine for himself or herself than someone with no formal education. The gender of the respondent did not have a significant effect on demand for either vaccine, but older respondents were less likely to want to purchase a cholera vaccine for themselves. Household size had no effect on typhoid demand, but respondents with more adults in their

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avoiding typhoid. It may also be, however, that respondents prefer the typhoid vaccine to the cholera vaccine because it is more effective (70% vs. 50%). Stated choice (SC) or choice model experiments provide a better opportunity to explore the importance of vaccine attributes to individual respondents and to make direct comparisons of vaccine demand between the two diseases without relying on cross-comparisons *between* respondents (Cook et al. 2006).

households were more likely to buy a cholera vaccine for themselves, and those with more young children were less likely to buy a cholera vaccine.

Controlling for income and other demographic differences, respondents in Tiljala were more likely to buy cholera vaccines than respondents in Beliaghata, but the difference in demand for typhoid vaccines across the two areas is not significant. Counteracting this effect, however, is the fact that Muslim respondents (who are the majority of Tiljala residents) were less likely to buy cholera vaccines than Hindu respondents (who are the majority of Beliaghata residents).

Knowing a person who had contracted typhoid increased the probability of agreeing to purchase a typhoid vaccine. Respondents who reported never boiling their drinking water were less likely to purchase a cholera vaccine. If someone in the respondent's household had received a typhoid or TABC vaccine in the past they were less likely to buy a typhoid vaccine. Distance to the nearest private health facility was negatively correlated with vaccine demand, although this relationship is significant at only the 10% level. The respondent's assessment of how serious the diseases were for adults was not statistically significant[40].

The third column on Table 3 reports mean WTP measures based on these parametric (probit) model results. These estimates generally fall within the estimates of the two nonparametric approaches reported in the same table.

[40] Because the respondents' assessments of how common the diseases were in their neighborhood was collinear with several other variables (seriousness of disease, likelihood of contracting disease, knowing someone with disease), it was not included in the multivariate models in Table 4. When this measure was entered into the model without any of the other collinear variables, the effect was not statistically significant ($p=0.73$ for cholera models, $p=0.68$ for typhoid models). Similarly, the variable tracking whether the respondent failed the test of their understanding of effectiveness was highly correlated with education levels. It was not significant in models where it was included with education levels, and was not reported in Table 4 for brevity.

Results from the "sliding scale" payment card exercise

All of the results presented thus far have been based on responses to the first valuation question – "Would you buy this (cholera or typhoid) vaccine for yourself if it costs *$x*?". Figure 1 reports results from the "sliding scale" payment card exercise. It shows the percentage of respondents who reported that a certain price was "green" (they were "completely sure" they would purchase the vaccine at that price). The percentage of respondents who were sure that they would buy the vaccine clearly declines with as price increases, is smaller in Tiljala than in Beliaghata at all prices, and is lower for TTT respondents than for NTTT respondents.

Discussion

This study passes two important tests of internal validity. Both the vaccine price offered to respondents and respondents' incomes influenced stated intentions to purchase vaccines for themselves in the manner hypothesized by economic theory. We believe that respondents who were given time to think gave more considered answers—indeed, they told us that they were more certain of their answers.

Our results suggest that about 5% of respondents in both Beliaghata and Tiljala would not accept a typhoid vaccine, even if free. Refusal of a free cholera vaccine was higher, especially in Tiljala (12%). An additional 10% of respondents would take a free vaccine but would pay nothing for it. These "out-of-market" respondents tended to have lower incomes and education levels and were more likely to engage in risky health behaviors (not boiling drinking water). Similarly, results from the multivariate models indicate that respondents with lower levels of education are less likely to purchase typhoid vaccines. The direction of the effect of education on demand for cholera vaccines was the same, but was smaller in magnitude and not statistically significant. Respondents who

reported never boiling water were significantly less likely to buy a cholera vaccine, though not a typhoid vaccine.

Several other independent variables had weak or no effects on demand. Older respondents were slightly less likely to say they would buy a cholera vaccine, but was not significant for typhoid vaccines. Men and women seem to have similar preferences for the vaccines. Respondents' perceptions of the seriousness and prevalence of the two diseases did not affect demand, and their self-assessed chances of getting the disease in the next five years was also not statistically significant. On the other hand, respondents who had either had typhoid themselves, or knew someone who had, were significantly more likely to say they would buy a vaccine.

If the respondent or someone in the respondent's household had at some point in the past received a typhoid or TABC vaccine, they were less likely to say they would buy the new typhoid vaccine for themselves, though this effect was not significant for cholera vaccines. Respondents may think that the vaccine is still protecting them or their household members; in fact, they told us that they believed the vaccines were still protecting 73% of the household members who had been vaccinated. The result may also reflect a negative reaction to previous experience with vaccines, although only 6% reported being unsatisfied with the old vaccine[41].

Household composition did not affect demand for typhoid vaccines, but respondents who had more young children were less likely to buy a cholera vaccine for themselves, perhaps a reflection that they would prefer to spend scarce household resources on a vaccine for the child rather than themselves, especially since cholera incidence is much higher for young children (Sur et al 2006). On the other hand, those with more adults in the household were more likely to buy a vaccine.

Tiljala and Beliaghata are very different neighborhoods in Kolkata. However, controlling for income and education and the other independent variables in Table 4, demand for a typhoid vaccine was similar in the two neighborhoods. Respondent demand for a cholera vaccine was higher in

[41] A dummy variable tracking whether the respondent was unsatisfied with the old vaccine was not significant in models not reported here.

Tiljala, but this was balanced against the result that religious affiliation was also correlated with demand for cholera vaccine: it was higher among Muslims (who lived chiefly in Tiljala) than Hindus (who lived chiefly in Beliaghata).

On the basis of the information that respondents gave us in the first WTP question we estimate that the average respondent WTP for these two vaccines is at least Rs. 70 (US$1.6) in the wealthier neighborhood of Beliaghata. However, the responses to our sliding scale exercise suggest that only 25%-30% of Beliaghata respondents were completely sure they would purchase either vaccine at a price of Rs. 70. Largely because of lower income levels, average WTP is lower in Tiljala. The most conservative estimate of average WTP in Tijala would be on the order of Rs. 60 for cholera vaccines and Rs. 40 for typhoid vaccines, though again a fraction of the population has a significantly higher WTP.

Cholera and typhoid vaccines have historically been provided free of charge in Kolkata. Public health resources in India, however, are scarce; as a point of reference, the WHO reports that average per capita expenditures on public health in 2002 were on the order of US$6 – US$20[42]. Our results indicate that the government of India *could* charge a modest price for vaccines to recover at least part of the costs of any future mass vaccination or targeted vaccination program and still achieve fairly high coverage rates.

The decision of whether or not to undertake a vaccination program against cholera and typhoid fever in Kolkata is not a simple one, and we do not attempt to answer this question here. The diseases do not have an especially high prevalence in Kolkata (~2 cases per 1000, higher among children, but probably lower in Beliaghata). Both diseases are treatable, afflict the patient for a small amount of time (relative to diseases like HIV or tuberculosis), and are rarely fatal. However, vaccines provide a positive externality through indirect protection of unvaccinated individuals, a result which has been documented recently for cholera vaccination programs in Bangladesh by Ali et al (2005).

[42] The range represents assumptions about whether resources should be adjusted for purchasing power parity. http://www.who.int/whr/2005/annex/indicators_country_g-o.pdf.

Little effort has been devoted, however, to quantify this herd immunity benefit and incorporate it into careful policy analyses of vaccination programs.

TABLES AND FIGURES

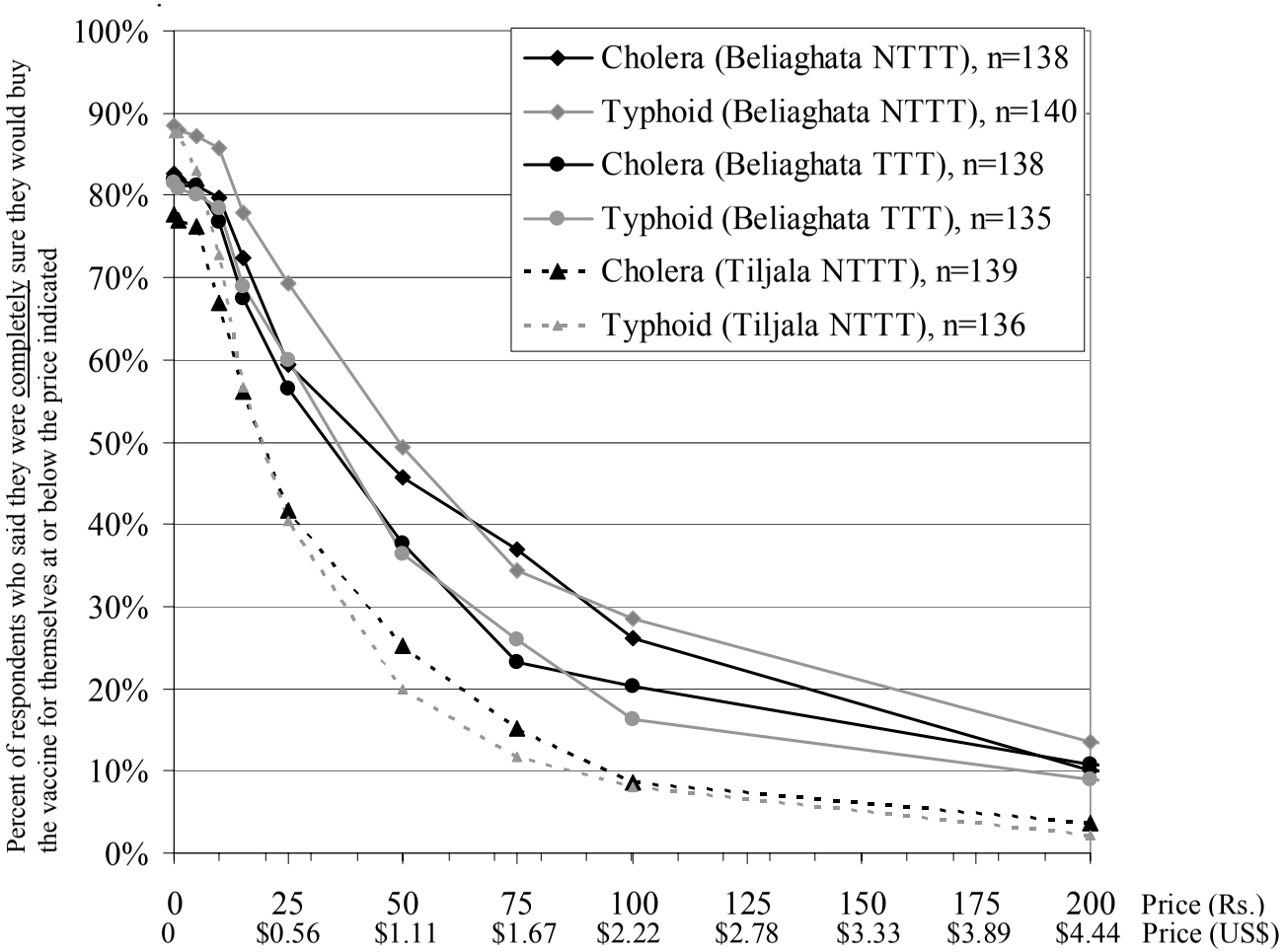


Figure 1. Percent of respondents who were certain that they would purchase a 50%- 3yr cholera vaccine or 70%-3yr typhoid vaccine for themselves, by price, time-to-think (TTT), and neighborhood (based on raw data from sliding scale exercise).

