INCORPORATION OF PRIVATE DEMAND AND HERD PROTECTION INTO VACCINE POLICY MODELS: AN EXAMPLE FOR CHOLERA VACCINATION IN MATLAB, BANGLADESH

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ABSTRACT

This dissertation examines cholera vaccination policy in a developing country context based on a combination of epidemiological and microeconomic data representing private demand for purchasing vaccinations, cost of illness, cost of vaccination, and herd protection impacts of vaccination. The dissertation incorporates data from Matlab, Bangladesh. Matlab's population is subdivided into four distinct population groups based on variation in disease burden and age. Mathematical optimization is used to solve for the socially optimal prices across population groups that maximize either 1) societal net benefits or 2) the number of DALYs saved across subject to a budget constraint. This analysis demonstrates that is optimal to charge the lowest prices to children in high incidence villages and the highest prices to adults in average incidence villages. Sensitivity analysis reveals that the use of cross-subsidies has only a small impact on program outcomes including both net societal benefits and total DALYs saved (e.g., adults who purchase vaccines in average incidence villages would pay more per vaccine to subsidize children in high incidence villages). This analysis shows that cross-subsidies may be less useful for scenarios in which the herd protection impacts of vaccination are similar across population groups.

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Abbreviations

CBA	Cost benefit analysis
CFR	Case fatality rate
COI	Cost of illness
CV	Contingent valuation
DALY	Disability adjusted life years
DOMI	Diseases of the Most Impoverished
EPI	Expanded Program on Immunization
ICDDR,B	International Center for Diarrhea Disease Research, Bangladesh
IVI	International Vaccine Institute
HDSS	Health and Demographic Surveillance System
MCS	Monte Carlo Simulation
NTTT	No time to think
ORS	Oral rehydration solution or therapy
TTT	Time to think
WHO	World Health Organization
WTP	Willingness-to-pay
VSL	Value of a statistical life

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Executive Summary

This dissertation develops new models to aid in improving vaccine policy in developing countries. The goal of the dissertation is to improve vaccine policy in light of the challenging health problems and scarce financial resources available in developing countries. The new models incorporate empirical data for private demand and the epidemiology of cholera vaccination herd protection. The rural Matlab, Bangladesh area is used as a case study to illustrate the models. A number of studies about the epidemiology of cholera have been conducted at this site. In addition, I led a study to estimate private household demand for cholera vaccinations in 2005.

One objective of this dissertation examines the reliability of monetary estimates of vaccination benefit, which are often controversial. Specifically I compare independent estimates of vaccine benefits: direct willingness-to-pay (WTP) estimates for cholera vaccines compared to additive estimates of the private cost of illness (COI) estimates plus valuations for reductions in non-specific mortality risk. The value of generic mortality risk reduction is estimated from a separate contingent valuation scenario included with the cholera vaccination household demand survey conducted in Matlab in 2005.

The overall average WTP for children's vaccination is US$1.6.If children are split into two groups, the average WTP for vaccinations for 1-5 year olds is US$2.4 compared to US$1.2 for older children age 5-17 years. Thus, WTP is considerably greater for younger children who also face a higher baseline risk of death from diarrhea. The expected private COI savings for 3 years of vaccine protection are about US$0.04 for young children and US$0.02 for school-age children. These values are about 1-2% of the estimated private WTP as estimated from my contingent valuation survey. This suggests that private COI savings in isolation are a poor estimate of the

private benefits of vaccination. *Ex ante* mortality risk reduction benefits are estimated to be US$1.70 for young children and US$0.24 for older children. These are equivalent to 70% of WTP estimates for young children and 20% of WTP estimates for school-age children. Thus, the vaccine WTP estimates are very close to the COI + mortality risk reduction benefits for young children. There is some discrepancy for older children who appear to face a very small risk of cholera mortality. It should be noted that the COI + mortality risk estimates neglect the cost of pain and suffering for those that contract cholera. The fear of suffering may lead to increased WTP for cholera vaccination for older children despite the small mortality risk.

Another objective of this dissertation is to incorporate empirical private demand and herd protection data into cost benefit and cost utility models that consider multiple subgroups. The newly developed optimization models should allow for a more thorough evaluation than is possible with the commonly used approach in which price (and thereby coverage rates) are fixed. These optimization models can examine the potential for cross-subsidies to improve program efficiency both in consideration of social net benefits and in consideration of health impacts based on the number of disability adjusted life years (DALYs) saved given similar budget constraints. Specifically, I split the population into four subgroups: 1) adults in average incidence villages, 2) children in average incidence villages, 3) adults in high incidence villages and 4) children in high incidence villages. These models can then be solved for a set of four user fees that would maximize either net benefits or total DALYs saved given a revenue constraint.

A third objective of this dissertation is to examine the advantages and disadvantages of cost-benefit analysis relative to cost utility analysis, especially in accounting for herd protection effects. Judging from published literature, it appears that cost utility analysis is often preferred to cost benefit analysis, probably because it is difficult and controversial to monetize mortality risk reduction and avoided pain and suffering.

I examined a number of different pricing models for vaccination programs. These include simple models in which all four groups are charged the same price and optimized models in

which different subgroups are charged different prices. The optimized models attempt to maximize either net societal benefits or total DALYs saved. The net societal benefit curve is almost flat over the range of likely prices, US$1.00 to US$3.00, for a cholera vaccination program in Matlab. Over this range of prices, net societal benefits vary between US$200,000 and US$220,000. Thus, there is very little difference in the absolute maximum net benefits, US$220,000, and the maximum net societal benefits possible from a revenue neutral program, US$210, 000. A public or donor contribution of US$32,000 could be used to boost net societal benefits by about US$5,000, a 2% change.

The optimal prices that maximize net societal benefits tend to fall within tightly bound ranges around the marginal cost of vaccination. As a result, the prices for each of the four groups would typically fall within US$1 of one another when societal net benefits are maximized. This occurs because the demand functions are found to be independent of incidence differences across villages. Since demand functions drive the calculation of direct and indirect benefits, the difference in optimal prices result solely from small differences in herd protection effects and public COI savings. However, public COI savings tend to be small relative to direct and indirect benefits. In the deterministic model, it is assumed that herd protection effects are the same for vaccinating adults or children. Thus, the targeting of vaccinations across age groups is unnecessary for maximizing herd protection.

Program outcomes are very similar for models that maximize DALYs saved. Relative to net benefit maximization models, the optimal prices derived from models that maximize DALYs show more variability across subgroups. The optimal prices for groups with high incidence tend to be smaller (i.e. for children relative to adults and for high incidence villages relative to average incidence villages). As a result, predicted coverage rates at optimal prices are greater for groups in which the numbers of cases avoided per vaccination are greater. However, the population-average coverage rates remain about the same. Thus, herd protection effects, which accrue equally to vaccinated and unvaccinated persons, are assumed to be independent of who is

vaccinated. As a result, there are very small differences in the numbers of DALYs saved for the net benefit maximization model versus the DALY maximization model, despite the differences in optimal prices. Monte Carlo Simulation results indicate that the differences in net societal benefits or DALYs saved for the Net Benefit or DALY models are less than 10% across a range of 500 independent parameter draws.

The uncertainty in optimal pricing is driven primarily by uncertainty in the fixed and variable costs of vaccination programs. If program costs are greater than expected, it would be necessary to charge all subgroups higher prices in order to maintain revenue neutrality. When higher prices are charged, coverage rates decline, herd protection effects are diminished, and fewer cholera cases are avoided. Thus, variation in societal net benefits and DALYs are also strongly impacted by uncertainty in program costs. Uncertainty in net societal benefits is also driven by uncertainty in demand function parameters. If demand is greater than expected, net societal benefits increase because cholera protection is perceived to be more valuable to the community. The uncertainty in DALYs saved is primarily driven by variability in case fatality and incidence rates, such that more DALYs are saved when incidence and case fatality rates are greater. It is believed that cholera case fatality rates may be lower in Matlab relative to other rural communities because Matlab's ICDDR,B hospital is available to provide high quality treatment. If case fatality rate were greater than 1%, it is likely that cholera vaccination in the Matlab area could be considered 'very cost-effective' based on World Bank Standards, but only at modest coverage rates (20-40%). At higher coverage rates, the cost per DALY saved would be higher due to diminishing returns to scale of herd protection.

It is possible to increase the number of DALYs saved if external funding is available. However, the marginal cost per DALY saved tends to be high. The cost per DALY saved varies depending on the coverage rate of the program. At very low coverage rates, the average cost per vaccination is very high because fixed costs are spread across a small number of vaccinated individuals. As a result, the cost per DALY saved is also high. As coverage increases, the cost per

DALY saved decreases as more people become vaccinated and fixed costs are spread across a larger number of vaccination recipients. The cost per DALY is minimized when the average price charged is about US$3 and the average coverage rate is about 20%. As coverage rates increase beyond 20% the average cost per DALY saved decreases. This is because of the diminishing returns to scale of herd protection. This dissertation provides useful insight into planning vaccination programs in rural areas of developing countries.

1 Description of Policy Problem

1.1 Introduction

As more and more new vaccines and other health interventions are developed, public health ministries and international donor agencies face increasingly difficult decisions for investing limited resources to improve health in less developed countries. One approach to increasing the adoption of new vaccines at limited cost to government and donors is to charge user fees for vaccinations. This would allow recipients to contribute to the cost of the vaccination program. However, the imposition of user fees would reduce vaccination coverage rates because some people would be either unwilling or unable to purchase vaccinations.

When determining user fees, it is important to consider that vaccinations have both public good and private good aspects. Recipients have a physiological response to vaccination, leading to increased immunity to disease. This is the private good aspect; the physiologic response is often exclusive to those who receive the vaccine. Since these recipients are less likely to become ill, they are less likely to expose family members and other community contacts to disease. As vaccination coverage rates increase, disease prevalence declines and unvaccinated persons are less likely to encounter infected persons or other disease vectors in the community (i.e. there is a herd protection effect). This is the public good aspect since each individual vaccination has an impact on the indirect protection for the community. For vaccinations with less than 100% efficacy, vaccinated persons would also benefit from herd protection.

Cost benefit analysis and cost utility analysis are typically used to evaluate the economic attractiveness of vaccination programs. Both approaches have advantages and disadvantages, which will be discussed in this dissertation. However, when demonstrated in the literature, most authors assume that vaccination coverage rates are pre-determined and that economic

attractiveness must be determined for these pre-determined coverage rates (e.g., free or mandatory provision as part of mass vaccination or infant vaccination programs). This dissertation attempts to evaluate how the choice of user fees (and implicitly the choice of coverage rates) impacts cost benefit and cost utility metrics commonly used to judge the economic attractiveness of vaccination programs.

The goal is to improve the allocation of scarce resources for a prospective vaccination programs in a developing country. My analysis focuses on how empirical price-coverage and indirect protection-coverage relationships can be used to optimize the setting of vaccination user fees. Empirical data from a number of cholera vaccination studies conducted in rural Matlab, Bangladesh are used to demonstrate these models. Empirical estimates of household demand for cholera vaccinations are based on a contingent valuation survey conducted in 2005. Empirical estimates of coverage-indirect protection relationships are based on recent studies of cholera incidence following a 1985 vaccination trial that was conducted in Matlab. These studies found that incidence rates for both vaccinated and unvaccinated subgroups were inversely correlated with vaccination coverage rates (Ali et al., 2005; Ali et al., 2008). Thus, unvaccinated persons that lived in areas with high coverage rates were considerably less likely to contract cholera than unvaccinated persons who lived in areas with low coverage rates. In addition, an empirical model of coverage versus expected incidence was developed for cholera vaccination in the Matlab area (Longini et al., 2007).

My dissertation incorporates both price-coverage and coverage-incidence expressions into cost-benefit and cost utility models to solve for socially optimal prices. While I focus on examples using cholera vaccination data from Matlab, I believe that these models should be illustrative of potential approaches for other locations and for different vaccines. I examine both cost benefit and cost utility approaches to identify if different policy models influence either the theoretically optimal prices or the expected program outcomes that would result from those prices.

For cost benefit models, health outcomes must be expressed as monetary benefit estimates via a welfare-theoretic approach. For cost utility analysis, health outcomes are expressed as non-monetary health utility units based on the number of life years and disability-impaired years saved via the intervention. Both types of benefit measures can then be compared to program costs. In the absence of herd protection, the change in disease morbidity per vaccination delivered is constant (given a population with homogenous incidence). However, in the presence of herd protection, the change in disease morbidity is no longer a constant function of coverage. Thus, it may be possible to use price-coverage relationships in combination with coverage-herd protection relationships to solve for socially optimal coverage rates. For each model, I assume that vaccination programs face budget constraints that limit government or donor contributions to program financing.