Table 1. Descriptive statistics of sample respondents

Variable name	Description		Beliaghata (n=559)	Tiljala (n=276)
			Mean (SD)	Mean (SD)
Respondent characteristics				
Male	Gender =1 if male, =0 if female		52%	48%
Age	Age, years		36 yrs (8.0)	35 yrs (9.4)
Muslim	Religion =1 if Muslim, 0=else		1%	76%
Education Low	=1 if respondent completed 1- 9 years of school		44%	44%
Education Mid	=1 if respondent completed 12 years of school or vocational school		30%	13%
Education High	=1 if respondent completed university, post-graduate or prof. course		17%	3%
Household characteristics				
Monthly per capita income[a]	Monthly household income divided by household size, Indian Rs.		Rs. 1246 (1912)	Rs. 585 (546)
Num. young children	Number of young children (0-5 yrs.)		0.5 (0.65)	0.6 (0.8)
Num .school-aged children	Number of older children and teens (6 - 18 yrs)		1.2 (0.93)	2.0 (1.5)
Num. of adults	Number of adults (18+ yrs),		3.6 (1.9)	2.8 (1.3)
Health and disease-related characteristics				
Know person with disease	=1 if knows someone who has had disease (incl. respondent and hh members)	Cholera Typhoid	41% 46%	47% 55%
Disease is common	=1 if disease is common or very common in my neighborhood	Cholera Typhoid	24% 22%	43% 37%
Likely to get disease	=1 if "somewhat likely" or "very likely" that respondent will get disease in the next 5 years	Cholera Typhoid	40% 38%	42% 48%
Disease is serious for adults	=1 if disease is "serious" or "very serious" for adults	Cholera Typhoid	65% 58%	65% 65%
HH member had vaccine	=1 if someone in household had vaccine	Cholera or TABC Typhoid or TABC	26% 23%	17% 15%
Never boil drinking water	=1 if household never boils drinking water & has does not have Aquaguard water filter		58%	65%
Distance to health facility	Distance to nearest private health facility, minutes		8.9 (6.7)	12.5 (13.5)

[a] 37 Beliaghata respondents (6.6%) and 9 Tiljala respondents (3.3%) could not (or would not) provide income information. These missing values were replaced with the neighborhood median income. Log monthly per capita income is used in the regression models to reduce the effect of high-income outliers in the income distribution. 1 US$ = 45 Rs.

Table 2. Percent yes to respondent referendum question, by price[a]

Price(Indian Rs.) Price (US$)	**Rs. 10** (US$ 0.22)	**Rs. 25** (US$ 0.56)	**Rs. 50** (US$ 1.11)	**Rs. 500** (US$ 11.11)
Beliaghata Cholera NTTT	89%	68%	63%	18%
Beliaghata Cholera TTT	82%	60%	49%	18%
Beliaghata Typhoid NTTT	91%	86%	63%	20%
Beliaghata Typhoid TTT	83%	69%	52%	9%
Tiljala Cholera (NTTT)	83%	53%	54%	9%
Tiljala Typhoid (NTTT)	82%	66%	46%	9%

[a] Excludes nine respondents who rejected the scenario

Table 3. Respondent willingness-to-pay (mean, Indian Rupees)

	Non-parametric estimates		Parametric estimates: Multivariate probit
	Turnbull lower-bound	Kristrom midpoint estimator	
Beliaghata Cholera NTTT	Rs. 114 ($ 2.5)	Rs. 234 ($ 5.2)	Rs. 199 ($ 4.4)
Beliaghata Cholera TTT	Rs. 109 ($ 2.4)	Rs. 204 ($ 4.5)	Rs. 163 ($ 3.6)
Beliaghata Typhoid NTTT	Rs. 128 ($ 2.8)	Rs. 248 ($ 5.5)	Rs. 248 ($ 5.5)
Beliaghata Typhoid TTT	Rs. 72 ($ 1.6)	Rs. 175 ($ 3.9)	Rs. 154 ($ 3.4)
Tiljala Cholera (NTTT)	Rs. 57 ($ 1.3)	Rs. 174 ($ 3.9)	Rs. 112 ($ 2.5)
Tiljala Cholera TTT[a]	n/a	n/a	Rs. 77 ($ 1.7)
Tiljala Typhoid (NTTT)	Rs. 70 ($ 1.5)	Rs. 164 ($ 3.6)	Rs. 131 ($ 2.9)
Tiljala Typhoid TTT[a]	n/a	n/a	Rs. 39 ($ 0.9)

Estimates in parenthesis are in USD converted at 45Rs.=1USD

[a] Tiljala respondents were not given time to think. These estimates adjust WTP for time-to-think effects by using the coefficient from the Beliaghata sample.

Table 4. Results of multivariate probit model of respondent demand[a]

	Respondent yes/no to "would buy for yourself?"	
	Cholera	Typhoid
Price (Rs.)	$-4.1e^{-3}$ ($4.3e^{-4}$)***	$-4.8e^{-3}$ ($4.6e^{-4}$)***
Log monthly per capita income	0.76 (0.13)***	0.41 (0.12)***
Time-to-think	-0.15 (0.19)	-0.44 (0.18)**
Education Low[b]	0.27 (0.23)	0.52 (0.21)**
Education Mid[b]	0.38 (0.27)	0.60 (0.27)**
Education High[b]	0.18 (0.32)	0.24 (0.35)
Male	-0.020 (0.18)	-0.034 (0.16)
Age	-0.032 (0.012)**	-0.006 (0.011)
Num. young children	-0.27 (0.14)*	0.039 (0.15)
Num. school-aged children	0.026 (0.091)	-0.073 (0.071)
Num. adults	0.19 (0.045)***	0.049 (0.038)
Muslim	-0.63 (0.28)**	0.35 (0.33)
Tiljala	0.86 (0.26)***	-0.38 (0.33)
Never boil drinking water	-0.47 (0.16)**	-0.14 (0.16)
Distance to health facility	-0.015 (0.008)*	-0.011 (0.007)*
Likely to get disease	-0.13 (0.16)	-0.11 (0.15)
Know person with disease	0.11 (0.16)	0.43 (0.15)***
Disease is serious for adults[b]	0.030 (0.16)	-0.032 (0.15)
HH member had vaccine	0.102 (0.20)	-0.35 (0.20)*
Constant	-3.8 (1.0)***	-1.8 (0.85)**
N=	415	411
Pseudo-R^2	0.34	0.33
Wald Chi-sq ($p <$ Wald χ^2)	137 (0.000)	128 (0.000)

[a] Robust standard errors are in parenthesis. * Indicates significance at the 10% level, ** at the 5% level, *** at the 1% level. Excludes nine scenario-rejecters.

[b] Excluded categories are: No education, disease is not common or don't know how common, disease is not serious for adults or don't know how serious for adults.

Manuscript Appendix. Description of diseases and contingent valuation scenario

Description of Cholera

Next I'd like to talk about the spread and prevention of cholera. Cholera is spread primarily through eating food and drinking water contaminated by the feces of patients. You can help protect yourself from cholera by consuming only safe, clean food and water.

Cholera is caused by a type of bacteria. When someone becomes ill with cholera, he/she can develop severe diarrhea that can cause him or her to lose large amounts of fluids and salts. When the body loses too many fluids and salts, it can no longer work properly. The patient's kidneys can stop working, and the patient could die. The patient with cholera should drink fluids with salt and sugar and when severe, take fluids through a vein (intravenous or IV fluids). If the patient takes antibiotics right away, the diarrhea should not last as long.

The diarrhea caused by cholera will stop in a few days. Giving fluids works well to prevent and treat the worst problems caused by cholera, and giving fluids also makes the patient feel better. However, without treatment a person with cholera can become severely sick or die.

Description of Typhoid

Next I'd like to talk with you about the transmission and prevention of typhoid. Typhoid is transmitted primarily by food and water contaminated by the feces of people already infected. Flies can contaminate food. You can help protect yourself from typhoid by consuming only safe, clean food and water.

A type of bacteria (not a virus) causes typhoid. People can transmit the disease as long as they have the bacteria. If someone becomes infected with typhoid taking antibiotic drugs can treat him or her. Although the patient will have to take antibiotics for about 4 weeks, they should feel better in 2 to 3 days. Early treatment in combination with new antibiotics is usually quite effective. Without antibiotic treatment a person with typhoid can be sick for weeks or months with a high fever, and there is a small chance of death. Typhoid is more common in children and young adults. Older adults are less likely to get typhoid than children or young adults.

Cholera vaccine scenario

(*The script here is the direct translation of the Bengali used in the survey instrument. To keep the respondent engaged, however, it was broken up at several points. The first break was to educate the respondents about effectiveness and test whether they understood. We omit this description and would refer the interested reader to Suraratdecha et al (2005), although the full script is available from the authors. The second break allowed the respondent to ask any questions or request clarification from the respondent. Finally, half of Beliaghata respondents were given time to think at the place indicated in the script*).

Doctors and scientists have developed a new vaccine that can prevent people from getting cholera. We'd like to know what you would do if the new cholera vaccine was available for sale at a convenient location like a vaccination camp or vaccination clinic. This new vaccine could be given to individuals to prevent them from having cholera in the future. It could not be used to treat someone who currently has cholera. This vaccine cannot be used for children under 1 year and pregnant women. This vaccine is different from the old cholera or TABC vaccine that you or your household members may have received.

Suppose that this vaccine has no side effects, and is safe, that is, after you were vaccinated you would have no chance to get cholera from the vaccine. Suppose that you could drink the vaccine (like the polio vaccine) so that the vaccine would be painless. Assume that two doses of the vaccine would be required taken about 2 weeks apart. Suppose that taking the two doses of cholera vaccine would be 50% effective for 3 years.

Suppose that the government will not supply the new vaccine for free. Those who want a vaccine would have to pay a fixed price for it. Everyone would pay the same price.

Now I'd like to know whether you would buy the vaccine if it was available at a specified price. Some people say they cannot afford the price of the vaccine or that they are actually not at risk of getting this disease. Other people say that would buy the vaccine because the protection is really worth it to them. In other studies about vaccines, we have found that people sometimes say they want to buy the vaccine. They think: "I would really like as much protection from this disease as possible." However, they may forget about other things they need to spend their money on. Please try to think carefully about what you would actually do if you had to spend your own money. There are no right or wrong answers. We really want to know what you would do.

> [Time to think respondents only]
>
> We are almost at the end of our first interview, and I want to thank you very much for your time. I would like to return again tomorrow to ask you more questions. I will ask you whether you would want to buy this vaccine for yourself as well as for other members of your household if it were sold at a certain price. I would encourage you to think overnight about how much this new vaccine is worth to you, and the range of prices you might be willing to pay for this vaccine for yourself and for your household members. You may also want to discuss these decisions with other members of your household. *<First interview ends>*

When you give your answer about whether you would or would not buy the vaccine, please consider the following: yours and your family's income and economic status compared with the price of the vaccine, and your risk of getting cholera. Apart from the vaccine, remember that we still have other ways to treat cholera such as oral rehydration solution. Also, remember that the benefit of the vaccine in preventing cholera is [50% effective for 3 years]. Again, the cholera vaccine cannot be used by children under 1 year and pregnant women.

Suppose that this cholera vaccine costs (Rs. X) for the two doses needed for one person. Would you buy this vaccine for yourself?

Typhoid vaccine scenario

Doctors and scientists have developed a new vaccine that can prevent people from getting typhoid. We'd like to know what you would do if the typhoid vaccine were available for sale at a convenient location like a vaccination camp or vaccination clinic. This vaccine would be given to individuals to prevent them from having typhoid in the future. It would not work to cure someone who currently has typhoid. This vaccine is different from the old typhoid or TABC vaccine that you or other members of your household may have received.

Suppose that this vaccine was safe and had no side effects (i.e. feel sick, light fever, headaches, etc.). Suppose that you could take the vaccine as an injection. Assume that only one dose of the vaccine would be required. Suppose this vaccine was 70% effective in preventing typhoid for 3 years.

Suppose that the government will not supply the new vaccine for free. Those who want a vaccine would have to pay a fixed price for it. Everyone would pay the same price.

Now I'd like to know whether you would buy the vaccine if it was available at a specified price. Some people say they cannot afford the price of the vaccine or that they are actually not at risk of getting this disease. Other people say that would buy the vaccine because the protection is really worth it to them. In other studies about vaccines, we have found that people sometimes say they want to buy the vaccine. They think: "I would really like as much protection from this disease as possible." However, they may forget about other things they need to spend their money on. Please try to think carefully about what you would actually do if you had to spend your own money. There are no right or wrong answers. We really want to know what you would do.

[*Time to think, as above*]

Keep in mind that when you give your answer about whether you would or would not buy the typhoid vaccine, please consider the following: your own income and your family's income and economic status compared with the price of the vaccine, and your risk of getting typhoid. Apart from the vaccine, remember that we can still treat typhoid with antibiotics. Also remember that the benefit of the vaccine in preventing typhoid is 70% effective for 3 years. (

Suppose that this typhoid vaccine costs (Rs.X) for the one dose needed for one person. Would you buy this vaccine for yourself?

APPENDIX C: Household WTP Measures

Modeling approach

Theoretical approach

Following the approach of Cropper et al (2004) and Cahn et al (2006), I assume the household decision-maker's utility function depends on each family member's consumption of some numeraire good (X_i), leisure time (L_i), a vector of household characteristics, and the amount of time spent ill with either cholera or typhoid (S_i). Assuming n family members, the utility function is:

(1) $U = u(X_1,\ldots,X_n, L_1,\ldots,L_n, S_1,\ldots,S_n, \boldsymbol{Z})$

The decision-maker maximizes utility subject to the household budget constraint, given in Eq. 2.

(2) $$I + \sum_{i=1}^{n} w_i (T - L_i - S_i) = \sum_{i=1}^{n} X_i + p_V \sum_{i=1}^{n} Q_i + p_m \sum_{i=1}^{n} M_i$$

The left-hand side of Eq. 2 is the amount of income available for prevention and treatment of cholera or typhoid, and is sum of household non-earned income (I) and earned income, where w_i is the wage and the total time available is T. The right-hand side of the equality is the sum of household expenditure on the numeraire good, household expenditures on prevention (p_v is price of prevention and Q_i indexes the quantity of prevention purchased for the i^{th} household member), and household expenditures on treatment of the disease (p_m is treatment cost and M_i indexes whether the quantity of treatment for household member i.

The head of household selects values of $\boldsymbol{X}$, $\boldsymbol{L}$, Q_i and $\boldsymbol{M}$ to maximize household utility subject to the budget constraint and to their health production functions (Grossman 1972). The solution to this maximization problem yields a demand function for preventive care:

(3) $$q^* = \sum_{i=1}^{n} q_i$$

where q^* is the amount of prevention chosen by the decision-maker, e.g., the number of vaccines the decision-maker purchases. Note that uncertainty is modeled implicitly here; we assume the decision-maker takes into account the probabilities of getting ill in arriving at q*. Rather than define household demand for prevention as an additive function of demand for individual members, let's define household demand more generally as some function g(·) of the prices of prevention and treatment, household non-wage income (I), a vector of each household member's wage (**w**), a vector of household characteristics (**Z**), and a vector of the health characteristics of family members (**H**):

$$(4) \qquad q^* = g(p_v, p_m, I, \mathbf{w}, \mathbf{Z}, \mathbf{H})$$

To find the total value (WTP) to the decision-maker for preventing the disease in themselves and in their *n* household members, I integrate the inverse demand function $g^{-1}(\cdot)$ from 0 to *n* vaccines[43]:

$$(5) \qquad WTP = \int_0^n g^{-1}(q, I, \mathbf{w}, Z, H)dq$$

Estimation Approach and WTP measures

The model requires some additional structure in order to estimate the parameters of the demand function g(·) in eq. 4 and calculate WTP. First, combine the characteristics of household *i*, the vaccine and prevention (including terms I, w, p_m, Z and H in eq. 4, as well as variables for our study like whether the respondent was given time to think and the respondent's neighborhood) into the vector $\mathbf{X}_i$. Further define the bid price of the vaccine offered to respondents in the contingent valuation survey as *A*.[44] Assuming an additive and separable utility function, the model we estimate statistically is:

$$(6) \qquad g(\mathbf{X}_i, A) = \exp(\mathbf{X_i\beta} - A\beta_p) + \varepsilon_i$$

[43] As a Marshallian demand function, this assumes that the marginal utility of income is constant.
[44] We use *A* to maintain some consistency with the notation used in Hanemann and Kanninen 2001

To estimate $\boldsymbol{\beta}$ and β_p from the observed data, we use the negative binomial regression model (NBREG), a variant of the Poisson count model. The Poisson-distributed probability of observing the respondent buying vaccines for all *n* household members is:

$$(7) \qquad P[observed = n] = \frac{\exp(\exp(X_i\beta - A\beta_p)) \cdot \exp(X_i\beta - A\beta_p)^n}{n!}$$

The Poisson model constrains the conditional mean and conditional variance in the data to be the same. Relaxing this assumption, the negative binomial model adds a gamma-distributed error term to $\mathbf{X_i\beta}$ to allow the two to differ. The predicted number of units $\hat{q}$ purchased by household *i* at price *A* is given by eq. 8. Notice that when the bid price is zero (i.e. there are no user charges), A=0, and $\hat{q}$ is simply $\exp(\mathbf{X_i\beta})$.

$$(8) \qquad \hat{q} = \exp(\mathbf{X_i\beta} - A\beta_p)$$

Again, willingness-to-pay[45] to vaccinate the entire household (<u>not</u> an individual person) is the area under the inverse demand curve $g^{-1}(\cdot)$ and to the left of household size *n*:

$$(9) \qquad WTP_i = \int_0^n g^{-1}(q, \mathbf{X})\, dq$$

Equivalently, we can also integrate the demand function g(·) over prices A. Define p* as the fee that users pay for the vaccine.

$$(10) \qquad WTP_i = \int_0^\infty \exp(\mathbf{X_i\beta} - A\beta_p)dA =$$

$$(11) \qquad = -\frac{1}{\beta_p}\exp(\mathbf{X_i\beta} - A\beta_p) \Big|_{p^*}^{\infty} =$$

[45] The theoretically correct measure of WTP is the Hicksian compensating variation. Because we ask respondents how many vaccines they would buy at price A, we actually observe a Marshallian demand function; consumer surplus, not Hicksian CV, is the area we calculate with eq. 9. This "uncompensated" demand should theoretically be adjusted for income in order to observe true Hicksian compensating variation, but we make the common assumption that the income effect is likely to be so small that the Marshallian CS which we observe is a reasonable approximation of Hicksian CV (Willig 1976).

(12) $$WTP_i = [\exp(\mathbf{X_i\beta} - p^*\beta_p)] / -\beta_p$$

Put another way, WTP is simply the expected count of vaccines purchased for the household at price p* (the term in braces in eq. 12) normalized by the negative of the coefficient on bid price. When the vaccine is provided without user charges (p*=0), WTP is the entire area under the demand curve and the expression collapses to:

(13) $$WTP_i = [\exp(\mathbf{X_i\beta})] / -\beta_p \quad \text{when } p^*=0$$

When p* is non-zero, the household's WTP is now comprised of the remaining consumer surplus and the expenditures on the vaccine. Eq. 12 characterizes the remaining consumer surplus, and household expenditures are:

(14) $$\text{Expenditures} = p^* \cdot \exp(\mathbf{X_i\beta} - p^*\beta_p)$$

and total HH WTP is:

(15) $$\text{HH WTP} = \underbrace{p^* \cdot \exp(\mathbf{X_i\beta} - p^*\beta_p)}_{\text{Expenditure}} + \underbrace{[\exp(\mathbf{X_i\beta} - p^*\beta_p)] / -\beta_p}_{\text{CS}}$$

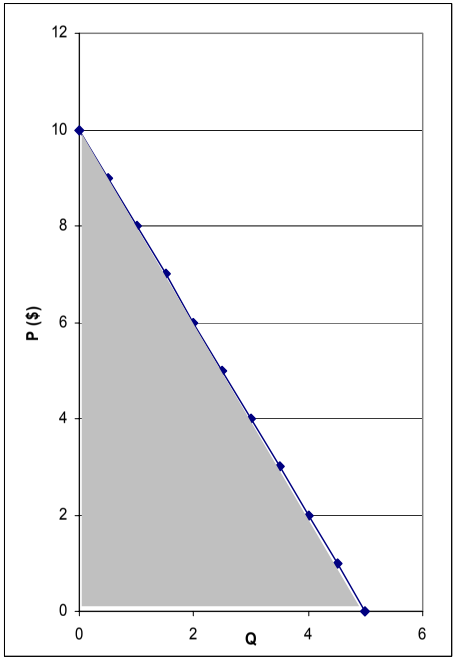
Note that the entire framework above can be applied for vaccine demand for household members of a specific age group (i.e. young children, school-children or adults). The only differences will be 1) *n* indexes only the number of household members in that age group, and 2) the characteristics included in the vector $\mathbf{X_i}$ may differ somewhat.

Furthermore, for policy analysis, we would like to know WTP to vaccinate one household member in a given age group rather than WTP to vaccinate the entire household or entire age group. Before explaining how to derive these per-person WTP benefits, I'll demonstrate the calculation of household WTP graphically.