This dissertation aims to answer three distinct, but related questions. First, how do private vaccine willingness-to-pay estimates compare with other economic estimates of disease prevention based on *ex ante* reductions in private treatment costs and mortality risk? I use the results of two contingent valuation surveys to answer this question. I calculate average willingness-to-pay (WTP) per vaccination by age group from the household cholera vaccination demand survey. An alternative vaccination benefit estimate can be calculated from separate studies that estimated cholera incidence, private cost of illness and willingness-to-pay for mortality risk reduction. This value of mortality risk reduction is estimated from a survey of willingness-to-pay to reduce mortality risk for each household's youngest child.

Second, how can cost utility methods be used to incorporate herd protection effects to optimize vaccination policy making? To answer this question, I use existing cost utility methods but I attempt to maximize the number of DALYs rather than simply estimating an average cost per DALY. I used standardized methods ((WHO), 2003) to convert changes in incidence to changes in disability adjusted life years (DALY). The number of life years lost depends on incidence rates and case fatality rates by age group. Since cholera does not cause long term

disability (e.g., blindness or paralysis), the disability impact is calculated from the average duration of disease and a weight that represents the degree of incapacitation experienced. When comparing different health interventions, an average cost per DALY saved is often used as the definitive metric. In an appendix, I demonstrate how to calculate average and marginal costs per changes in DALYs saved as functions of coverage to demonstrate how variation in coverage rates impacts cost utility. In addition, I solve for a set of optimal prices for specified population subgroups that maximize the number of DALYs saved in the community.

Third, given a common set of constraints and model input parameters, how different are the hypothetical socially optimal outcomes derived from cost benefit versus cost utility analyses? A related question is what are the underlying causes of differences in the hypothetical socially optimal outcomes from cost benefit and cost utility analyses? To answer these questions, I create optimization models that maximize either social net benefits or DALYs saved for a given revenue constraint. The optimization models solve for a set of prices to be charged to each of four different subgroups. The societal net benefits are calculated from the sum of expected WTP benefits and discounted public treatment cost savings less program costs. The net revenue constraint is the difference between program costs and the sum of sales revenue and discounted public treatment cost savings. Both of these models incorporate herd protection versus coverage functions in addition to price versus coverage functions. By solving each of these optimization problems, it is possible to identify how the choice of outcome measure affects decision making.

This type of comprehensive vaccination policy analysis is not always conducted prior to making decisions about introducing new vaccines. DeRoeck et al (2005) interviewed policy makers in seven Asian countries to understand their views on vaccines against cholera and other enteric disease. Policy makers in Bangladesh and other countries reported that they did not place a high priority on providing cholera vaccines to areas with high endemic incidence rates. They cited a number of reasons for this preference, including 1) the success of oral rehydration solution (ORS) also known as oral rehydration therapy in reducing cholera mortality, 2) a desire to spend

limited resources on water and sanitation infrastructure or other health interventions (e.g. Hib and hepatitis B vaccines) that are believed to have greater potential for reducing childhood mortality, 3) the limited duration and effectiveness of cholera vaccines, 4) the higher cost of cholera vaccines relative to Expanded Programme of Immunization (EPI) vaccines, and 5) the inability to administer the cholera vaccine as part of the existing EPI schedule. Policy makers may also fail to consider whether private spending might help offset the cost of vaccination programs (via charging user fees). In addition, empirical evidence of herd protection from cholera vaccination was not yet available when policy makers were interviewed for DeRoeck's report.

The policy makers' opinions of cholera vaccines demonstrate the need to consider Bangladeshi health policy in light of very limited financial resources, which are insufficient to adopt every newly-developed health intervention. As increasingly more vaccines and other interventions are developed, policy makers should take care to consider both herd protection-induced efficiencies and private willingness-to-pay considerations when forming health policy. Planning should be flexible enough to allow increasing localization of planning efforts and freedom for household decision makers to invest in their favored interventions.

The models developed in my dissertation differ from more common approaches to vaccine policy for developing countries, which traditionally revolve around simple binary decisions about whether or not to introduce specific vaccines. In low income countries, it is also often assumed that these vaccines must be provided free of charge because residents' budgets are too tightly constrained to spend money on preventive efforts. However, the provision of free vaccines places a large burden on already strained health ministry budgets and reduces prospective purchasers' abilities to assess their own local health priorities. It is uncommon for policy makers to consider charging user fees or how to determine what amounts should be charged.

Recently economists have been researching private demand for newly developed vaccines. Their studies use surveys that present respondents with a carefully described

hypothetical vaccine and ask how many vaccines would be purchased for the respondent's household. This allows researchers to estimate demand functions for vaccination purchases and also provides direct monetary estimates of the private value of vaccination (e.g., Canh et al., 2006; Cook et al., 2006; Lucas et al., 2007; Islam et al., 2008; Kim et al., 2008; Whittington et al., 2009).

Longini et al. (2007) developed an epidemiological model of the cholera vaccination coverage-incidence relationship in Matlab and reported the expected incidence reduction as a function of coverage (relative to a baseline scenario without vaccination). At a vaccine coverage rate of 30%, they predicted that probability of cholera infection would decrease by 90% for vaccinated persons and by 70% for unvaccinated persons. If coverage were increased to 50%, risk of infection would further decrease, by 97% for vaccinated persons and by 89% for unvaccinated persons. These findings demonstrate that the impact per vaccine varies as a function of coverage and that the attractiveness of cholera vaccination almost certainly depends on the coverage rate. Because of this nonlinear relationship between coverage and vaccination impact, common economic modeling approaches that rely on a single point-coverage estimate may not be well suited to policy making.

By combining private demand and epidemiological data, I can develop more helpful economic models that demonstrate the impact of user fees on program outcomes. The work included this dissertation makes an important contribution to the literature in a number of ways:

- It provides the first estimate of WTP to reduce the mortality risk of children in a developing country;
- It is one of the first attempts to include private demand and herd protection data into a vaccination policy model for a specific location;
- It demonstrates a new method of cost utility modeling, namely I define the marginal cost per DALY saved, which is a function of coverage

- It is the first to examine how to set user fees in consideration of multiple subgroups with independent vaccine demand functions, incidences, cost of illness, and impacts on herd protection. (The use of cross-subsidies in the presence of herd protection has not been previously considered).

1.2 Dissertation goals

The goal of this dissertation is to provide policy models and recommendations to improve vaccination decision making in developing countries. This is accomplished through the development of new vaccination policy models that aim to better understand the tradeoffs involved in charging user fees for vaccinations in less developed countries, using Matlab, Bangladesh as an example. The framework developed in this dissertation should be applicable to policy makers working on other vaccines and in other countries. The dissertation focuses on data collected for a cholera vaccination program in the Matlab, Bangladesh area. This site was chosen because of an opportunity to conduct empirical research in the area and the availability of empirical data for cholera vaccination herd protection effects from a 1985 trial (Ali et al., 2005; Longini Jr. et al., 2007). The area may consider a cholera vaccination program as a medium term preventative measure prior to future water and wastewater infrastructure improvements. Thus, one objective of the dissertation is to develop models that improve understanding of the inter-relationships between price, coverage, and health outcomes for a potential set of cholera vaccination policies. While these models are demonstrated with Matlab data, I believe that the underlying models will prove to be broadly applicable for other vaccines and in other locations. The recommendations derived from these models may provide a template for other rural communities in Bangladesh and other countries that suffer from endemic cholera; however, I caution that differences in social, cultural, economic, and environmental conditions must be taken into consideration prior to extrapolation.

In this dissertation I attempt to incorporate empirical private demand and herd protection data into cost benefit and cost utility models that consider multiple subgroups. The models should allow for a much more thorough evaluation than is possible with the commonly used approach in which price (and thereby coverage rates) are fixed. In addition, I demonstrate that the marginal cost per DALY saved is strongly dependent on the coverage rate achieved. This demonstrates the importance of considering target coverage rates after deciding whether to conduct the vaccination program. The optimization models can examine the potential for cross-subsidies to improve program efficiency both in consideration of social net benefits and in consideration of DALYs saved given similar net revenue constraints. Specifically, I split the population into four subgroups: 1) adults in average incidence villages, 2) children in average incidence villages, 3) adults in high incidence villages and 4) children in high incidence villages.[1]

In addition to the development of new localized vaccination policy models, this dissertation examines a number of additional objectives that aim at improving the current state of the art in developing economic analyses of vaccines and the collection of the data necessary to inform vaccine policy. A third objective of this dissertation examines the reliability of vaccination benefit estimates, which are often controversial. Specifically I compare independent estimates of vaccine benefits: direct WTP estimates for cholera vaccines compared to additive estimates of the private cost of illness estimates plus valuations for reductions in non-specific mortality risk. The value of generic mortality risk reduction is estimated from a separate contingent valuation scenario included with the cholera vaccination household demand survey conducted in Matlab in 2005.

[1]The Matlab case study is unique because of the amount of data available. It is unusual to have detailed data for private vaccine demand, herd protection epidemiology, and even disease incidence in other locations. In fact, it would be prohibitively expensive to collect these data prior to determining vaccine policy at all locations for all diseases. However, I believe it is possible to apply some of the lessons learned from this dissertation in a variety of contexts.

An additional objective of this dissertation is to examine the advantages and disadvantages of cost-benefit analysis relative to cost utility analysis, especially in accounting for herd protection effects. Judging from published literature, it appears that cost utility analysis is often preferred to cost benefit analysis, probably because it is difficult and controversial to monetize mortality risk reduction and avoided pain and suffering. This dissertation examines how different outcomes arise from cost benefit versus cost utility analyses. Further, I examine what conditions would lead to differences in optimal pricing for cost benefit versus cost utility analysis.

It is important to note that I approach cost utility analysis differently in that I attempt to maximize the number of DALYs saved given a revenue constraint (rather than simply calculate the costs and saved DALYs for a pre-specified intervention. For cost benefit analysis, the difference between benefits and costs is defined as the net benefits. After determining an optimal allocation for a specific intervention, policy makers should attempt to maximize either net benefits or DALYs saved across interventions. At present, vaccine policy decisions in developing countries are generally limited to allocating resources across interventions. Little attention is typically given to program design within a particular intervention. This issue has been raised by a number of authors (Philipson, 1996; Gersovitz and Hammer, 2003; Francis, 2004; Boulier et al., 2007); however, I am unaware of any attempts to use empirical demand data to design vaccination programs.

Another objective of this dissertation is to define a marginal cost per DALY function that varies as a function of coverage. As shown by Longini et al. (2007), the marginal changes in incidence are highly variable. It is possible to reduce incidence of unvaccinated persons by 70% by increasing cholera vaccination coverage from 0% to 30%; however, a further increase in coverage from 30% to 50% only increases effective protection for unvaccinated persons from 70% to 89%. Thus, it is important to quantify not just the average cost per DALY saved, but also the marginal cost per DALY saved. This will help prevent wasting resources on additional vaccinations, once an acceptable threshold of protection has been achieved.

1.3 Summary of the dissertation's contribution

This chapter highlights my dissertation's important and novel contributions to the literature. First, the study incorporates a large data set of cholera vaccine benefits for a rural, cholera-endemic setting. This combination of data sources has not been available for any previous evaluation at a single location. Many economic evaluations of vaccine programs miss important private economic benefits such as increased productivity and reductions in risk of death or pain and suffering. In addition, most economic models are hindered because program planners do not include price-coverage relationships. I can estimate these relationships from the results of the stated preference studies. The estimated demand curves can also be used to calculate total willingness-to-pay for the community. The Matlab study site is unique in that very specific data on different causes of mortality are available to inform policy. Unlike other vaccination policy studies, all of these data are available at a single location and thus benefit transfer models are not necessary.

Second, value of statistical life estimates are notoriously difficult to obtain because of difficulties in educating respondents about the very small risks of deaths faced and the ability of the proposed intervention to reduce those already small risks of death. This study (Maskery et al., 2008) is only the second known attempt to elicit estimates in a rural area of a developing country (Mahmud, 2009) and the first to elicit estimates of parents' willingness-to-pay to reduce their children's risk of death. In addition, cholera vaccine WTP estimates are compared to cholera cost of illness and generic mortality risk reduction estimates to test for consistency.