Household WTP - A graphical approach

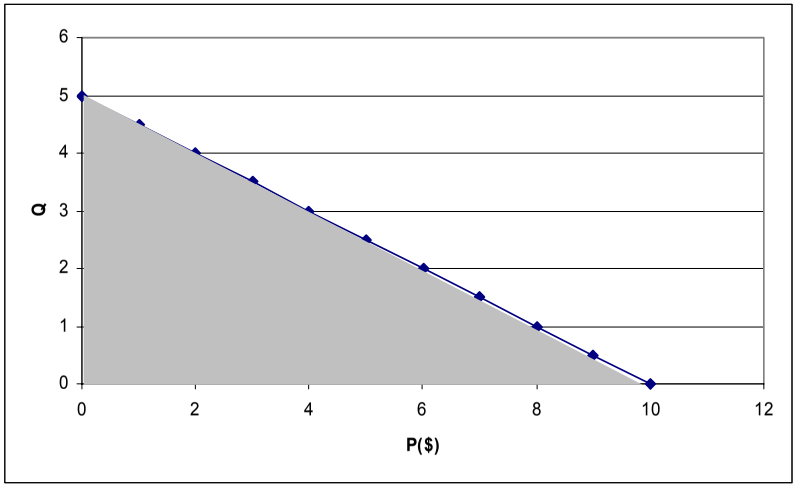
For simplicity, assume a linear demand function. Figure 1a plots the inverse demand curve $g^{-1}(\cdot)$ with prices as a function of quantities. WTP for a vaccine with no user charge is the area under this curve, and is calculated by integrating $g^{-1}(\cdot)$ over quantities (shown here for a household with 5 members). Figure 1b shows the exact same relationship between price and vaccines demanded, but now as the demand function $g(\cdot)$, where quantities are shown as a function of prices. WTP for a vaccine with no user charges is calculated by integrating $g(\cdot)$ over prices.

Figure 1a. Calculate WTP for a vaccine with no user charges by integrating the inverse demand curve over quantities….



Rotated

Figure 1b. …. or by integrating the demand curve over prices.



When users are charged some fee p* for the vaccine, they demand q* vaccines for their household. Household expenditures (or revenues to the vaccine provider) are the rectangle with area p*q*, and the household loses consumer surplus equal to the darker shaded triangles below. In Figure 2a, the remaining consumer surplus is the area under the inverse demand function between vaccine quantities 0 and q*, less the household's expenditures on the vaccine. In Figure 2b, the equivalent area is calculated as the area under the demand curve between vaccine prices p* and ∞ (here shown as a choke price of $10).

Figure 2a. Expenditures and consumer surplus with a user charge, in price-quantity (inverse demand) space

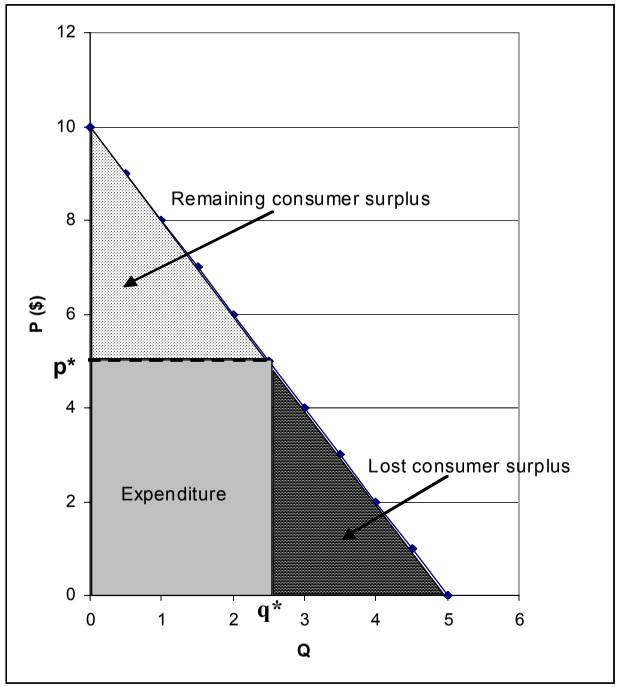


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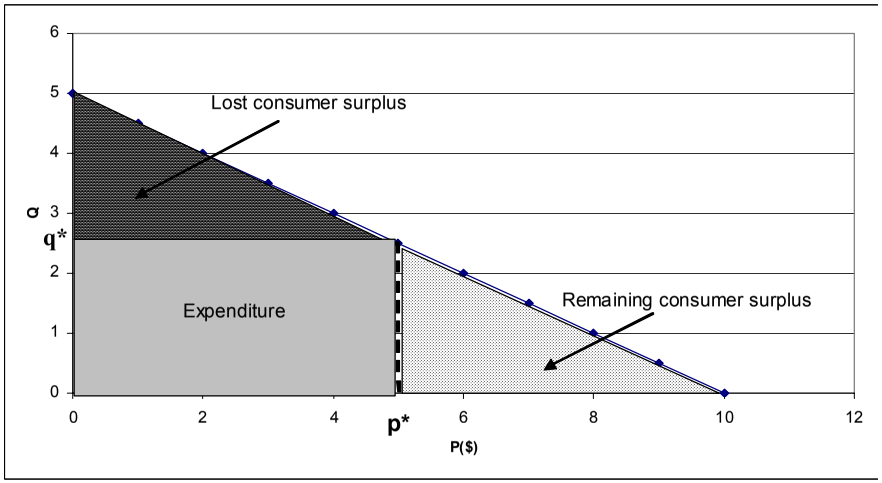
Figure 2b. Expenditures and consumer surplus with a user charge, in quantity- price (demand) space



Per-person WTP for vaccine with no user charge

To calculate per-capita WTP of a vaccine with no user charge, I divide the total household (or age group) WTP by the predicted number of vaccines demanded for the household (or age group) when the price is zero. All household-level characteristics $\mathbf{X_i}$ drop out and the per-capita benefit of the vaccine collapses to the negative inverse of the price coefficient:

$$(16) \qquad \frac{HHWTP}{predicted\_count} = \frac{\frac{\exp(X_i\beta)}{-\beta_p}}{\exp(X_i\beta)} = \frac{-1}{\beta_p}$$

To account for important differences in WTP by neighborhood (Tiljala vs. Beliaghata) and time-to-think treatment, we could include as independent variables interaction terms between price and neighborhood and between price and time to think. Per-capita WTP for a vaccine with no user charges would then become:

$$(17) \qquad \frac{HHWTP}{predicted\_count} = \frac{\frac{\exp(X_i\beta)}{-(\beta_p + \beta_{price*Tiljala} + \beta_{price*TTT})}}{\exp(X_i\beta)} = \frac{-1}{-(\beta_p + \beta_{price*Tiljala} + \beta_{price*TTT})}$$

(18) Per-capita WTP = $-1 / \beta_p$ (Beliaghata respondents, No TTT)

(19) Per-capita WTP = $-1 / (\beta_p + \beta_{price*TTT})$ (Beliaghata respondents, TTT)

(20) Per-capita WTP = $-1 / (\beta_p + \beta_{price*Til})$ (Tiljala respondents, NTTT)

(21) Per-capita WTP = $-1 / (\beta_p + \beta_{price*Til} + \beta_{price*TTT})$ (Tiljala respondents, TTT)

To calculate the percent of our sample who would take a free vaccine I sum the expected number of vaccines purchased in all *H* households in the sample and divide by the total number of household members in the sample (eq. 22)[46]. The equivalent percentage for a specific age group

[46] To extrapolate to the whole population in our study areas, we need the percent of household members who would take the free vaccine. We could use the raw percent of respondents who either said yes to the offer price

divides the sum of the predicted number of vaccines purchased for that age group in all *H* households (with a member that age) by the total number of people in that age group in the sample.

(22) Percent coverage for free vaccine = $\sum_{i=1}^{H} \exp(\mathbf{X_i\beta})$ / $\sum_{i=1}^{H}$ (*Members in household i)*

In practice, however, we prefer results from separate models for each of the two neighborhoods results to models which pool Tiljala and Beliaghata responses (see below). With separate models, there is obviously no need for the price-neighborhood interaction ($\beta_{price*Til}$). Because there was no time-to-think experiment in Tiljala, however, we need to extrapolate time-to-think results in Beliaghata to Tiljala. We apply to Tiljala the average change in the intercept (eq. 22) and slope (β_p) observed comparing the Beliaghata NTTT and TTT experimental groups (see below).

Per-person WTP with user charge

Using a similar approach, the per-capita household (or age group) WTP with a user fee of p* will be:

HH WTP = Per-capita expenditures + Per-capita CS

(23) = $\frac{[p^* \cdot \exp(\mathbf{X_i\beta} - p^*\beta_p)]}{\exp(\mathbf{X_i\beta} - p^*\beta_p)}$ + $\frac{[\exp(\mathbf{X_i\beta} - p^*\beta_p)] / -\beta_p}{\exp(\mathbf{X_i\beta} - p^*\beta_p)}$

(24) = p* + $-1/\beta_p$

As in eqs.17 – 21 above, the per-capita CS term could include interactions of price with neighborhood and price with time to think (suppressed in eq. 24 to avoid notational clutter), although in practice we run models on the two neighborhood separately.

The percent of household members (or age group members) covered at price p* is:

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plus the percent who said they would take a free vaccine and extrapolate that percent to all household members, adults and children (or use the respondent "stoplight" information).

(25) Percent coverage at $p^* = \sum_{i=1}^{H} \exp(\mathbf{X_i\beta} - p^*\beta_p) \; / \; \sum_{i=1}^{H} (\textit{Members in household i})$

Household WTP results

Raw demand

Figures 3 – 8 show the raw percentage of age groups covered in the two neighborhoods by vaccine type and time to think treatment.