Third, the economic model developed in this dissertation is believed to be one of the first to account for both the heterogeneous demand and herd protection. Most economic models that incorporate herd protection have assumed that cholera vaccination benefits are the same for everyone in the community (Brito et al., 1991; Francis, 1997; Francis, 2004; Boulier et al., 2007). I also contributed in the development of a simplified model (Cook et al., 2009). This article uses

empirical private vaccine demand and epidemiological data to examine vaccination outcomes for Kolkata, India. This article uses a different method for calculating direct and indirect vaccination benefits and assumes a single demand function and incidence for the entire population. My model includes consideration for separate incidence and demand functions for each of four subgroups. The Cook et al. article is discussed in more detail in Section 3.6.

Fourth, I think my dissertation provides one of the first attempts to examine vaccination program optimization with different objectives, namely the maximization of net benefits versus the maximization of DALYs saved given a common revenue constraint.

2 Background

This chapter includes background information of the biology of cholera, information about available cholera vaccines, a comparison of vaccination programs relative to water and sanitation programs, and the Matlab study site. A more thorough review of economic and epidemiological vaccine research is included as Chapter 3.

2.1 Cholera

Appropriate vaccination policies depend on the epidemiology of disease. Cholera is an endemic and epidemic diarrheal disease that primarily strikes low income persons in certain parts of the developing world. It is endemic where the local climate is conducive to the survival of *vibrio cholerae* outside of human hosts. Epidemic cholera may also strike communities with poor-quality water and sanitation infrastructure, which allows the disease to spread from person to person even though the natural environment is not conducive to survival of the causative bacteria. The Matlab community suffers from endemic cholera.

The primary symptoms of cholera include intense, watery diarrhea, fever, and rapid dehydration. It is easily treated by quickly re-hydrating the patient with oral rehydration solution (ORS) or IV fluids. The severe dehydration caused by cholera can kill patients within 24-48 hours; however, the introduction of ORS has reduced the case fatality rate (CFR) to less than 1% in areas with high quality treatment (Ryan et al., 2000; Sack, 2003).

Ali et al. (2002) constructed a spatial map of cholera risks in the Matlab area and observed that the risk of dying from cholera increased with distance from the nearest health clinic. Thus, vaccinations may be especially useful in reducing mortality risk in areas that lack convenient access to health clinics. In the Matlab area, the centralized ICDDR,B diarrhea hospital

treats the majority of severe cholera cases. This hospital is unique in that it has tested all diarrhea patients that presented cholera symptoms and has maintained surveillance records for almost 40 years (Longini Jr. et al., 2002). Historically, cholera incidence in the Matlab area has been highly variable. Cholera incidence data for the Matlab area are examined in detail in Section 5.1.

The bacteria that causes cholera live 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). The bacteria that causes cholera is *Vibrio cholerae*, which has 2 major serogroups (O1 and O139). The O1 serogroup has two biotypes (classical and El Tor), each of which has 2 major serotypes (Ogawa and Inaba). Usually, one of the two serotypes is responsible for the majority of epidemic cases in any geographic area, but the two serotypes usually replace one another over time in an endemic area. The change in serotype is believed to depend on the immune status of the population (Longini Jr. et al., 2002).

The epidemiology of cholera is dependent on both the bacteria that cause the disease and the water and sanitation infrastructure. If communities had properly functioning, self-contained indoor piped water and sewerage, it would be uncommon for cholera to be transmitted across households. In Matlab, however, most bathing is performed in nearby ponds, which are shared by small groups of households. Emch et al. (2009) have shown that cholera vaccination herd protection effects are highly localized among households sharing these ponds. Since cholera infection requires the ingestion of a large number of bacteria, even small changes in local incidence via vaccination may help to inhibit transmission to unvaccinated persons by reducing the concentration of *vibrio cholerae* in any particular pond.

2.2 Vaccines

This dissertation examines the next generation whole-cell-killed cholera vaccines (either with or without a recombinant b-subunit). This vaccine is delivered orally in two doses. It was originally believed to have about 65% direct efficacy for three years (Clemens et al., 1990a);

however, after accounting for herd protection, the vaccine has been found to have a 65% direct efficacy (Longini et al., 2007) at least in the first year. The next generation whole cell vaccines have not been proven safe in infants less than 1 year of age. 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. Research into the whole-cell-killed vaccine is ongoing with recent trials in Vietnam, Beira, Mozambique, and Kolkata, India (Thiem et al., 2003; Lucas et al., 2005; Cavallier et al., 2006; Thiem et al., 2006). The Kolkata trial is the only one to use the International Vaccine Institute's newly developed vaccine, which is being made available for technology transfer to producers in less developed countries.

2.3 Comparing vaccines with water and sanitation improvements

Most households in the Matlab area retrieve their potable water from shallow hand pumps located near their homes. These shallow tube wells have helped to reduce all-cause diarrheal disease, but have also exposed the population to hazardous concentrations of arsenic naturally found in shallow Bangladeshi aquifers. Exposure to arsenic has led to chronic health problems over the past 20 years. Basic pit latrines and hanging latrines are used for urination and defecation throughout the area. These latrines have also helped reduce diarrheal disease, but are less than ideal. Some hanging latrines introduce pathogens directly into bathing areas and the shallow pit latrines may not effectively remove pathogens from the source water of the shallow tube wells.

While these water and sanitation facilities are an improvement over the use of surface water and open defecation practices, they are only the first step to reducing water borne illness. The next developmental step would be the construction of large scale water and sanitation infrastructure. Cholera vaccines are unnecessary in wealthier countries because of advanced water and wastewater treatment, better hygiene practices, and an overall higher standard of living. The

next steps in major water and wastewater infrastructure would be an expensive network of pipes to carry treated, clean water to households and transport wastewater away from households. If properly operated and maintained, this new system should improve health, assuming that hygiene practices simultaneously improve. Disease incidence can be further improved with the ultimate construction of wastewater treatment facilities that would remove pathogens and other pollutants prior to discharge into Bangladeshi streams or rivers. This step would reduce exposure to pathogens during bathing or play in local water bodies. Thus, long term infrastructure improvements would likely have a great impact on public health, but these require significant financial commitments, at least on the order of US$20 per month per household. The necessary local, national, or international financial resources will not likely become available over the next 20 years given that the average monthly household income in the area is only about US$75 per month.

Point-of-use treatment is considerably less expensive than the construction of new infrastructure and may be used to reduce diarrheal disease from multiple types of bacteria and viruses. Point-of-use treatment may incorporate one of many different technologies including some type of water filter, disinfecting additive (e.g., chlorine), or sedimentation additive. Considering that Matlab suffers natural arsenic contamination, sedimentation additives may be preferred if reagents are selected to precipitate and remove this arsenic. There have been some point-of-use treatment pilot programs in the Matlab area, and some of the survey respondents continue to employ point-of-use treatment devices. Accurate effectiveness data for point-of-use treatment in Matlab are not available, but other studies have demonstrated a 30-50% decrease in all-diarrhea incidence at costs of about $15 to $50 per household per year (Fewtrell et al., 2005; Brown et al., 2007; Sobsey et al., 2008). The effectiveness of point of use treatment has not been measured Jeuland and Whittington (2009) compared generic investments into point-of-use treatment versus cholera vaccination in low income countries. They concluded that point-of-use

treatment is often more cost effective, but that results vary across locations depending on the incidences of disease.

The microbiological quality of water from hand pumps has not been rigorously investigated across the Matlab study area, but it is widely believed that cholera is more likely to be spread through contaminated food sources or bathing areas (St. Louis et al., 1990; Emch et al., 2009). Cholera infection requires a large dose of the infecting bacteria, which is unlikely to be present in tube well water. It is important to note that point-of-use treatment should reduce other types of diarrheal disease in addition to cholera, which is an important consideration in comparing investments. However, these devices require considerably greater effort to properly use and maintain. Cholera vaccination reduces cholera incidence, but would have no impact on other diarrheal disease. After receiving the required two doses, vaccinated individuals will be protected for 2-4 years, but should continue to avoid contaminated water sources that cause other diseases. In addition, cholera vaccination leads to reduced cholera exposure for both vaccinated and unvaccinated individuals in the immediate area. Thus, it is also important to adjust for herd protection when comparing investments, although, point-of-use treatment devices may also have indirect protection benefits. The examination of point-of-use treatment is not a focus area for this dissertation, but it is important to consider this alternative when developing health policy in Matlab and other localities.

2.4 Description of Study Site

Centered on the town of Matlab, the study area lies some 55 km southwest of Dhaka and has a population of approximately 224,000 ((ICDDRB) 2005). The ICDDR,B operates a hospital in Matlab town whose services include free treatment to anyone with diarrhea; this hospital treats most of the serious diarrhea cases in the area. ICDDR,B also provides basic health services to approximately 111,000 people in Matlab town and 67 outlying villages. Once a month, ICDDR,B's Health and Demographic Surveillance System (HDSS) gathers information from

each person in the ICDDR,B service area as well as from an additional 113,000 people in 75 other nearby villages who receive basic health care services from government facilities. ICDDR,B has collected this information for more than 40 years. Over the years, a number of health intervention studies have been conducted in both the ICDDR,B and government service areas.

The HDSS data include annual mortality rates for a number of causes by age group, as summarized in Table 2.1 (ICDDRB 2002, 2003, 2004). The most common causes of death differ by age group. For children less than 1 year of age, respiratory disease is the most likely cause of death; next most common are diarrhea and nutritional deficiency. For children age 1 to 4, drowning is the most likely cause of death; next are diarrhea and respiratory disease. Mortality rates drop significantly for children age 5 to 9 years relative to younger children. Mortality rates for children age 10 to 19 drop again by half relative to children age 5 to 9 and are six times less than among children age 1 to 4 years. In comparison to the United States, mortality rates in the Matlab area are about 6.5 times greater for children less than one year of age, about 14 times greater for children age 1 to 4 years and about 5 times greater for children age 5 to 14 years ((NCHS) 2005). The mortality rates for older children and young adults are similar for the two countries.

I collected data for the sociodemographic characteristics of sample households that participated in a 2005 contingent valuation survey that estimated household willingness to pay for cholera vaccinations and willingness to pay for mortality risk reductions for households' youngest children. The survey is described in more detail in Chapter 4. Some household socioeconomic data from the survey are summarized here. These data only include households with at least one child less than 18 years of age, and located within two hours (via traditional transportation options) of the ICDDR,B hospital. The average household size is about 5.8 persons, including, on average, 0.1 infants less than one year old, 0.7 young children (1 to 5 years), and 1.7 school-age children (6 to17 years). The average respondent age was about 40 years and the youngest child

was 6.5 years old, and about 50% of the children were less than 5 years of age. The gender split for the sample is almost even. Many of the adult males leave the area to pursue employment in the national capital of Dhaka or in other countries because of a lack of economic opportunity. The respondents had attained an average of about 3.6 years of education; about 35% of the sample reported that they had never attended school. Average monthly household income is about US$75 and median income was US$60. A frequency distribution of average household income per month is shown in Figure 2.1. This figure shows that most households earned between US$35 and US$75 per month, although a small fraction earned considerably more. Thirty nine percent of respondents received electricity directly at their house from a grid. A few other respondents had installed solar panels or used large batteries because of the lack of electrical supply to their village.

The primary source of drinking water for most respondents was hand pumps. About 60% of respondents shared a hand pump with their neighbors; another 30% had their own. Only 3% used surface water. Because of the widespread use of hand pumps, nearly all households (92%) surveyed did not boil their drinking water, though some did treat water with bleach (5%), via sedimentation with alum (4%) or with filters made of cloth, ceramic, sand, or composite material (7%). The respondents primarily used improved pit, unimproved pit, and hanging latrines for waste removal, the latter two of which may promote increased prevalence in the environment of the bacteria that cause cholera. People in the Matlab area have had previous experience with cholera vaccines, including the new-generation oral vaccines and a combined typhoid, paratyphoid A and B, and cholera injectable vaccine. Currently, no cholera vaccine is available in the area. Seven major cholera vaccine field trials were conducted in Matlab between 1963 and 1989. Between 1963 and 1968, there were 5 trials of injectable vaccines: whole-cell, serotype-specific, and purified antigens. The combined vaccine was discontinued in the 1970s 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 1974, there was a sixth trial of a toxoid

vaccine. The seventh and final trial estimated the effectiveness of oral cholera vaccines similar to the vaccine analyzed in this dissertation (Longini Jr. et al., 2002). ICDDR,B's 1985 field trial administered two oral cholera vaccines and a placebo. More than 62,000 people took three doses, approximately 27,000 took one or two doses, and about 31,000 were absent or refused to participate (Clemens et al., 1990). Although the vaccination program only targeted children and mothers, significant herd protection effects were observed even at modest coverage rates (Ali et al., 2005; Longini Jr. et al., 2007). Empirical herd protection data from Matlab is examined in more detail in Section 3.5.