Figure 3. Raw demand: Beliaghata **cholera** without time to think

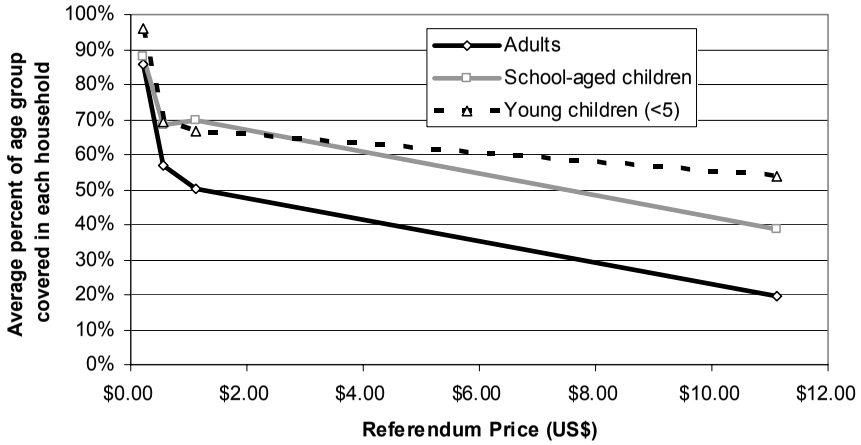


Figure 4. Raw demand: Beliaghata **cholera** with time to think

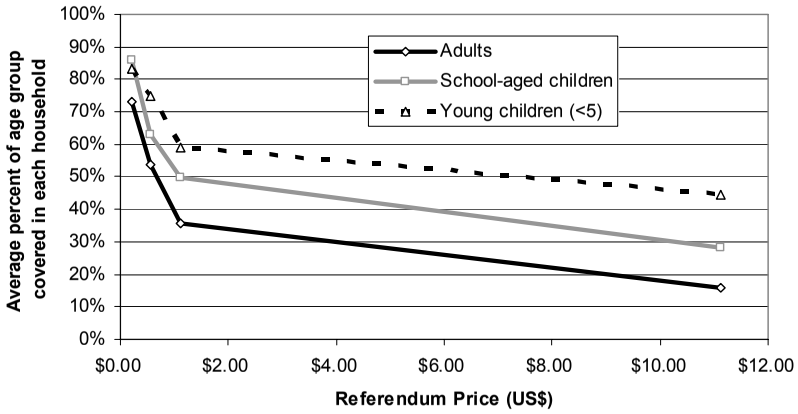


Figure 5. Raw demand: Beliaghata **typhoid** without time to think

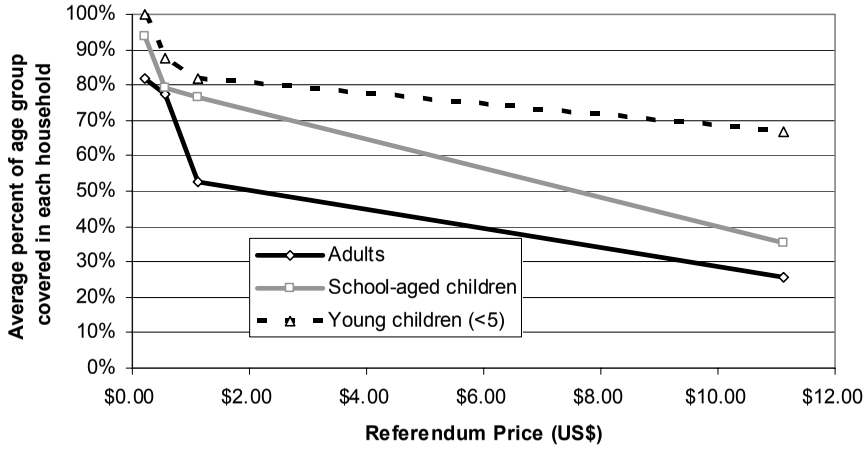


Figure 6. Raw demand: Beliaghata **typhoid** with time to think

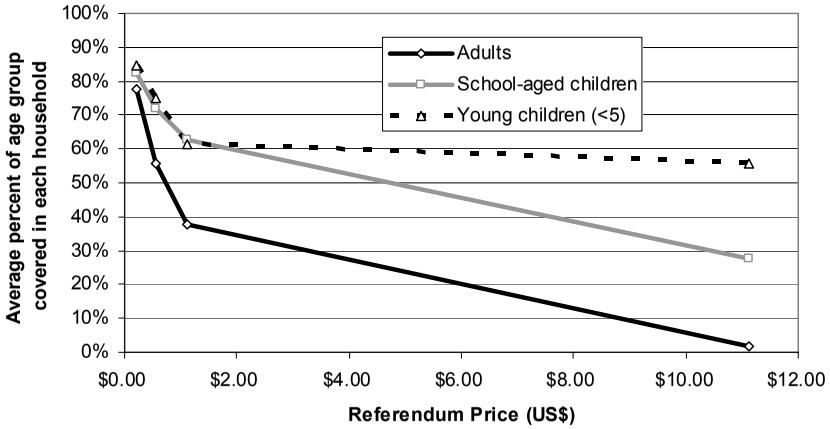


Figure 7. Raw demand: Tiljala **cholera** without time to think

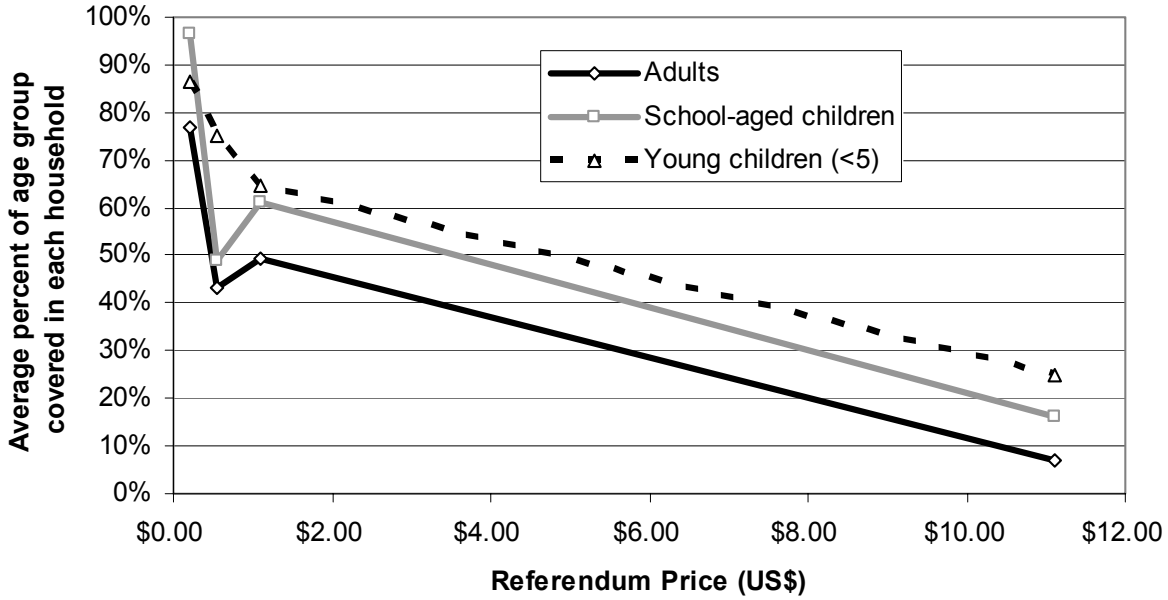
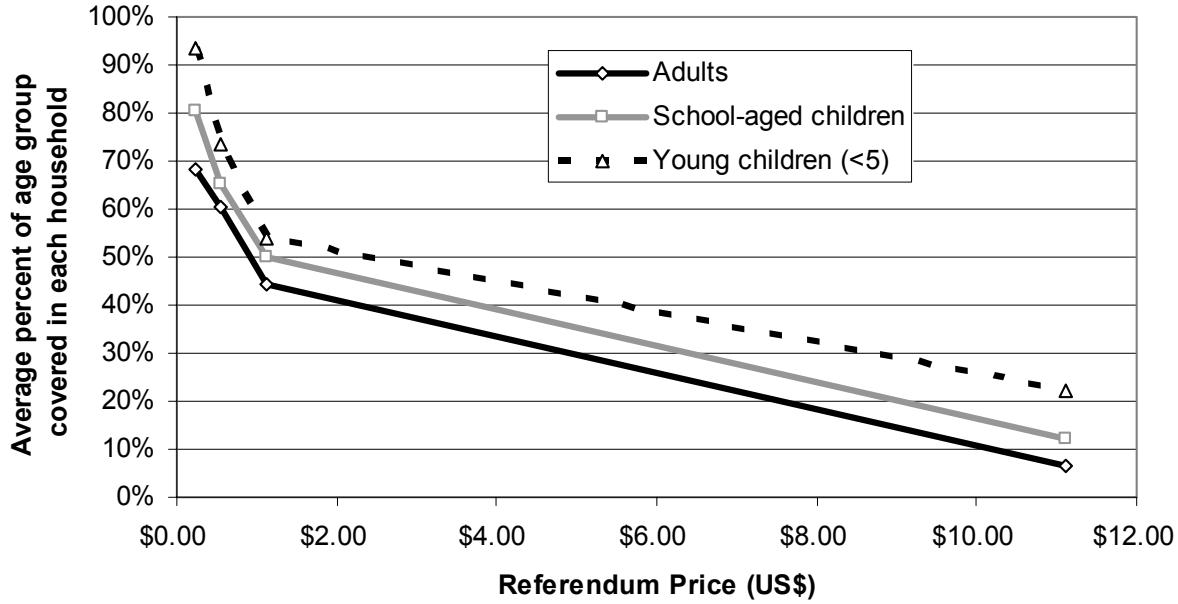


Figure 8. Raw demand: Tiljala **typhoid** without time to think



Multivariate results

Table 1 gives descriptive statistics for the explanatory variables used in the multivariate household demand (the same explanatory variables were used in the estimation of respondent demand). Tables 2 and 3 presents results from negative binomial regressions of the number of vaccines purchased for 1) young children (1-4yrs), 2) school-aged children (5-14yrs) and 3) adults over 15. These pool demand for both diseases but run separate regressions by neighborhood. I present both a "parsimonious" and a "full" specification.

Table 1. Descriptive statistics of sample respondents

Variable name	Description		Beliaghata (n=559)	Tiljala (n=276)
			Mean (SD)	Mean (SD)
Respondent characteristics				
Male	Gender =1 if male, =0 if female		52%	48%
Age	Age, years		36 yrs (8.0)	35 yrs (9.4)
Muslim	Religion =1 if Muslim, 0=else		1%	76%
Education Low	=1 if respondent completed 1- 9 years of school		44%	44%
Education Mid	=1 if respondent completed 12 years of school or vocational school		30%	13%
Education High	=1 if respondent completed university, post-graduate or prof. course		17%	3%
Household characteristics				
Monthly per capita income	Monthly household income divided by household size, Indian Rs.		Rs. 1246 (1912)	Rs. 585 (546)
Num. young children	Number of young children (0-5 yrs.)		0.5 (0.65)	0.6 (0.8)
Num .school-aged children	Number of older children and teens (6 - 18 yrs)		1.2 (0.93)	2.0 (1.5)
Num. of adults	Number of adults (18+ yrs),		3.6 (1.9)	2.8 (1.3)
Health and disease-related characteristics				
Know person with disease	=1 if knows someone who has had disease (incl. respondent and hh members)	Cholera Typhoid	41% 46%	47% 55%
Disease is common	=1 if disease is common or very common in my neighborhood	Cholera Typhoid	24% 22%	43% 37%
Likely to get disease	=1 if "somewhat likely" or "very likely" that respondent will get disease in the next 5 years	Cholera Typhoid	40% 38%	42% 48%
Disease is serious for adults	=1 if disease is "serious" or "very serious" for adults	Cholera Typhoid	65% 58%	65% 65%
HH member had vaccine	=1 if someone in household had vaccine	Cholera or TABC Typhoid or TABC	26% 23%	17% 15%
Never boil drinking water	=1 if household never boils drinking water & has does not have Aquaguard water filter		58%	65%
Distance to health facility	Distance to nearest private health facility, minutes		8.9 (6.7)	12.5 (13.5)

[a] 37 Beliaghata respondents (6.6%) and 9 Tiljala respondents (3.3%) could not (or would not) provide income information. These missing values were replaced with the neighborhood median income. 1 US$ = 45 Rs.