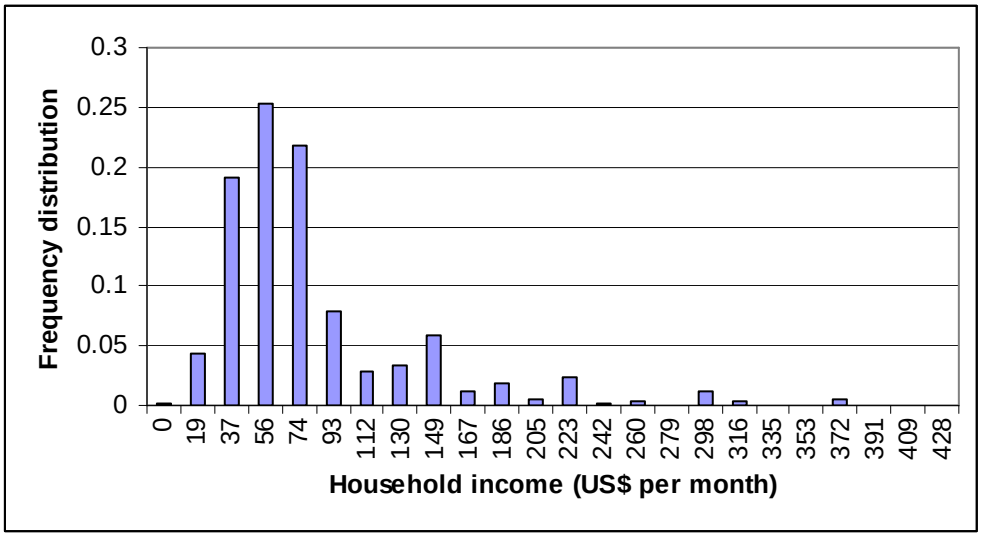

Figure 2.1. Frequency distribution of average monthly income per household

In my 2005 survey about 31% of the respondents had reported receiving the oral cholera vaccine during the 1985 trial. Most respondents, 90%, reported that they were satisfied with the vaccines received by themselves and their family members. They thought that most of the vaccinated persons in their households (72%, including themselves and other members), were sufficiently recently immunized to still have some protection against cholera infection. In addition to their experiences with the oral cholera and cholera-typhoid combined vaccines, people in the Matlab area have had access to vaccines from the EPI program. The free EPI vaccines for children include those against diphtheria, tetanus, pertussis, polio, measles, and tuberculosis. EPI

also provides tetanus vaccines for women of child bearing age (14 to 49 years) ((IVD), 2005). ICDDR,B's community health workers distribute the EPI vaccines throughout the Matlab area once per month. The private market for vaccines in the area is minimal, with only a few pharmacies in Matlab town providing tetanus vaccines (US$0.30–$1.34, Tk 20–Tk 90) and rabies vaccines (US$5.95–$6.40, Tk 400–Tk 430). Nationwide, Levin et al. (1999) report that the private sector only accounts for about 2% of vaccines delivered in Bangladesh.

Table 2.1. Average annual number of deaths for children in Matlab area by cause (based on data from HDSS annual reports ((ICDDRB), 2003; (ICDDRB), 2004; (ICDDRB), 2005)

Age range	<1	1-4	5-9	10-14	15-19	Total
(Population)	(5,764)	(21,024)	(24,985)	(27,024)	(23,944)	(102,741)
Disease related						
Respiratory	70	8.7	2.0	1.0	1.3	83
Diarrhea	17	9.3	2.0	1.0	0	29
Cancer	0.0	2.0	1.3	2.0	0.7	6.0
Infectious	7.0	2.7	1.0	1.3	1.3	13
Nutritional	12	4.3	1.3	1.0	0.3	19
Gastro-intestinal	2.3	0.3	1.0	0.7	1.0	5.3
Cardio-vascular	0.3	0	0	0.3	0.7	1.3
Neonatal	130	0	0	0	0	130
Avg. no. deaths due to disease	245	34	14	11	9	314
Rate of death (per 1,000 children per year)[a]	43	1.6	0.57	0.41	0.39	3.1
Accidents, Injuries	0	0	0	0	0	0
Drowning	3.3	49	8.0	1.3	0.7	63
Homicide/Suicide	1.0	1.0	0.3	1.0	3.0	6.0
Other accident	2.3	1.3	2.0	2.3	1.3	9.3
Avg. no. deaths due to accident/injury[a]	17	58	16	8	9	108
Rate of death[a] *(per 1,000 children per year)*	2.9	2.8	0.6	0.31	0.38	1.1
Other/Unknown	19.7	13.3	11.0	7.4	8.0	59
Avg. no. of deaths (all causes)	260	92	30	19	18	420
Rate of death (all causes) (per 1,000 children per year)	45	4.4	1.2	0.72	0.77	4.1
Rate of death in United States[b] (per 1,000 children per year)	6.8	0.29	0.24	0.18	0.65	0.3

[a] Deaths attributed to other/unknown were split evenly between disease and accident/injury.
[b] Data taken from NCHS (2005)

3 Review of related literature

Policy analysis typically involves the application of natural and social science to public decision making (Friedman, 2002). This dissertation focuses primarily on the application of economics and epidemiology to public vaccination. Economics is the study of the efficient allocation of scarce resources. Epidemiology is the study of how disease is transmitted throughout a community. This chapter summarizes the current state of economics and epidemiology research for public vaccination programs.

This chapter is subdivided into seven sections. It begins with a discussion of the most common approaches to the economic modeling of vaccination programs and their limitations. The next two sections examine studies that can be used to monetize vaccine benefits, either directly or indirectly. Section 3.2 summarizes existing stated preference studies of cholera vaccination in developing countries. Section 3.3 summarizes the value of statistical life literature with an emphasis on studies conducted in developing countries and studies that estimated value of statistical life for children. Section 3.4 summarizes existing economic analyses of cholera vaccination policy. Empirical estimates of cholera vaccination herd protection are described in Section 3.5. The final section (3.6) evaluates the economic epidemiology literature, which merges epidemiological disease spread information with economic theories of behavioral responses to changes in the risk of becoming ill (i.e. changes in averting behaviors in response to changes in disease prevalence). These insights aid the development of a long term vaccine policy model that incorporates changes in vaccine demand after prospective purchasers have observed herd protection effects.

3.1 Common approaches to economic evaluation of vaccine programs

As more and more new vaccines and other health interventions are developed, public health practitioners and international donor agencies face increasingly difficult decisions for investing limited resources to improve health in poor countries. Economic analyses of the costs and benefits of various interventions are one approach to prioritizing these interventions. Many vaccines have a considerably longer duration than the cholera vaccine or protect against diseases that are especially dangerous for infants. For these vaccines, it is usually optimal to vaccinate children as young as possible. In contrast, cholera, typhoid, influenza, and other short-duration vaccines require a more nuanced approach in which it may be necessary to identify which age groups should be vaccinated to optimize impacts. For short-duration vaccines with herd protection or herd immunity effects, analysis is further complicated by the need to consider the indirect protection provided by vaccinating different age groups.

Prior to examining modeling approaches, it is illustrative to define the various types of vaccine costs and benefits. All vaccine interventions potentially offer five principal private benefits and three public benefits. The five private direct protection benefits result from a reduction in the risk of contracting cholera and accrue directly to vaccinated individuals:

(1) avoided direct medical treatment costs, such as medicine and doctor fees,

(2) avoided productivity losses (e.g., wages, school, housework) for patients and their caretakers,

(3) avoided disutility of enduring the pain and suffering of illness,

(4) reduced risk of death from illness, and

(5) reduced expenditures on activities or products that would specifically decrease the risk of contracting the disease that is prevented by vaccination.

These benefits represent the private hardships caused by cholera symptoms. In addition to the private benefits of direct protection, vaccination leads to public benefits that accrue to the entire

community in which the vaccinated persons reside. These public benefits result from reduced public expenditure or via indirect protection:

(6) reduced government expenditure on subsidized treatment for the disease prevented,

(7) indirect protection (a decrease in disease risk resulting from reduced exposure to infected community members or other disease vectors), and

(8) macroeconomic benefits due to increased tourism or trade that may result from a decrease in cholera prevalence.

The indirect protection benefits (7) are essentially the same as the direct protection benefits identified in (1-5), except that the decrease in hardships results from reduced exposure to disease (indirect protection) rather than direct vaccine protection. Thus, indirect protection benefits accrue to the whole community while direct protection benefits only accrue to vaccinated persons. The government treatment cost savings (6) represent the government contribution to subsidized treatment at public clinics, which can vary between 0-100% of total treatment costs. The macroeconomic benefits would accrue if tourism or trade increased as a result of a decline in cholera incidence. The seafood industry may be especially affected by presence of cholera in Bangladesh. It is unlikely that macroeconomic benefits would result if cholera vaccination were limited to the Matlab area exclusively.

Vaccination costs include…

(1) manufacturing costs,

(2) transportation costs from manufacturing sites to local distribution sites,

(3) refrigeration and storage costs at distribution sites

(4) building rental or construction costs (if cholera vaccination cannot be absorbed into existing vaccination infrastructure),

(5) Labor costs to administer vaccines to recipients.

In addition to provider costs, vaccine recipients incur the following costs…

(6) productivity and leisure losses due to time spent traveling to and waiting at the clinic,

(7) transportation costs if buses, cars or other vehicles are used,

(8) pain and suffering caused by vaccine side effects or injections.

Any vaccine user fees paid are considered to be a transfer payment from vaccine recipients to providers. The average cost per vaccinated individual is the sum of the average provider and recipient costs.

While there are many economic analyses of vaccines available in published literature, few incorporate private vaccine demand functions or herd protection-coverage relationships. The journal, *Pharmacoeconomics,* is devoted to economic analyses of health interventions including vaccines. An excellent review of research in developing countries has been compiled by Walker and Fox-Rushby (2001). There is considerable heterogeneity in the methods used to conduct economic analyses. Methodological discrepancies primarily arise from difficulties in benefit estimation and/or a lack of the data necessary to conduct analyses. It may be impossible to explicitly account for all the costs and benefits of a vaccination program; however, there is no consensus in practice as to which costs or benefits must be included or how to quantify them. The remainder of this section examines the strengths and weaknesses of various approaches to the economic modeling of vaccination programs. The most common methods include cost effectiveness analysis, cost minimization analysis, cost utility analysis, and cost benefit analysis, listed in order of increasing complexity.

Cost effectiveness analysis is the simplest method, and requires estimates of 1) the provider costs and 2) the public health outcomes of the vaccination programs.[2] Programs are assessed based on the expected cost per unit change in health outcomes. Examples of cost

[2]In this section, I use cost utility analysis to refer to analyses that examine the cost per disability adjusted life years. This is because the DALY is a utility-based or subjectively determined unit. In contrast, deaths and cases are objective units of measurement, which I refer to as cost effectiveness analysis. In the literature, cost effectiveness analysis and cost utility analysis are often used interchangeably.

effectiveness metrics include the cost per case avoided, the cost per death avoided, or the cost per hospital-day avoided. After calculating the cost per outcome, the least costly health interventions are prioritized. However, these metrics typically omit important benefits. The cost per case avoided metric omits differences in the severity of disease. The cost per death avoided metric neglects the impacts of long term disability and the economic benefits associated with reduced pain and suffering. The primary advantage of cost effectiveness analysis is simplicity due to the avoidance of assigning monetary or utility values to health outcomes, an often controversial endeavor.

Cost minimization analysis evaluates health interventions based solely on a comparison of expected vaccination provider costs and expected public treatment cost savings. Vaccination programs are deemed worthwhile if expected treatment cost savings exceed expected vaccination costs. Obviously, this approach completely ignores the private benefits and costs of vaccination. This approach is also poorly suited for countries that do not use public funds to subsidize treatment, especially if potential vaccine recipients do not have insurance. The advantage for this approach is again simplicity; only the public sector benefits and costs need to be quantified.