Table 2. Negative binomial regressions of demand for vaccines in Beliaghata

	Adults		**School-aged children**		**Young children**	
	Full	Parsim.	Full	Parsim.	Full	Parsim.
Price ('000 Rs.)	-3.437***	-3.431***	-1.962***	-1.919***	-0.750**	-0.741**
	(-0.564)	(-0.562)	(-0.517)	(-0.515)	(-0.333)	(-0.334)
Cholera	-0.154*	-0.096	-0.106	-0.09	-0.174	-0.199**
	(-0.093)	(-0.08)	(-0.098)	(-0.081)	(-0.106)	(-0.1)
Price * Cholera	0.867	0.869	0.144	0.112	0.148	0.179
	(-0.746)	(-0.754)	(-0.688)	(-0.688)	(-0.545)	(-0.55)
Time to think	-0.326***	-0.318***	-0.166**	-0.177**	-0.159	-0.178**
	(-0.076)	(-0.076)	(-0.074)	(-0.074)	(-0.1)	(-0.09)
Monthly per capita income	0.041***	0.045***	0.034	0.046*	0.008	0.008
	(-0.013)	(-0.013)	(-0.027)	(-0.027)	(-0.007)	(-0.007)
Education Low	0.258	0.259	0.229	0.24	0.123	0.166
	(-0.167)	(-0.169)	(-0.174)	(-0.175)	(-0.251)	(-0.251)
Education Mid	0.433**	0.468***	0.370**	0.379**	0.208	0.245
	(-0.171)	(-0.172)	(-0.174)	(-0.174)	(-0.257)	(-0.253)
Education High	0.204	0.292	0.292	0.312*	0.145	0.222
	(-0.176)	(-0.177)	(-0.183)	(-0.181)	(-0.269)	(-0.262)
Num. young children	-0.236***	-0.219**	-0.271**	-0.243**	0.500***	0.485***
	(-0.088)	(-0.09)	(-0.115)	(-0.115)	(-0.07)	(-0.069)
Num .school-aged children	-0.282***	-0.272***	0.460***	0.460***	-0.277***	-0.267***
	(-0.054)	(-0.054)	(-0.048)	(-0.049)	(-0.086)	(-0.086)
Num. of adults	0.165***	0.167***	0.006	0.005	-0.007	-0.006
	(-0.021)	(-0.021)	(-0.018)	(-0.018)	(-0.025)	(-0.025)
Know person with disease	0.147*	0.146*	0.045	0.05	0.093	0.076
	(-0.077)	(-0.076)	(-0.076)	(-0.075)	(-0.092)	(-0.088)
Never boil drinking water	-0.138*		-0.134*		-0.073	
	(-0.075)		(-0.069)		(-0.098)	
Disease is serious for adults	0.018		-0.093		-0.092	
	(-0.078)		(-0.08)		(-0.096)	
Likely to get disease	0.037		-0.082		-0.061	
	(-0.075)		(-0.079)		(-0.083)	
Wait time at private clinic	-0.005**		0.000		-0.002	
	(-0.002)		(-0.002)		(-0.002)	
Had cholera or TABC vaccine	0.12		0.039		-0.083	
	(-0.124)		(-0.105)		(-0.18)	
Had typhoid or TABC vaccine	-0.11		-0.081		-0.04	
	(-0.13)		(-0.131)		(-0.148)	
Constant	0.573***	0.297	-0.602***	-0.811***	-0.413	-0.590**
	(-0.216)	(-0.198)	(-0.22)	(-0.202)	(-0.27)	(-0.257)
N =	551	551	398	398	169	169

Robust standard errors in parentheses, * significant at 10%; ** significant at 5%; *** significant at 1%

Table 3. Negative binomial regressions of demand for vaccines in Tiljala

	Adults		**School-aged children**		**Young children**	
	Full	Parsim.	Full	Parsim.	Full	Parsim.
Price (‘000 Rs.)	-4.594***	-4.587***	-4.441***	-4.508***	-3.501***	-3.213***
	(-1.323)	(-1.341)	(-1.311)	(-1.337)	(-0.812)	(-0.817)
Cholera	-0.106	-0.104	-0.146	-0.207	-0.014	0.036
	(-0.138)	(-0.122)	(-0.141)	(-0.142)	(-0.178)	(-0.18)
Price * Cholera	0.39	0.308	2.01	2.231	0.841	0.692
	(-1.594)	(-1.6)	(-1.616)	(-1.587)	(-1.301)	(-1.312)
Monthly per capita income	0.342***	0.348***	0.273***	0.203**	0.691***	0.438***
	(-0.122)	(-0.117)	(-0.099)	(-0.103)	(-0.213)	(-0.166)
Education Low	0.254*	0.271**	0.390**	0.453***	0.546***	0.555**
	(-0.134)	(-0.131)	(-0.176)	(-0.175)	(-0.212)	(-0.22)
Education Mid	0.183	0.269	0.537***	0.649***	0.845***	0.915***
	(-0.185)	(-0.184)	(-0.208)	(-0.195)	(-0.3)	(-0.304)
Education High	0.05	0.174	0.212	0.429	0.591	0.24
	(-0.274)	(-0.273)	(-0.265)	(-0.266)	(-0.43)	(-0.399)
Num. young children	0.013	0.016	-0.046	-0.013	0.397*	0.307
	(-0.088)	(-0.086)	(-0.089)	(-0.092)	(-0.212)	(-0.204)
Num .school-aged children	-0.089*	-0.080*	0.303***	0.344***	0.006	0.002
	(-0.047)	(-0.046)	(-0.059)	(-0.055)	(-0.064)	(-0.058)
Num. of adults	0.255***	0.262***	0.019	0.025	0.074**	0.085**
	(-0.028)	(-0.028)	(-0.034)	(-0.036)	(-0.035)	(-0.036)
Know person with disease	-0.042	-0.05	-0.039	-0.039	0.012	-0.053
	(-0.125)	(-0.121)	(-0.135)	(-0.132)	(-0.161)	(-0.148)
Never boil drinking water	-0.187*		-0.209		0.024	
	(-0.112)		(-0.128)		(-0.148)	
Disease is serious for adults	0.082		0.328**		-0.105	
	(-0.122)		(-0.142)		(-0.183)	
Likely to get disease	-0.099		0.106		0	
	(-0.115)		(-0.132)		(-0.155)	
Wait time at private clinic	-0.004		-0.008**		0.003	
	(-0.004)		(-0.004)		(-0.003)	
Had cholera or TABC vaccine	0.152		-0.365*		-0.246	
	(-0.157)		(-0.187)		(-0.298)	
Had typhoid or TABC vaccine	0.058		-0.273		-1.505	
	(-0.176)		(-0.251)		(-0.964)	
Constant	0.143	-0.164	-0.163	-0.405**	-0.591**	-0.815***
	(-0.237)	(-0.192)	(-0.234)	(-0.182)	(-0.269)	(-0.202)
N =	275	275	210	210	104	104

Robust standard errors in parentheses, * significant at 10%; ** significant at 5%; *** significant at 1%

Fitting exponential demand functions and calculating WTP per vaccinated person

I next plotted the predicted coverage at various prices from the parsimonious specifications for each group and fit an exponential demand function to the data. Table 4 presents the intercepts and slope parameters for those fitted exponential functions for Beliaghata, and the implied average WTP per vaccinated person. The values in bold type are the ones used in the investment case. Because no respondents were given time to think in Tiljala, I adjust the slope and intercept parameters by the average time to think effect in Beliaghata (the percentage change in slope and intercept from NTTT to TTT). The adjusted and unadjusted parameter values for Tiljala are given in Table 5.

Table 4. Demand function parameters for Beliaghata

	Intercept (coverage at zero)	**Slope** (price, US$)	**WTP per vacc. person** (US$)
Adults			
Beliaghata Cholera No TTT	62%	-0.080	$12.5
Beliaghata Cholera TTT	60%	-0.181	**$5.5**
Beliaghata Typhoid No TTT	69%	-0.117	$8.5
Beliaghata Typhoid TTT	67%	-0.220	**$4.6**
School-aged children			
Beliaghata Cholera No TTT	70%	-0.072	$13.9
Beliaghata Cholera TTT	69%	-0.100	**$10.0**
Beliaghata Typhoid No TTT	78%	-0.070	$14.2
Beliaghata Typhoid TTT	78%	-0.099	**$10.1**
Young children			
Beliaghata Cholera No TTT	76%	-0.022	$46.2
Beliaghata Cholera TTT	81%	-0.036	**$27.8**
Beliaghata Typhoid No TTT	88%	-0.026	$38.7
Beliaghata Typhoid TTT	93%	-0.040	**$25.1**

Table 5. Demand function parameters for Tiljala

	Intercept (coverage at zero)	**Slope** (price, US$)	**WTP per vacc. person** (US$)
Adults			
Tiljala Cholera (Unadjusted)	63%	-0.194	$5.2
Tiljala Cholera Adjusted	60%	-0.435	**$2.3**
Tiljala Typhoid (Unadjusted)	70%	-0.207	$4.8
Tiljala Typhoid Adjusted	69%	-0.389	**$2.6**
School-aged children			
Tiljala Cholera (Unadjusted)	65%	-0.104	$9.7
Tiljala Cholera Adjusted	59%	-0.145	**$6.9**
Tiljala Typhoid (Unadjusted)	80%	-0.203	$4.9
Tiljala Typhoid Adjusted	80%	-0.284	**$3.5**
Young children			
Tiljala Cholera (Unadjusted)	89%	-0.095	$10.6
Tiljala Cholera Adjusted	93%	-0.157	**$6.3**
Tiljala Typhoid (Unadjusted)	87%	-0.158	$6.4
Tiljala Typhoid Adjusted	91%	-0.243	**$4.2**

APPENDIX D: Results for Beliaghata

It is useful to begin by thinking about how the results for the Beliaghata neighborhood might be different from the Tiljala analysis presented in the main body of the dissertation. Recall that information on incidence and cost of illness was collected in Narkeldanga, a poor slum with what NICED believed were the highest cholera and typhoid incidences in the city. We argued that Tiljala is a similar neighborhood and applied the Narkeldanga data to our case study without adjustments. However, incidence is likely to be smaller in Beliaghata. One might also suspect that the private costs of illness would be higher in Beliaghata as incomes are higher – Beliaghata residents may spend more on medicines and treatment and the opportunity cost of their time will be higher on average than in Tiljala. VSL measures (from Matlab, Bangladesh) are also likely to be higher because average incomes in Beliaghata are higher than in Matlab. We would seem to have two options: apply the incidence, COI, and VSL data without adjustment, or guess at an adjustment factor to decrease incidence and increase COI and VSL.

How would an *ad hoc* adjustment affect benefit measures? The COI, VSL and BPC net benefit measures all have a constant marginal benefit per case (i.e. they do not change with user fees). If this constant benefit per case is larger than costs, it will pass and a user fee of zero is optimal, regardless of private demand or the coverage rate at zero user fee. Both the COI and VSL marginal benefit measures would use no data collected in Beliaghata: the parameters that drive this calculation are incidence, public and private COI, CFR and VSL. Because incidence is likely to be lower in Beliaghata, but VSL and COI are likely to be higher, these two might offset each other and the Tiljala results for COI and VSL net benefits would equally apply to Beliaghata. If they did not offset each other and the policy advice changed, this would be driven entirely by our assumptions about how to adjust the parameters. This will also be true of all the cost-effectiveness measures.

The WTP and BPC net benefit measures would change, however, because they are based on data collected in Beliaghata. These measures are driven almost entirely by two factors: vaccine cost

and average WTP per vaccinated person (public COI savings were a very small factor in these benefit measures for Tiljala, and they are similarly small for Beliaghata). As described in Appendix C, average WTP in Beliaghata was much higher than Tiljala (Tables 1 and 2), driven in large part because a large number of respondents bought vaccines for young children even at very high prices (see Figures 3 – 6 in Appendix C). Using these mean WTP estimates, it's clear that a program that provided either cholera vaccines (avg cost ~US$5) or typhoid vaccines (avg cost ~ US$2.5) without user fees to children would pass using the WTP net benefit measure. Programs for adults would be likely to pass. The demand intercepts are similar in Beliaghata and Tiljala (except for cholera vaccines for school children), and they would in any case only affect the absolute value of net benefits.