Over time cost effectiveness analysis and cost minimization analysis have become less common in the published literature, primarily because of the limitations mentioned above. Presently, cost benefit analysis and cost utility analysis are preferred because of their more comprehensive treatment of vaccination benefits. Cost utility analysis typically estimates the cost per change in a standardized utility measure such as the cost per disability adjusted life year (DALY) saved. A DALY is defined as the discounted sum of the life-years lost to premature mortality and the severity-adjusted mental and physical disutility of disease (Russel et al., 1996; (WHO), 2003).

The World Health Organization has developed a standardized set of guidelines for estimating the number of DALYs saved by a particular intervention ((WHO), 2003). This approach can be described in four steps. The first step sums the expected number of life years

saved by the intervention, which depends on the disease mortality rate, the effectiveness of the intervention, and the age distribution of lives saved (i.e. such that remaining life expectancy is greater for children than for adults). The second step sums the amount of time patients experience the symptoms of disease, including long term disability for chronic illnesses or for disabilities that persist after an illness is cured. The third step incorporates a scaling factor that assesses quality of life impairments caused by the disease in addition to long term disability caused by disease. This scaling factor is designed such that slight discomfort is rated close to zero, and complete incapacitation (such as coma or chronic excruciating pain) would be rated close to one. The scaling factor is typically determined based on surveys that ask respondents how they would trade off a greater number of years spent with the disease (or the disability caused by the disease) relative to a smaller number of years spent healthy (Ware Jr., 1987; Broome, 1993; Guyatt et al., 1993; Russel et al., 1996). For example, would the respondent prefer to live 5 more years with ovarian cancer or 3 more years in perfect health? Finally, the life years saved and the disability adjusted life years saved are discounted depending on 1) when the intervention's effects occur and 2) the future life span of the person saved. Thus, the calculation employs adjustments for life expectancy, future time, and severity of impairment caused by disease. Severity weights for some diseases are maintained by the World Health Organization to ensure consistency across studies. (Fox-Rushby and Hanson, 2001; (WHO), 2003). A DALY weight of 0.105 is cited for diarrhea, although there is no cholera-specific DALY weight.

Though considerable effort has been put into this approach, published papers exhibit significant discrepancies in the way DALYs are calculated (Szucs, 2005; Beutels et al., 2007). These discrepancies include the use of different severity, discount, and/or age weights. Some studies subtract public and private treatment cost savings from the provider cost, resulting in a net cost calculation. Many cost utility analyses have omitted herd immunity effects entirely (Beutels et al., 2002; Beutels et al., 2007; Cook et al., 2008; Kim et al., 2009). Other analyses incorporate herd protection data from other sites for a pre-specified coverage rate (Armstrong et al., 2007;

Lee et al., 2007; Lloyd et al., 2007; Jeuland et al., 2009). The confusion caused by differences in approach is often compounded by the authors' omissions of the assumptions they made in their calculations, making it difficult to draw conclusions across studies (Walker and Fox-Rushby, 2000; Beutels et al., 2007). Critics of the methodology also point to issues with the theoretical validity of the DALY as a welfare measure (Bala and Zarkin, 2000; Dolan and Edlin, 2002). For example, there is no way to examine how health preferences change over time, health status, or income (Klose, 2003).

Cost benefit analysis (CBA) requires monetization of the costs and benefits of a vaccination program. A vaccine program would pass a cost-benefit test if total benefits exceed total costs. A benefit-cost ratio can also be calculated by dividing total benefits by total costs. This ratio can be used to prioritize interventions, such that those with the highest ratios would be pursued first. The assignment of monetary values to benefits is both difficult and controversial (Klose, 2003). Returning to the numbered list of benefits, estimation of public and private expenditure on treatment (1 and 6 above) is relatively straight-forward and non-controversial (e.g., (Cookson et al., 1997; Fischer et al., 2005). The estimation of productivity gains (2 above) adds another layer of complexity, but is still common (e.g., Bahl et al., 2004; Cropper et al., 2004). Reductions in treatment expenditures and productivity losses can be estimated from surveys with patients and reviews of public facilities' operating records. The expected annual cost of illness per person can be estimated by multiplying the average cost of illness per case by the change in disease incidence resulting from the health intervention. It is straightforward to monetize these benefits, which would represent a lower bound estimate of intervention benefits.

Private averting expenditures (5 above) can also be estimated from surveys. In contrast to COI studies, it would be important to also interview previously uninfected persons. It may be difficult to isolate averting expenditures for cholera relative to other types of diarrhea. After receiving a cholera vaccination, it would be unwise for recipients to stop attempting to avoid non-cholera diarrhea.

Valuations for reductions in pain and suffering or mortality risk reductions (3 and 4 above) are both cognitively and empirically difficult. In addition, attempts to value mortality risk reduction have often been challenged on moral and ethical grounds by authors who believe it is immoral to attempt to assign values to human life, even on a statistical basis (Heinzerling, 1998; Heinzerling, 1999; Heinzerling, 2000). Much of this objection applies to the governmental regulation of the environment, in which persons have no say about the deleterious impacts on their health. Thus, controversy may be reduced for preventative health programs that aim to improve health of participants in contrast to environmental degradation, which harms health of affected persons. The estimation of indirect protection benefits (7 above) is often complicated by a lack of empirical epidemiological data.

Many published economic evaluations of vaccine programs in developing countries have been mislabeled as CBA, when in fact, the authors used a cost minimization analysis (i.e. they assess whether vaccines were more or less costly than *ex ante* public treatment expenditure). In their review, Walker and Fox-Rushby (2000) found that 13 of 23 evaluations labeled as CBA were actually cost minimization analyses (i.e. these studies only calculated benefit number 6 from the list above). Thus, vaccination programs were only deemed worthwhile if they saved money from the health provider context. Any program that is cost-saving from the provider perspective would definitely pass a benefit-cost test. However, it is also possible for a program to pass a social benefit-cost test even if it is not cost-saving from the provider perspective. Thus, these studies should not be labeled as CBA. At best, they might confuse the audience. At worst, the omission of these benefits can introduce considerable bias in the conclusions drawn (Fox-Rushby and Hanson, 2001). For example, if mortality risk and/or pain and suffering considerations are omitted from an analysis of a disease with high case fatality rates or long term disability rates, benefit estimates would be greatly underestimated.

3.2 Stated preference studies of cholera vaccines in developing countries

In the previous section, I report that most monetary estimates of vaccine benefits are incomplete. Cholera vaccines are sparsely available in cholera endemic areas. Historically, cholera vaccines have been provided in vaccine trials or free of charge in developing countries. The use of stated preference studies to estimate vaccine benefits is a relatively new approach in the literature. The two most common types of stated preference studies are contingent valuation (CV) and stated choice surveys. CV studies typically use surveys to assess whether respondents would be willing to purchase a carefully defined vaccine at a specific price. The design of the valuation scenario must ensure that respondents understand the important attributes of the specific vaccine. In addition, respondents must be encouraged to consider the purchase decision as realistically as possible relative to their existing budget constraints (Arrow et al., 1993; Carson, 2000). The valuation can be based on a yes/no response to a single price or a series of prices. The use of a single price is more representative of a real world purchasing decision, while a series of prices allows for a more tightly bound estimate of the valuation for each person (Alberini, 1995). If the single price approach is used, the researcher will randomly (exogenously) assign one of a carefully designed set of prices to each respondent. The use of CV allows the researcher to estimate a household demand curve as a function of price for the vaccine. This demand curve can then be used to calculate an average willingness-to-pay for vaccines based on consumer surplus estimates.

Historically, stated preference studies have been used by environmental economists to value the public benefits or costs of changes in environmental quality (Carson, 2000). The use of CV for health interventions has recently become more common, although many health economists still favor the cost utility approach (Dolan and Edlin, 2002; Klose, 2003; Lancsar and Savage, 2004). In fact, most economists dismiss stated preference estimates because respondents are not bound to follow through on their stated responses (Arrow et al., 1993; Carson, 2000).

Vaccine CV surveys may inquire about demand for the respondent only (e.g., (Whittington et al., 2002; Whittington et al., 2003), the respondent's household (e.g., Cropper et al., 2004; Canh et al., 2006; Islam et al., 2008; Lucas et al., 2007), one of the respondent's children (e.g., Hsu et al., 2003; Prosser et al., 2004), or all children in the community (e.g., Prosser et al., 2004). Theoretically, analysis is most straightforward for estimating the respondent's own WTP because there are no constituency concerns about purchases for others. In contrast, household demand studies are complicated by the fact that decision-makers would be required to make valuations based on the preferences of others.

Surveys that measure WTP for cholera vaccines would be inclusive of all four types of the private benefits identified in Section 3.1. Respondents should consider all of these benefits when stating whether or not they would purchase at the offered price. If CV estimates of WTP for vaccines are accurate, this approach is better than attempting to estimate each benefit separately. Comparisons of WTP and COI estimates are available in some articles. Since COI estimates exclude valuations for reduced pain and suffering and reduced mortality risk, WTP estimates should be greater than COI estimates. For example, household WTP estimates for a 100% effective, 1-year duration malaria vaccine were about twice as great as the expected household COI in Tigray, Ethiopia (Cropper et al., 2004). In one study, Hsu et al. (2003) estimated that WTP for a varicella vaccine was actually less than their estimate of private COI; however, their survey only included recovered patients and it was unclear for whom the vaccine would be purchased. Note that varicella (or chickenpox) patients achieve lifetime immunity after recovery; thus, there is no need to purchase vaccines for children that have already suffered from the disease. It should also be noted that varicella symptoms are much more severe and mortality risk is greater if contracted later in life. Since vaccine effectiveness wanes with time, prospective purchasers may prefer that their children contract the disease while young to acquire lifetime immunity and avoid the more severe symptoms that would be experienced if contracted later in life.

My research group has conducted a number of CV studies of cholera vaccine demand, several of which have been published in the literature (Lucas et al., 2007; Islam et al., 2008; Kim et al., 2008; Whittington et al., 2009). These studies were conducted as part of the International Vaccine Institute's Diseases of the Most Impoverished (DOMI) multidisciplinary examination of cholera and typhoid disease burden and attitudes toward vaccination. I am not aware of any other cholera vaccine WTP estimates. The results of the cholera vaccine studies are summarized in Table 3.1. Incidence was highest in Beira, Mozambique and lowest in Hue, Vietnam. In Hue, public vaccination programs in 1998 and 2000 achieved 75-80% coverage of residents, and reduced incidence to almost zero during the period from 2000 to 2003 (Thiem et al., 2006). A vaccine trial was also undertaken in the bairro of Esturro in Beira, Mozambique in 2003. The trial covered 57% of the bairro and conferred 75-85% protection for recipients in the first 6 months. Thus, respondents in these studies should have previous experience with cholera vaccines. It is unclear how the trials may have influenced WTP estimates; trial participants may expect free vaccines or they might suspect that their trial vaccines are still providing protection, which would have rendered another vaccine unnecessary.

The Beira and Kolkata private demand studies incorporated a time-to-think approach for survey respondents. This methodology uses a series of two interviews to allow respondents to spend overnight considering their purchasing decision. This has reduced demand relative to standard treatment among DOMI studies, and contributed to the lower WTP estimate for Beira (Cook et al., 2006; Islam et al., 2008; Lucas et al., 2007; Whittington et al., 2009). The Hue study collected data in a single interview. Thus, it is difficult to directly compare Hue estimates with Beira and Kolkata results. The Hue estimate is greater than that for Kolkata or Beira. This could suggest that income is more important than incidence. However, it is important to note that the Hue study was conducted during the first cholera outbreak after the successful vaccination campaigns in 1998 and 2000. This might have led respondents to believe a cholera epidemic was in progress.