Table 1. Demand function parameters for Beliaghata

	Intercept (coverage at zero)	**Slope** (price, US$)	**WTP per vacc. person** (US$)
Adults			
Beliaghata Cholera TTT	60%	-0.181	**$5.5**
Beliaghata Typhoid TTT	67%	-0.220	**$4.6**
School-aged children			
Beliaghata Cholera TTT	69%	-0.010	**$10.0**
Beliaghata Typhoid TTT	78%	-0.099	**$10.1**
Young children			
Beliaghata Cholera TTT	81%	-0.036	**$27.8**
Beliaghata Typhoid TTT	93%	-0.040	**$25.1**

Table 2. Demand function parameters for Tiljala

	Intercept (coverage at zero)	**Slope** (price, US$)	**WTP per vacc. person** (US$)
Adults			
Tiljala Cholera Adjusted	60%	-0.435	**$2.3**
Tiljala Typhoid Adjusted	69%	-0.389	**$2.6**
School-aged children			
Tiljala Cholera Adjusted	59%	-0.145	**$6.9**
Tiljala Typhoid Adjusted	80%	-0.284	**$3.5**
Young children			
Tiljala Cholera Adjusted	93%	-0.157	**$6.3**
Tiljala Typhoid Adjusted	91%	-0.243	**$4.2**

In conclusion, it seems as likely as not that the results using the cost-effectiveness ratios, the COI net benefits or the VSL net benefits will be similar to those discussed in the Tiljala case. Using WTP benefits (or BPC benefits with herd immunity), though, both programs would most likely pass a social cost-benefit test.

However, it seems even less likely that policymakers would be interested in using scarce public subsidies to provide vaccines for free in an area where incomes are higher and disease burden is probably lower. Because demand is much less responsive to price (especially for young children), the government could provide the vaccine at full cost and still cover a significant fraction of the population. We expect that 54%, 59% and 19% of the young children, school children and adults who heard about the program would receive a cholera vaccine if it were provided at the full cost of US$5. Assuming a population of 78,000 and using all of the same parameter values as in Tiljala except for those in Table 1, a program in Beliaghata with uniform user fees set to the full cost would produce about US$96,000 in WTP net benefits for cholera. It would not produce positive net COI benefits or VSL+COI net benefits. Including the herd immunity effects, the program would produce COI, VSL, WTP and BPC net benefits of (-$103k), (-$59k), $101k and $128k. To achieve revenue-neutrality but cross-subsidize free cholera vaccines for all children under 5, the price for adults and school-children would need to be set only a bit higher than full cost, around US$5.4(with herd immunity effects).

We expect that 68%, 53% and 36% of young children, school children and adults who hear about the program would take a typhoid vaccine if it were provided at the full cost of US$2.4. Again changing only the demand and WTP parameters and leaving all others at their Tiljala values, a full-cost recovery program with uniform user fees of US$2.4 would produce COI, VSL+COI, and WTP net benefits of (-$91k), $14k, and $128k. To achieve revenue-neutrality but cross-subsidize free typhoid vaccines for all children under 15, the adult price would need to be set around US$4.8 (about Rs.215). VSL+ COI and WTP net benefits would be $33k and $112k with this cross-subsidy program.

APPENDIX E: Vaccine Delivery Costs

As described in the main text, the best source of delivery cost data for the policy analysis comes from the cholera and typhoid vaccine trials in the Narkeldanga neighborhood of Kolkata. To summarize, the cholera trial was able to deliver 139,000 doses of vaccine for an average cost of US$1.7 per dose (excluding manufacturing costs). The typhoid trial delivered 39,000 doses of typhoid vaccine at an average cost of US$2.4 per dose. How do these values compare with other delivery cost estimates in the literature?

Several studies have examined delivery costs in the context of cholera vaccination campaigns or trials. Cookson (1997) found the delivery cost of providing 240,000 doses of the live CVD cholera vaccine (which requires only dose) in two provinces in Argentina to be about US$0.32 (in 2006$). Costs to deliver about 63,000 doses of the killed oral cholera vaccine in a refugee camp in Uganda were on the order of US$0.30 per dose (Legros et al. 1999). A similar study in Vietnam (Naficy et al. 2001) found delivery costs of US$0.14 per dose for 631,000 doses of the killed oral cholera vaccine. A large trial in Beira, Mozambique had delivery costs of US$0.67 per dose (Cavailler et al. 2006). In another study in Vietnam, the cost of mass vaccination using whole-cell killed cholera vaccine was about $0.89 per fully vaccinated individual (Thiem *et al.* 2003) . Finally, a mass campaign against cholera in Indonesia following the tsunami in December 2004 cost approximately US$17.6 per fully immunized person, although the conditions on the ground were extremely harsh and unlikely to apply to an endemic setting like Kolkata (WHO 2006). We know of no published study on the cost of typhoid programs, although Poulos et al (2004) extrapolate (unpublished) estimates from Vietnam that indicate that total costs <u>including</u> manufacturing, transport and delivery are on the order of US$0.90 – US$1.7 per dose. None of the estimates above include the financial cost to users of traveling to receive the vaccine or the opportunity cost of their time spent traveling and waiting. Lauria (2007) reviews data from 19 vaccine cost studies in low income countries and finds that the

median delivery cost per dose is US$0.68 (mean US$1.36), with estimates ranging from US$0.10 to US$5.7 per dose. Only 30% of the delivery cost estimates were larger than US$1 per dose.

This presents somewhat of a dilemma. Based on Lauria's (2007) summary of the literature, the best estimate for delivery costs is on the order of US$0.7 – $1 per dose. Data from actual vaccine trials in Kolkata, in a neighborhood similar to Tiljala, however, indicate that delivery costs are considerably higher than most other published vaccine studies – US$1.7 - $2.4. This higher cost may be due to the research nature of the vaccine trials (although most of the studies cited above were also research trials or demonstration projects), or a systematic downward bias in existing published studies. It may, however, reflect the reality that delivering vaccines is more expensive in slums in Kolkata than in other settings, perhaps because staff needs and salaries are higher. In the analysis below, we present several approaches for examining the existing vaccine delivery cost data in order to estimate the most plausible delivery costs for the programs in question.

Table 1. Existing data on delivery-only costs for cholera or typhoid vaccines

Site	Disease	Number clinics N	Days of operation D	Number of doses Q	Total cost (2007 $) C	Average cost C/Q
India[a]	Cholera	34	33	139k	$236k	1.60
India[b]	Typhoid	20	30	38k	$90k	2.31
Mozambique[c]	Cholera	10	14	98k	$57k	0.59
Uganda[d]	Cholera	15	35	63k	$11k	0.17
Vietnam[e]	Cholera	192	20	591k	$66k	0.11

References: [a] NICED 2007; [b] NICED 2007; [c] Cavailler et al. 2006; [d] Legros et al. 1999; [e] Naficy et al. 2001

Approach 1: Estimate fixed cost + constant average cost based on Kolkata data only

Because the two vaccine trials were done in the same area over roughly the same time frame, there is a unique opportunity to use differences in the number of doses delivered and differences in costs to identify whether there are economies of scale in delivery. The Kolkata data would seem to indicate that there are: *ceteris paribus*, the cholera trial delivered 3.7 times more doses than the

typhoid trial but cost only 2.5 times more (or viewed more simply, the larger cholera trial had a lower average cost). In this first approach, we fit a simple OLS model to the data from the Kolkata trial, regressing the number of doses (139k and 38k) on total cost ($221k and $87k), with a constant. This approach by definition assumes economies of scale because average cost will decline with a larger numbers of doses delivered. This OLS approach yields a delivery cost function:

(1) Total delivery cost (C) = $36,000 + $1.44 · doses

Approach 2: *Fit a power function to Kolkata data only*

The second approach uses the data to estimate the parameters of a two-parameter power function ($C = \alpha \cdot Q^{\beta}$). The first parameter of the power function α, an intercept, gives the delivery cost if only one person is vaccinated. The second parameter β represents economies of scale: if $\beta=1$ then there are constant returns to scale, and α will be the constant marginal cost of delivering the vaccine. If $0<\beta<1$, there are economies of scale and the marginal and average costs decrease as more people are vaccinated. If $0<\beta<1$, there are diseconomies of scale and the marginal and average delivery costs increase as more people are vaccinated. Substituting the data from Table 1 gives:

(2) Typhoid: $\$90{,}000 = \alpha \cdot (38{,}000)^{\beta}$

(3) Cholera: $\$236{,}000 = \alpha \cdot (139{,}000)^{\beta}$

(4) $\$90k / \$236k = (38k/139k)^{\beta}$

(5) $\beta = \log(\$90k / \$236k) / \log(38k/139k) = 0.74 = \beta$

These results suggest that there are economies of scale: for a 1% increase in the number of doses delivered, costs rise only 0.74%. After solving for β, one can solve for α using either equation, giving a value of $38, so the total delivery cost function is:

(6) $$\text{Total costs} = \$38 \cdot Q^{0.74}$$

Approach 3: *Predict costs for smallest and largest possible programs with power function and fit OLS*

One drawback of the first approach is that the fixed costs implied by the model ($38,000) is likely to be too high for a small, targeted program. In Tiljala, the smallest possible program would be a typhoid program that targets only children aged 2 -5 (about 6,000 children). It would require the delivery of only 6,000 doses. Eq. (1) implies that the average delivery cost of this program would be about US$7.4 per dose, which seems implausibly high. This raises the more general point that we need to estimate delivery costs for programs that are outside the domain of the functions we're estimating (smaller than 38,000 doses or larger than 139,000 doses).

The third approach, therefore, is a hybrid of the first two. We assume that the power function estimated above is the "true" model and use it to predict the total costs of the smallest and largest possible programs (the largest possible program is one in which all 120,000 residents of Tiljala receive two doses of cholera vaccine). We then fit an OLS model to these two data points to estimate a cost function with fixed costs and constant marginal costs:

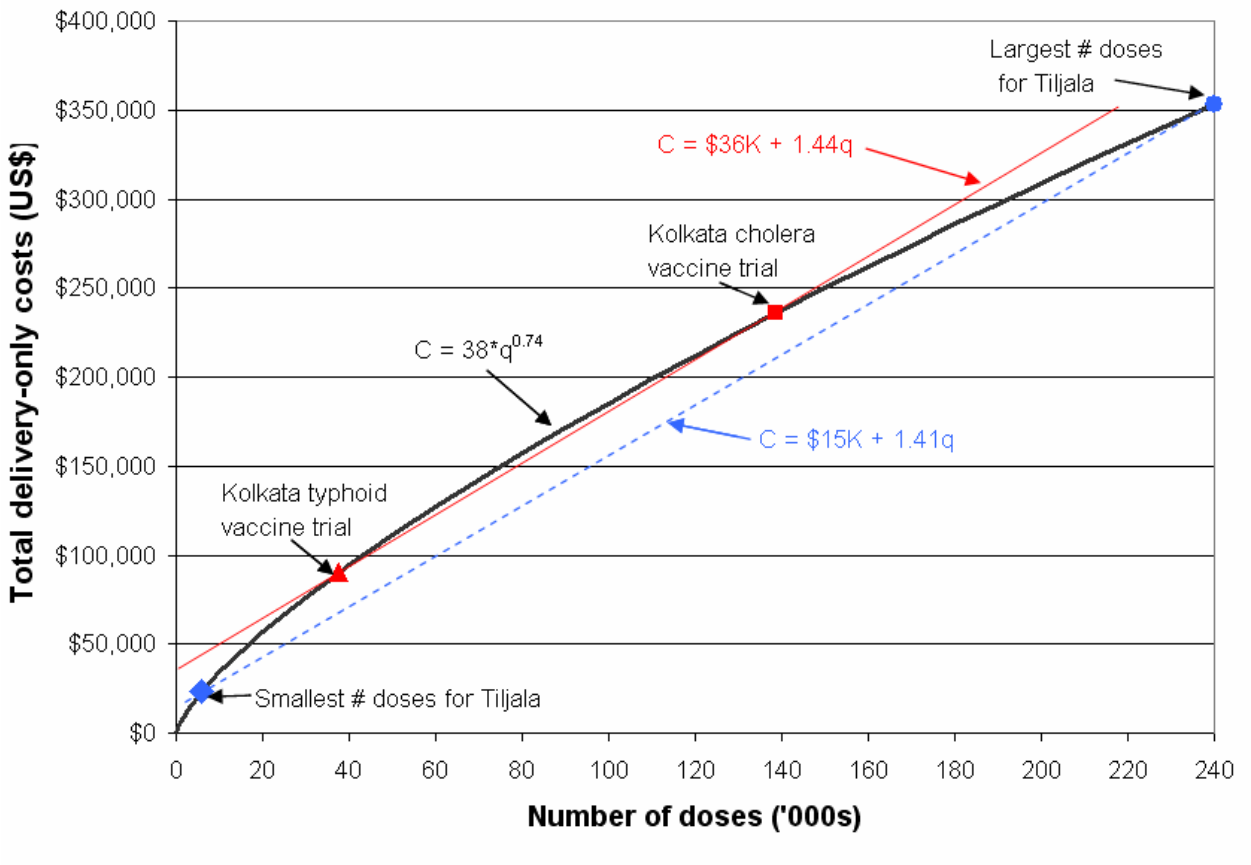
(7) $$\text{Cost (smallest program)} = \$38 \cdot (6000)^{0.74} = \$23{,}000$$

(8) $$\text{Cost (largest program)} = \$38 \cdot (240{,}000)^{0.74} = \$353{,}000$$

Fitting an OLS model to these two points give a cost function of the form:

(9) $$C = \$15{,}000 + \$1.41\, Q$$

Figure 1. Estimating total delivery costs with three different approaches



Differences between cholera and typhoid trials

These simple exercises, however, ignore differences between the two trials programs that may affect our estimate of the returns to scale. First, the cholera trial was done two years after typhoid trial and there may have been price or salary inflation. Adjusting cholera costs downward to account for inflation make the economies of scale look even larger (a smaller β in Eq. 6). Over a period of only two years, this effect would seem to be minimal, and inflation was in any case only about 5-6% over that period (IMF)).

Second, the typhoid vaccine requires a needle injection whereas the cholera vaccine is oral. However, dropper-like syringes were used in the cholera trial (apparently because the smell of the vaccine was bad), and in fact average cost for syringes and safety boxes per dose delivered was higher for cholera.

Third, the typhoid vaccine has more stringent cold chain requirements than cholera. In fact, average cost for cold chain per dose was US$0.21 for typhoid vs. US$0.10 for cholera. This would mean that Eq. 6 overestimated economies of scale (β closer to 1). If we set the average cold chain cost per dose equal for both programs, β increase from 0.74 to 0.79.

Fourth, since the program was administered by the same staff at NICED in the same neighborhood, there may have been a learning effect from typhoid trial so that the cholera trial was more efficient. This would mean that the lower average cost in the cholera trial was not the result of economies of scale but rather learning. This would again mean that Eq. 6 overestimated economies of scale (β closer to 1). Although this effect seems likely, we have no data to bound its effect on β.

Finally, it is obvious that what is really driving the calculation is the differences in staff cost per dose. Setting them equal in both programs implies a β much closer to 1 (β=0.95). However, this is precisely where you might expect to see returns to scale – the same salaried nurse can vaccinate more people.

Overall, it seems that there are important reasons to think that our estimate of β is too small, and that we may be overstating economies of scale for a vaccine program in a Kolkata slum. Table 2 shows how varying our assumption of the β parameter in eq. (6) changes the results for Method #3. As the economy of scale factor approaches 1, fixed costs get smaller and constant marginal costs increase.

Table 2. Effect of varying scale parameter of power cost function

β	Implied α	Implied cost equation from Method #3
0.74	38	C = $15,000 + 1.41Q
0.80	18	C = $10,000 + 1.48Q
0.85	10	C = $ 7,000 + 1.54Q
0.90	6	C = $ 4,400 + 1.59Q
0.95	3	C = $ 2,000 + 1.65Q

Approach 4: Regressions based on number of clinics

One final approach would be to use data from several studies on the number of vaccination clinics or outposts operated for each campaign to calculate fixed or set-up costs as a function of the scale of the program. For example, suppose that the vaccine would be distributed as part of a mass campaign. Vaccines are distributed from temporary clinics set up specifically for the purpose of vaccination. Suppose each clinic could vaccinate 100 people per day. If the campaign targeted 60,000 people and was to last 30 days, the government would need to set up 20 vaccination clinics. The total delivery cost of the program would be the cost of setting up those 20 clinics plus any additional marginal delivery cost (i.e. cost of syringes, record-keeping, etc.). One might think that the vaccination costs would be "lumpy" in that much of the costs of the program would be in deciding how many clinics to set up and for how long, since that would determine overall staffing levels. With this approach, total costs would be:

(10) $\text{Total costs} = \alpha \cdot \text{Number of Clinic-Days} + \beta \cdot Q$

We can estimate this model based on only the Kolkata data. The total number of clinic-days was 1,122 for the cholera campaign and 600 for the typhoid campaign ($N \cdot D$ in Table 1). Note that this implies that the cholera campaign was able to deliver more doses per clinic-day than the typhoid campaign (124 per clinic-day vs. 63). This gives:

(11) Cholera $\$236{,}000 = \alpha \cdot 1122 + \beta \cdot 139{,}000$

(12) Typhoid $\$90{,}000 = \alpha \cdot 600 + \beta \cdot 38{,}000$

Solving the equations simultaneously, gives the total cost equation:

(13) $\text{Total costs} = \$89 \cdot \text{Number of Clinic-Days} + \$0.98 \cdot Q$

This cost function will only have economies of scale if the number of doses delivered per clinic-day increases with the size of the program. For example, suppose that a vaccination clinic in Kolkata can deliver 100 doses/day (mid-way between the cholera and typhoid trials). A program targeting 6,000 people lasting 30 days would require 2 clinics. The total delivery cost of the program (using eq. 13) would be $11,220, and the average cost per dose would be $1.87. A program targeting 60,000 people lasting 30 days would require 20 clinics, the total cost would cost ten times as much ($112,200) and the average cost would remain $1.87 per dose. If a clinic in the larger program can deliver 200 doses per day, however, then only 10 clinics would be needed, and the average cost drops to $1.43.

Again, though, we only have two data points in Kolkata, so it is difficult to generalize a relationship between the size of the program and the doses delivered per day. (Plugging the doses per day observed in the two trials back into Eq. 13 will, of course, just give you back the two observed average costs - $1.7 and $2.4 – and these will not vary depending on scale of the program.) To try to find a more general relationship between the size of the program and the doses delivered per day, we use data from five studies (including the Kolkata studies) which provide information on the number of clinics and days they were operated (Table 1). Fitting an OLS model of Q and the number of clinic-days on total costs, without a constant, gives:

(14) $$\text{Total costs} = \$120 \cdot \text{Number of Clinic-Days} - \$0.57 \cdot Q$$

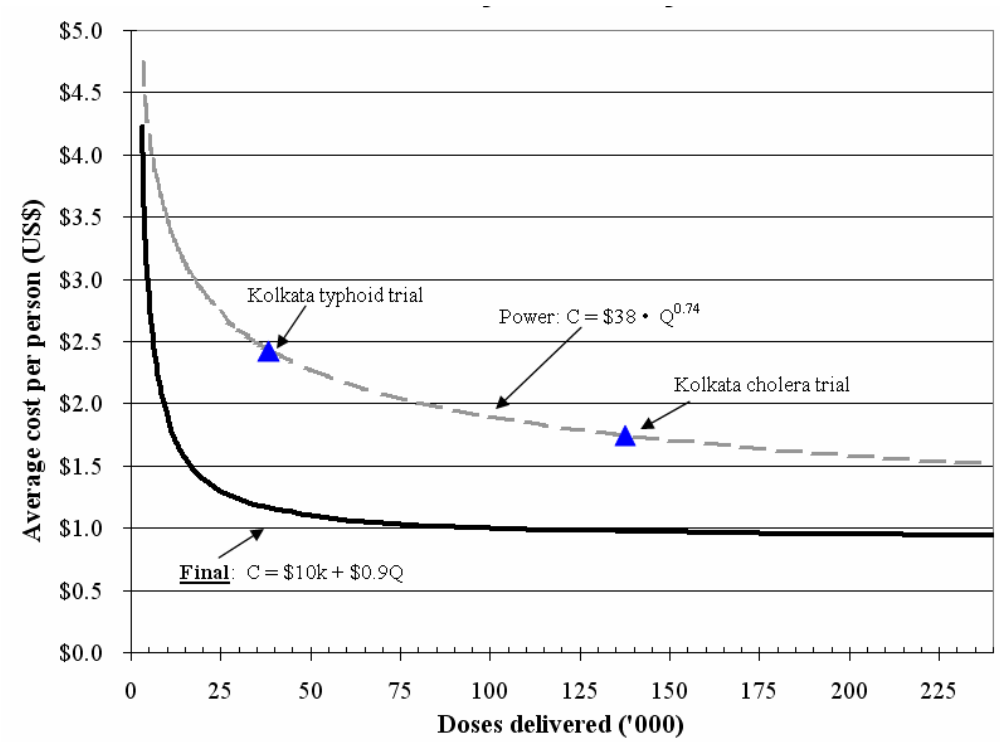
This model is inconclusive because the parameters of the model were not statistically different from zero (one reason to disregard the puzzling negative coefficient on marginal cost).

Final estimates for investment cases

Our best estimate of delivery costs for the investment case is the one provided by Approach 3 (eq. 9). It assumes fixed delivery costs of $15,000 and constant variable (marginal) delivery costs of $1.40 per dose. However, we have no data on the vaccination costs that were related only to research, so it is impossible to carefully exclude these from the final estimates. Also, as noted earlier, the average cost estimates implied by these parameters (approximately $1.5 per dose for programs ≥ 50K doses), is considerably higher than the studies reviewed by Lauria (2007).

To account for research-related costs, we reduce the constant marginal delivery costs from US$1.4 to US$0.9 (a reduction of 35%) and reduce fixed costs from US$15,000 to US$10,000. Figure 2 plots average costs per dose with these assumptions, and shows that delivery costs are on the order of US$1 per dose for moderately-sized programs . The figure also includes the actual observed costs in Narkeldanga for reference (blue triangles in Figure 2) and the average costs implied by a power function of the form $C = 38 \cdot Q^{0.74}$ (dashed gray line in Figure 2).

Figure 2. Final average delivery costs compared with power function and Kolkata trials



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