Table 3.1. Comparison of *ex ante* COI and WTP estimates from DOMI project sites

Location	Annual incidence (1/1000)[a]	Annual *ex-ante* COI (US$) [a]		WTP per person (US$)	Time-to-think (y/n)	Self reported annual household income (US$) [b]
		Private	Public			
Hue, Vietnam	NA [c]	NA	NA	$7.4 [d]	N	$1,200
Kolkata, India	1.6	0.02	NA	$2.7 [e]	Y	$700
Beira, Mozambique	2.4	0.08	0.11	$1.4 [f]	Y	$800

[a] Data taken from Poulos et al. (2008)
[b] All income measures are from the WTP studies. Estimates from COI studies would be biased if the infected population is significantly different than the rest of the population.
[c] Large scale cholera vaccine programs were conducted in 1998 and 2000. As a result, cholera incidence was reduced to near zero for a number of years prior to an outbreak in 2003. There were not enough cases to generate COI or incidence estimates.
[d] Data taken from Kim et al. (2008)
[e] Data taken from Whittington et al. (2009)
[f] Data taken from Lucas et al. (2008)

Both private *ex ante* COI and private WTP estimates are available for Beira and Kolkata, India. The estimated WTP was about 150 times greater than annual COI in Kolkata and about 20 times greater in Beira. Together, these results suggest that private COI estimates compose a small fraction of total private benefits. The Hue study included four different cholera vaccine scenarios, which varied in expected efficacy and duration. These included (1) the baseline 50% effective, 3-year duration vaccine, (2) a 70% effective, 3-year vaccine, (3) a 70% effective, 20-year vaccine, and (4) a 99% effective, 20-year vaccine. The order from 1 to 4 should rank the various vaccines in terms of desirability as longer lasting and more efficacious vaccines should provide more value to consumers. However, there was only a slight increase in stated household WTP (US$40 for the least desirable vaccine compared to US$50 for the most desirable vaccine) (Kim et al., 2008). This might suggest that some respondents had trouble understanding their interviewers' descriptions of vaccine effectiveness and duration. It could also suggest a very high discount rate for future protection.

The stated choice approach is the other common type of stated preference survey. In stated choice surveys, respondents typically are presented with 4 or more pair-wise sets of alternative vaccines and are asked to choose which one of the pair they would prefer. The choices sets are variable in attributes (e.g., price, effectiveness, duration, side effects, and convenience of vaccine receipt). By analyzing the repeated choice tasks, researchers can quantify the value of vaccine attributes based on tradeoffs between attributes and vaccine prices (Hall et al., 2002; Cook et al., 2006). The Cook et al. (2006) stated choice study was performed in the same areas of Hue as the Kim et al. (2008) cholera vaccine CV study. This study allowed for comparisons between respondent valuations for cholera and typhoid vaccines with varying attributes. They found that cholera vaccines are preferred to typhoid vaccines and that vaccine effectiveness was a more important attribute than duration. The Cook et al. WTP estimate for a 50% effective cholera vaccines was close to zero, which was much less than the estimate from the CV study. Since all WTP estimates in the stated choice experiment are evaluated relative to other choices, it is difficult to directly compare estimates. In contrast to the CV results for individually presented vaccines, this might suggest that prospective purchasers would spend considerably more on a more effective vaccine.

There has been little effort to estimate vaccine demand under varying incidence rates. In Table 3.1, there is some variance in incidence rates, but there are also important differences in socioeconomic status, cultural beliefs, and health system operation. There are some studies that examine influenza, pneumococcal, and/or measles vaccine uptake rates relative to disease incidence or mortality rates in previous years. However, it is not possible to generate WTP estimates from these studies because the price was not variable. In Section 3.6, I examine these studies as part of the economic epidemiology literature review. It is important to note that I am not aware of any attempts to estimate the indirect protection benefits of vaccinations relative to direct protection benefits.

3.3 Review of value of statistical life literature

It is usually preferable to directly estimate benefits for the vaccine of interest as demonstrated in Section 3.2. However, this requires considerable effort to obtain separate estimates in each location of interest. In Section 3.1, I identified five primary private benefits of vaccination, including mortality risk reduction. If I can estimate a generic value for the population average willingness-to-pay to reduce mortality risk, this generic value could be standardized across interventions based on the magnitude of risk reduction. Private COI estimates are already available for Matlab. I can compare the direct cholera vaccine WTP estimates to the value of *ex ante* COI plus a generic mortality risk reduction WTP estimate after adjusting the generic risk to the cholera-specific risk. In this section, I examine the mortality risk reduction WTP research.

A number of studies in the developed world have attempted to estimate the value of reduced mortality risk (for excellent reviews, see (Hammitt and Graham, 1999; Mrozek and Taylor, 2002; Viscusi and Aldy, 2003; Blomquist, 2004). Three methods commonly employed for this purpose include (1) hedonic wage or compensated wage studies, which measure how employees trade off higher wages for riskier jobs; (2) stated-preference techniques, which use surveys to ask how much respondents would pay for hypothetical products that could reduce risk of death; and (3) averting-expenditure studies, which examine how much people spend in time and money on products that reduce risk of death (e.g., seatbelt and bicycle helmet use, car safety).

The hedonic wage literature is the most widely implemented of the three approaches and includes studies in some less developed countries. However, results are generally limited to male blue collar workers facing risk of death by accident. The averting-expenditure studies include some estimates of parents' values for risk reductions for their children, but the method is limited by risk misperception and difficulties in valuing the non-monetary disutility of averting behaviors (e.g. time expenditure and discomfort from helmets, seat belts, and car seats). Estimates from stated preference studies are also available for some less developed countries and avoid some of the limitations of hedonic wage and averting expenditure product studies. However, these may

introduce bias if respondents are not properly informed of risk magnitudes and because people are not bound to actually pay for the hypothetical risk intervention.[3]

The average WTP per person divided by the magnitude of risk reduction per person is the normalized value of a statistical life (VSL) or population total WTP per expected life saved. The United States Environmental Protection Agency (USEPA) has used a VSL of US$6.1 million when monetizing the value of reduced mortality risk in its analyses of air pollution programs (Alberini et al., 2004a). In Europe, Environment Directorates-General adjusts VSL benefits for age, health, and cause of death and uses a central VSL measure of €1 million (Alberini et al., 2004a). Mortality risk reductions often contribute the main benefits of health and environmental initiatives; VSL estimates from less developed countries would be useful for conducting cost benefit analyses.

Table 1 presents results from illustrative hedonic wage, stated preference, and averting expenditure studies, with special emphasis on meta analyses, studies conducted in developing countries and of parents' valuations for reducing their children's mortality risks. If available, I report the magnitude and type of risk reduction considered, average or median annual household income, as well as a ratio of VSL to annual household income. The VSL to income ratio is useful for identifying trends in VSL amongst high and low income countries and for identifying outliers.

Generally, the highest VSL estimates (both in value and ratio) have been obtained from hedonic wage studies. Viscusi and Aldy (2003) provides the most comprehensive review of existing work and reported that the median VSL in the United States was (year 2000) US$7 million based on the most reliable studies. Thus far, very few hedonic wage VSL studies focus on

[3]Knetsch (2004) points out an important distinction between these methods. The hedonic wage studies measure willingness to accept (WTA) increased mortality risk in exchange for higher wages. In contrast, the stated preference and averting expenditure methods measure willingness-to-pay (WTP) to reduce mortality risk. WTA measures are bound by the maximum wages or minimum risk available; WTP estimates are bound by family income. In general, VSL estimates based on hedonic wage studies (i.e., WTA measures) tend to be higher than those based on stated preference and averting behavior studies (i.e., WTP measures), although exceptions do exist.

the developing world, although there were three estimates for India and another for Taiwan. The VSL estimates from the United States are significantly higher than those from India, which range from US$150,000 to 360,000 in 1991 USD (Simon et al., 1999) to US$3 million in 1990 USD (Shanmugam, 2001). Liu, Hammitt and Liu (1997) provided an estimate of US$150,000 to 360,000 in US$1986 based on a study in Taiwan. The VSL to wage ratio for the Indian studies, especially those by Shanmugam, are much higher than most others in Table 1. Both Viscusi and Aldy (2003) and Mrozek and Taylor (2002) report income elasticity of VSL estimates in the range of 0.45 to 0.6 based on a review of international studies. The estimates from Simon et al. and Liu et al. appear to be consistent with such estimates of the income elasticity of VSL (this is not true of Shanmugam's studies[4]).

Mount et al. (2001) use a model that examined family composition in the context of tradeoffs between car safety and automobile purchase price and maintenance cost to estimate families' WTP to reduce mortality risks for all members, and then to calculate average VSLs by age group. They generate roughly equivalent VSL estimates for parents and children of (1997) US$2.6 to $7.7 million. Carlin and Sandy (1991) and Blomquist, Miller and Levy (1996) examine parents purchases and uses of child car safety seats to examine VSLs for children. Carlin and Sandy's estimate is much lower because they do not attempt to place a monetary value on the time and disutility costs to parents when placing children in the car seats.[5] Additionally, Blomquist et al. provide a comparison between adults and children and report slightly higher VSL estimates for children less than 5 years of age compared to other age groups. Jenkins, Owens and

[4]Shanmugam (2001) extended the work in Shanmugam (2000) by adjusting for individuals' abilities to select their jobs based on the assumption that some may have unobserved attributes that allow them to work more efficiently in risky occupations. Using a different econometric procedure, his VSL estimate increased about three-fold to US$3.0 million. This approaches the US estimates and demonstrated the sensitivity of results to underlying model assumptions.

[5]Because all states have passed laws requiring child safety restraints (either carriers or booster seats) for children 4 years of age or less, I can infer that the public agrees that the societal value of mortality risk reductions provided by car seats exceeds their costs.

Wiggins (2001) estimate lower bounds for VSL based on aggregate data for bicycle helmet purchases, prices, and uses. Their VSL estimates are slightly higher for adults, although it is important to note that helmet prices tend to be considerably greater for adults than for children.[6]

The VSL-to-annual-income ratios for the averting behavior studies (for a summary of averting behavior studies conducted in the United States, refer to Blomquist (2004)) are generally lower than the median US hedonic wage estimate from Viscusi and Aldy (2003). However, the ratios from studies that attempt to account for the disutility of using safety equipment and make adjustments for perceived versus actual risk (e.g., Blomquist et al., 1996; Mount et al., 2001) tend to be higher and approach estimates from hedonic wage literature. Although definitive conclusions cannot be drawn from these few studies, it appears that VSL estimates for children are quite similar in magnitude to those for adults.

Relative to the hedonic wage and averting behavior studies discussed above, the stated preference VSL estimates tend to exhibit more variation and depend on the magnitude of risk reduction presented in the hypothetic scenario. The North American and European scenarios from Alberini et al. (2004a) and Alberini, Hunt, and Markandya (2004b) present a "general purpose" scenario in which the hypothetical product reduce risk of death from all causes. The US VSL estimates from (Alberini et al., 2004a) are lower than those reported for other methods as summarized in reviews by Viscusi and Aldy (2003) and Blomquist (2004) above.

In contrast to the "general purpose" studies, with the exception of Mahmud (2009), the studies from less developed countries are based on hypothetical products/interventions that would reduce risk from one specific cause of death. While the use of specific interventions (e.g., air pollution, SARS, etc.) present a more realistic contingent valuation scenario, the baseline mortality risk from one cause necessarily become much smaller relative to risk from all causes. It

[6]The range of prices for youth helmets is US$9 to $40 compared to US$25-135 for adults. Because of the large difference in price for the two age groups, it is hard to estimate accurately the difference in WTP for mortality risk reduction for children in comparison to adults. These estimates are also very sensitive to assumptions regarding the useful life of a helmet, the amount of protection provided by helmets, and the allocation of the helmet's value between injury prevention and death prevention.

is more difficult to communicate a small change in risk compared to the larger general risk scenarios. In addition, the use of specific causes of death might influence results if those causes are dreaded, like cancer, or somewhat avoidable, like traffic accidents (Subramanian and Cropper, 2000). Thus, there is a tradeoff between providing a more realistic CV scenario and an easier to understand change in mortality risk when choosing between general and specific intervention scenarios.

Bhattacharya, et al. (2007) estimate VSL for commuters in Delhi, India to reduce their risk of death from road traffic accidents. As might be expected, they find that people who commute to work have the highest WTP for improved safety and estimated VSL at about PPP$150,000 (US$30,000). The ratio of VSL to average household income (US$3,000) in Delhi is low relative to most of the other studies, but within the general range. The study by Mahmud (2009) is the only known stated preference study for mortality risk reductions from Bangladesh and is the only study from a rural area. It is based on a CV scenario for which the hypothetical intervention (a series of vaccinations) reduces a respondent's baseline risk of death from all causes by either 25% or 50%. This is a much larger change in baseline risk than for any of the other studies. In addition, the scenario required an up-front payment for five years of protection, while other studies used an annual payment mechanism. The use of the large change in baseline risk in addition to the 5-year up-front payment requirements are probably major factors in the very small VSL estimates from that study, US$1,300 to 2,500 in US$2003. The VSL-to-annual-income ratio of 1 to 2 is by far the smallest ratio observed from any of the studies reported in Table 3.2.

Table 3.2. Summary of relevant literature for VSL hedonic wage and stated preference studies

Researcher	Location, date, and data source	Average risk (10^{-5})	Average annual wage (US$)	VSL estimate (US$)	VSL to annual wage ratio ($/$)
Hedonic Wage Studies					
Viscusi and Aldy 2003	US subsample, 2000[a]	0.1 – 2	30,000	7 million	230
	Summary of studies[a]				
Liu et al. 1997	Taiwan, 1982-1986	2.25 - 3.82	4,100 - 5,100	135,000 - 600,000	33 - 130
	Taiwan Labor Force Survey				
Simon et al. 1999	India, 1985-1991	1.5	1,150	150,000 - 360,000	130 - 310
	Occupational Wage Survey and Annual Survey of Industry				
Shanmugam 2000	Madras, India, 1987-1990	1.0	600	0.75 - 1 million	1,250 - 1,700
	Survey of blue-collar workers				
Shanmugam 2001	Madras, India ,1987-1990	1.0	600	3 million	5,000
	Survey of blue-collar workers				
Averting Behavior Studies					
Blomquist 2004	US subsample, 2000	Not reported	30,000[c]	1.7 - 7 million	60 - 240
	Summary of studies[b]				
Mount et al. 2001	US hedonic study of 1997 vehicle	7 - 50[d]	34,000	3.4 - 6.4 million	100 - 190
	fatality rates and costs (adults)				
Mount et al. 2001	US hedonic study of 1997 vehicle	7 - 50[d]	34,000	2.6 - 7.7 million	75 - 230
	fatality rates and costs (children)				
Blomquist et al. 1996	Adult car seat belt use	5	22,000	1.7 - 2.8 million	75 - 130
	with time and disutility costs, 1983				
Blomquist et al. 1996	Child seat use (under 5 years of age)	10	22,000	2.3 - 3.7 million	100 - 160

Researcher	Location, date, and data source	Average risk (10^{-5})	Average annual wage (US$)	VSL estimate (US$)	VSL to annual wage ratio ($/$)
	with time and disutility costs, 1983				
Carlin and Sandy 1991	US, 1985 IN survey of child car seat use; crash safety data in WA	10	23,000 [c]	430,000 - 550,000	19 - 24
Jenkins et al. 2001	US, 1997, aggregate bicycle helmet price, use, and protection (adult)	0.55	37,000 [c] (lower bound)	2.0 - 4.0 million	54 - 108
Jenkins et al. 2001	US, 1997, aggregate bicycle helmet price, use, and protection (children)	0.4-0.6	37,000 [c] (lower bound)	1.1 - 2.7 million	30 - 70
Stated Preference Studies					
Alberini et al. 2004a	Canada, 1999 and US, 2000	1	47,000 - 53,000	0.9 - 1.5 million	19 - 28
	General	5	47,000 - 53,000	3.7 - 4.8 million	79 - 90
Alberini et al. 2004b	UK, Italy, France, 2002	1	41,000	2.5 million	60
	General	5	41,000	1.1 million	28
Vassanadumrongdee and Matsuoka 2005	Bangkok, 2003	0.3	9,000	1.4 - 1.5 million	150 - 170
	Traffic accidents and air pollution	0.6	9,000	0.9 million	100
Bhattacharya, Alberini, and Cropper 2007	Delhi, 2005 Traffic accidents	4 – 30	3,000	30,000	10
Hammitt and Liu 2004	Taiwan, 2001 Lung and liver cancer/ non-cancer	0.2 - 0.8 [e]	14,000	0.5 - 2.2 million [e]	36 - 160
Liu et al. 2005	Taiwan and Taipei, 2003	0.18	13,000 - 21,000	4.7 - 11 million	220 - 850
	SARS	0.6	13,000 - 21,000	2.8 - 6 million	130 - 460

Researcher	Location, date, and data source	Average risk (10^{-5})	Average annual wage (US$)	VSL estimate (US$)	VSL to annual wage ratio ($/$)
	Bangladesh, 2003	7.5 - 45[f]	1,200	2,300	2
Mahmud 2009					
	General	15 - 90[f]	1,200	1,300	1

[a] Viscusi and Aldy compile a number of studies. The risk reduction, average wage and VSL are ranges shown after conversion to 2000 US$.
[b] Blomquist compiles a number of studies. The risk reduction, average wage and VSL are ranges shown after conversion to 2000 US$
[c] Average household income is not reported in the study. The income reported in the table is taken from (U.S. Bureau of the Census 2004).
[d] Risk of death is calculated based on the sum of risks from 1-car, 2-car, and multi-car crashes. The differences in risk are based on the average risk for different categories of vehicles.
[e] Estimated VSL is calculated by average VSL for 2 in 100,000 and 8 in 100,000 risk reductions. Separate estimates for each magnitude of risk reduction are not available. Only median VSL values are reported
[f] The risk reduction used was either 25% or 50% of the baseline risk by age group. Hence, different age groups received different magnitude reductions. Estimates based on subjective risk were also made, but I only include estimates for objective risk.

Vassanadumrongdee and Matsuoka (2005) provide VSL estimates from Bangkok, Thailand and find no statistically significant difference in VSL estimates for reducing risk from traffic accidents compared to air pollution-related cancer. In contrast, Hammitt and Liu (2004) find a reduction in cancer risk is preferred to a change in risk from accidental death. Liu et al. (2005) present very high VSL estimates based on reduction of mortality risk from SARS; however, the surveys were performed during an epidemic, which may have resulted in great uncertainty regarding the future incidence of disease.

The ratios of VSL to annual household income tend to be lower for the stated preference studies relative to other methods, with the exception of the SARS study. The ratios also appear to be sensitive to the magnitude of risk reduction; the use of smaller hypothetical risk reductions results in larger VSL estimates within a given study. The only stated preference study that examines parents' willingness-to-pay to reduce their children's risk of death is from the United States (Dickie and Gerking, 2003; Dickie and Gerking, 2006).[7] This dissertation reports the first stated preference estimates of parents' WTP to reduce their child's risk of death from a less developed country.

3.4 Cholera vaccine economic evaluations

This section examines eight economic evaluations of cholera vaccines, which are summarized in Table 3.2.[8] The first five evaluations were performed prior to the DOMI project

[7]Dickie and Gerking (2003) tested parents' WTP for protective sunscreen that would reduce morbidity and mortality risks of skin cancer for themselves and their children in the US. They found that parents were willing to pay about twice as much to protect their children than to protect themselves. In addition, they found that parents' stated WTP was about twenty times greater for mortality risk reduction than for non-fatal skin cancer risk reduction. They could not develop a VSL estimate comparable to those above, because of the latent nature of mortality risk from skin cancer, especially for children. The results from this study are similar to two studies that examine parents' WTP to avoid an episode of illness for their children. Liu et al. (2000) and Dickie and Messman (2004) both found that parents were willing to pay more for one of their children to avoid an episode of illness than for themselves. In both studies, WTP was about twice as high for very young children as for their parents; the ratio decreased with age of the children.

[8]The first five studies were initially identified in Cook (2007). Each of these studies have been

and are more simplistic than the DOMI analyses. Of these five, there are two cost effectiveness analyses, two cost minimization analyses, and a single cost utility analysis. None of these analyses account for herd protection. The last three studies include DOMI study results and are considerably more thorough. Each of these studies accounts for herd protection and two out of three incorporate private demand considerations. The remainder of this section provides more detail regarding each study.

MacPherson and Tonkin (1992) report the cost-effectiveness of vaccinating North Americans traveling to cholera endemic areas based on a 50%-effective whole-cell killed vaccine that costs C$28 per fully vaccinated person in (1992 US$). Further, they assume that some recipients would have adverse reactions to the vaccine including fever, malaise, and headache. Their estimates are based on a 1 in 500,000 risk of contracting cholera for travelers for which there would be a 1% case fatality rate. They find that preventing one case in travelers costs C$28 million, and recommend that travelers not be vaccinated. Given the 1% fatality rate, it would cost C$2.8 billion to save one life, which is greater than any of the estimates presented in Section 3.3. They suggest that the vaccine might be cost-effective for some travelers to very high risk epidemic areas (e.g., a doctor working in an area with an epidemic). This study is not representative for residents of the Matlab area.

Naficy et al. (1998) provide a cost effectiveness analysis of four different strategies for controlling cholera based on epidemic simulations in a hypothetical refugee camp in sub-Saharan Africa: (1) pre-emptive treatment set up at inception of the camp; (2) reactive treatment set up after an outbreak is identified; (3) pre-emptive vaccination with a whole-cell killed vaccine; (4) reactive vaccination; and various combinations of these four strategies. This study makes no attempt to monetize the vaccine's private 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 vaccination would become more cost effective than treatment alone if the cost per delivered dose

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independently summarized and reviewed for this dissertation.

were less than US$0.16 per dose, which is not possible for any existing cholera vaccine. While adding vaccination to preemptive treatment costs more per case or death avoided, it also prevents more deaths. They report that it would cost $1,700 per additional death avoided, which is quite reasonable compared to the VSL estimates in Table 3.1. In general, it may be difficult to compare refugee settings with endemic settings because the incidence and mortality rates tend to be much greater for refugees.

Murray et al. (1998) examine the cost-effectiveness of the whole-cell killed vaccine both for a hypothetical refugee population with epidemic cholera and a hypothetical community with endemic cholera. They compare vaccination to a post-infection treatment strategy and a theoretical water and sanitation improvement. Water and sanitation improvement is found to be more cost effective than vaccination in both settings. This conclusion is dependent on the assumptions they have made. They assume that the cholera vaccine would cost US$6.26 per fully vaccinated person, and that the annual cost of water + sanitation + hygiene education would be US$17 per capita (both estimates in 1990 dollars). Their estimates also assume that cholera incidence is about 0.3% of the total diarrhea incidence in an endemic setting and about 2% in an epidemic refugee setting. In addition, they assume that cholera mortality is about 10% of all diarrhea mortality in the endemic setting and about 40% in the epidemic setting (both without treatment). They find that combining a treatment strategy with water and sanitation improvements is the most cost-effective strategy.

I note that the cost effectiveness of vaccination compared to water and sanitation interventions generally depends on the difference between cholera mortality and all-diarrhea mortality. If cholera mortality is a large fraction of all diarrhea mortality, cholera vaccination will appear to be a better investment. For locations in which cholera mortality is a small fraction of diarrhea mortality, it would not make sense to prioritize cholera vaccination before other interventions that would reduce all types of diarrheal disease.

Using the Matlab area as an example, Sack (2003) compares the cost effectiveness of cholera treatment versus vaccination by performing break-even analyses of the cost per cholera death avoided using different incidence rates and vaccination costs. Sack estimates that the treatment cost per death avoided is about US$350 (based on a 20% case fatality rate without treatment versus 0.5% with treatment). He reports that vaccines might be more cost effective than the provision of free treatment if per capita vaccine cost were less than US$1 or if annual incidence exceeded 1 in 1,000. However, this analysis ignores the disutility and financial costs of illness prevented through vaccination. Also, it may not be necessary to choose between vaccination and treatment. Instead, one could assess the marginal benefit of adding vaccination efforts to existing treatment programs.

The fifth study evaluates the retroactive use of a live oral vaccine (CVD 103-HgR) during the 1992 cholera outbreak in Argentina (Cookson et al., 1997). Although the study is labeled as a cost-benefit analysis, the authors only consider the avoided public costs of treatment in benefit calculations. Thus, this analysis is really a cost minimization analysis. The public COI estimates of direct medical treatment were very high (US$602 per case) during the Argentina outbreak because their public health system was ill-prepared for the outbreak. The authors find that a 75% effective, 3-year vaccine that costs US$1.50 per fully vaccinated person would be cost-saving from the government's perspective. These results are of limited applicability to the situation in rural Bangladesh because the public COI per case is about 30 times less in Matlab (COI estimates are presented in section 4.3). One reason for the discrepancy is the inclusion of "managerial costs" for bimonthly helicopter trips used by medical staff to travel to the outbreak area in the Argentine public COI estimate. Helicopter flights would not be needed in the Matlab area, where local treatment is readily available.

The sixth study undertakes a cost-benefit analysis of cholera vaccination in Beira, Mozambique (Jeuland et al., 2009). This study is based on similar assumptions as the work included in this dissertation. Specifically, private willingness-to-pay, incidence, and public cost of

illness data were collected for Beira and Matlab as part of the DOMI series of studies. Further, the authors incorporated herd protection into their analysis by assuming that the pattern of herd protection observed for Matlab would be similar to that expected in Beira. The Beira estimates for WTP, incidence, and public COI are similar in magnitude to those I found for Matlab (see Chapter 6 for Matlab estimates).

The authors make parametric assumptions regarding WTP for indirect protection to perform cost benefit analyses of three types of programs: school-based vaccination of children age 5-14 years, expanded school-based vaccination of children age 1-14 years, and mass vaccination of all ages greater than 1 year. For each type of program, the authors investigate the implementation of 3 user fees: free, US$1, and US$2.2. The authors estimate benefit-cost ratios in a range from 0.9 to 4.7, depending on program type, user fee, and whether herd protection was incorporated. The programs with the highest benefit-cost ratios target all children age 1-14 years, but omit adults. In addition, programs with higher user fees tend to have higher benefit-cost ratio because 1) public COI savings tend to be small relative to program costs, 2) WTP per person estimates increase as the price charged increases, and 3) monetary estimates of herd protection benefits are greater at lower coverage rates. The authors also conduct a sensitivity analysis and report that child vaccinations are very unlikely to fail a benefit-cost test even under worst case conditions.

Next, I summarize the findings of a seventh article that I worked on. Our article performs a cost benefit analysis of a cholera vaccination program in Kolkata, India and determines an optimal user fee (Cook et al., 2009). The data used to conduct this analysis were taken from the DOMI studies performed in Kolkata, India. We found that the social benefits of vaccination were much greater than the private benefits at low coverage rates (i.e. when the vaccine is sold at high prices). Thus, partial subsidies should be used to attain maximum social benefits. We also considered a pair of second-best policies in case it was not possible to determine the optimal price prior to initiation of the program, namely free provision and full-cost pricing. In the Kolkata case,

full-cost pricing would lead to greater net societal benefits than free vaccination. Free provision would lead to the vaccination of too many persons. The marginal impact of an additional vaccine on community incidence decreased with coverage and would be very small at the high coverage rates that would result from free vaccination.

Finally, the eighth study is a cost utility analysis of four sites that were included in the DOMI cholera studies: Matlab, Beira, Mozambique, Kolkata, India, and N. Jakarta, Indonesia. The data used for Matlab should be about the same as the input data used in this dissertation. Like the Beira cost-benefit analysis, the authors examine three age-based vaccination programs: school-based vaccination of 5-14 year old, expanded school-based vaccination of 1-14 year olds, and mass vaccination of all ages greater than 1 year. Programs with lower coverage rates (e.g., school children only) have lower costs per DALY saved because the marginal herd protection effect per vaccine is greatest at low coverage rates. Programs are deemed to be 'very cost effective' if the cost per DALY is less than annual GDP). If herd protection effects are ignored, none of the vaccination programs would be considered 'very cost effective'. However, when herd protection effects are considered, school-age vaccination programs in Matlab, Kolkata, and Beira would be considered 'very cost effective'. Thus, the inclusion or exclusion of herd protection effects have a dramatic impact on cost effectiveness. Since the herd protection effect per vaccine delivered tends to be greatest at low coverage rates in endemic areas, cost effectiveness measurements depend on the number of people vaccinated and who is targeted. For Matlab specifically, school-based programs for either 5-14 year olds or 1-14 year olds would be right at the 'very cost effective threshold', while the cost per DALY saved for universal vaccination would be about 50% greater than the threshold.

Table 3.3. Summary of cholera economic evaluation studies[a]

Study	Vaccine type	Perspective	Setting	Key assumptions	Conclusions
MacPherson and Tomkin (1992)	Whole-cell killed, 50% effective	Cost effectiveness (per case and per death)	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	Cost minimization	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 (per case and death)	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 (per case and death) Cost utility (per DALY)	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 minimization	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
Jeuland et al. (2009)	Oral killed whole-cell vaccine (rBS-WC)	Cost benefit	Beira, Mozambique	Vaccine cost US$0.80 – 4.00, Incidence 1.4 – 18 cases per 1000, Public COI US$0-30, Private WTP US$0.7-3.20, Vaccine effectiveness 60% for 3 years, Herd protection is similar to that observed in Matlab	Vaccination program is likely to pass benefit-cost if children are targeted or if user fees are charged because WTP is higher for child vaccinations and herd protection reduces risk for unvaccinated.
Cook et al. (2009)	Oral killed whole-cell vaccine (rBS-WC)	Cost benefit	Kolkata, India	Vaccine cost US$2.40, Vaccine effectiveness 50% for 3 years, Incidence 1.6 cases per 1000,	Vaccination program is likely to pass benefit-cost. Net societal benefits are

				Public COI US$15, Private WTP US$2.30, Herd protection is similar to that observed in Matlab	maximized at price less than average cost.
Jeuland et al. (2009)	Oral killed whole-cell vaccine (rBS-WC)	Cost utility	Matlab, Bangladesh; Kolkata, India; N. Jakarta, Indonesia; Beira, Mozambique	Vaccine cost US$2.20-3.20, Incidence 0.9 – 8.8 cases per 1000, Public COI US$17-34, Vaccine effectiveness 60% for 3 years, Case fatality rate 1%; Herd protection is similar to that observed in Matlab	When herd protection is considered, vaccination is 'very cost effective' for school-based programs in Matlab, Beira, and Kolkata. When herd protection is ignored or when adults are included in the vaccination program, it is unlikely that programs would be 'very cost effective.'

[a] The layout of this table, as well as some of the data, is taken from (Cook, 2007)

In summary, while a number of studies have attempted to examine the economic attractiveness of cholera vaccines, many are limited relative to the analyses included in this dissertation. Of the non-DOMI studies, none considered any private benefits, much less the private demand for cholera vaccines or the herd protection impacts. It is very unlikely that any of these studies would have had access to detailed private demand or herd protection data. The DOMI studies tend to be much more similar to the work included in this dissertation. I have been involved at various levels on these studies; however, I expand upon these previous works.[9]

3.5 Cholera epidemiology and impact of herd protection

The first four sections of this chapter focus on the economics of vaccination policy. This section focuses on the epidemiology of cholera vaccination. Many vaccination programs provide indirect protection from disease as well as direct protection. Indirect protection effects are generally categorized as either herd protection or herd immunity effects. Herd immunity involves the transfer of live immunologic agents from vaccine recipients to non-recipients. Herd immunity only results from the use of vaccines that incorporate live bacteria or viruses. Herd protection indirectly reduces exposure to disease by reducing the number of susceptible persons that could otherwise spread disease if they were not vaccinated. Since the vaccine used in the Matlab trial

[9]Compared to the Kolkata cost-benefit model that uses a single estimate for incidence and a single price function for demand, this dissertation uses models that consider four different sub-populations with separate incidences and demand functions. In addition, the Kolkata cost-benefit model uses a different methodology for calculating indirect vaccination benefits, which incorporates an adjusted VSL estimates and expected case fatality rates. Because this approach uses different accounting methods for direct and indirect benefits, the total benefit calculation depends on how benefits are calculated, not just how many people are vaccinated.
There are also a number of differences between the Beira cost benefit study and this dissertation. The Beira cost benefit study omits any consideration of cost utility metrics, while this dissertation compares outcomes from cost utility and cost benefit analyses. Second, the Beira cost benefit analysis does not consider the herd protection benefits that would result from the reduced risk experienced by vaccinated persons, (i.e. herd protection benefits only accrue to unvaccinated persons). Third, this study does not solve for optimal prices. Rather, prices are assumed.

was a whole cell killed vaccine, there was no herd immunity effect; there was only a herd protection effect.[10]

At this point, it is useful to define some basic epidemiological concepts. Epidemiologists have historically been interested in determining the "critical threshold" vaccine coverage rates that "break the chain of transmission". The critical threshold (X_c) is based on the relationship (1 - 1/R) where R is the infectivity or reproductive rate of infection (i.e. the expected number of additional cases per infected individual). Illnesses with larger values of R require higher coverage rates to achieve the critical threshold. The initial reproductive rate, R_o, is a function of the biology of the disease (i.e. the ease of transmission from infected to susceptible individuals), the population density, average age at which infection occurs, and other socio-behavioral factors of transmission. After the initiation of an outbreak, the reproductive rate, R, declines from R_0 as individuals recover from disease and acquire temporary immunity (Fine, 1993). The reproductive rate can also be reduced by initiating a vaccination program. This reduces the number of susceptible persons by conferring partial or full immunity to some fraction of the population. The reduction in reproductive rate decreases disease prevalence in the community. The decrease in prevalence reduces disease exposure: both direct contacts with infected individuals and contacts with disease vectors that propagate from infected individuals.

Experimental epidemiology studies on rats in the 1930s first demonstrated the effects of herd immunity and protection for limiting or eradicating disease. Most efforts by epidemiologists have focused on highly-communicable diseases, which can have drastic impacts in short periods of time (e.g., smallpox and polio). 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.

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

A recent natural experiment offered an opportunity to examine the herd protection impacts of a school-based mandatory influenza vaccination program. The authors examine influenza mortality in elderly adults before and after the program (Reichert et al., 2001). They report that one excess influenza death of an elderly adult was averted for every 400 vaccinations of school children. Another study reports a 42% reduction in respiratory illnesses in the members of households with a flu-vaccinated child compared to households in which none of the children were vaccinated (Hurwitz et al., 2000). There is also evidence that intra-household herd protection would reduce incidence in non-vaccinated family members (Patel et al., 2005; Longini Jr. et al., 2007). Intra-family herd protection is especially important for diseases that are primarily spread via direct personal contact (such as influenza and varicella).

The basic model used to represent the epidemiology of disease spread is shown in Figure 3.1. In this model, there are five basic categories to represent the population. These categories are summarized as susceptible (S), infected (I), recovered (R), exposed (E), and passively immune (M). The susceptible population may or may not become infected after exposure. The infected population may either recover from disease or die. The recovered group will become immune for at least a short time. Depending on the disease, the recovered individuals either achieve lifetime immunity or become susceptible again. When children are born, they may receive passive immunity from their mothers, although they become susceptible again in time (Hethcote, 2000).

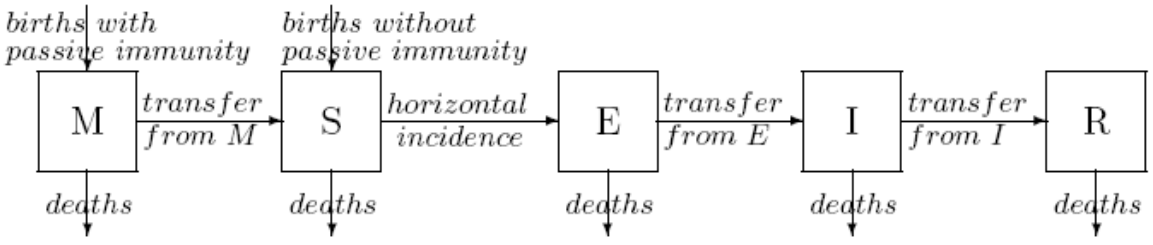


Figure 3.1. The general transfer diagram for the MSEIR model with the passively immune class M, the susceptible class S, the exposed class E, the infective class I, and the recovered class R (taken from Hethcote, 2000)

Any herd protection model must accurately capture the epidemiological factors associated with the spread and severity of disease as well as the effectiveness and duration of vaccine protection. For diseases like hepatitis A and varicella, infected individuals experience lifetime immunity after recovering from the illness. Recovered individuals should not be vaccinated because they already have immunity. These diseases are also unique in that disease symptoms are considerably more severe if the disease is contracted later in life. The varicella vaccine could actually increase varicella mortality because it does not confer lifetime immunity. As a result, adult mortality could increase after the vaccine is introduced. As varicella vaccine effectiveness wanes later in life, more adults would be susceptible because fewer adults would have developed lifetime immunity as children (Brisson and Edmunds, 2002; Brisson and Edmunds, 2003).

Next, I explore some of these considerations as they relate to cholera. The *Vibrio cholerae* species requires a specific tropical environment to survive endemically outside human hosts.[11] The global cholera incidence is mostly confined to a small number of locations where cholera is endemic. The bacteria are often present in the environment on a year round basis, although most cases occur during periodical outbreaks that emerge at specific times of the year. In areas where cholera is present, most individuals will have acquired some degree of immunity to infection. However, recovered cholera patients cannot acquire lifetime immunity to the disease (Longini et al., 2007), possibly because of changes in the dominant phenotype. Because the bacteria can survive outside human hosts, it would not be possible to eradicate cholera in a manner similar to smallpox. Although cholera can be spread via direct contact with infected individuals (Hartley et al., 2006), cholera is primarily acquired from ingesting contaminated food and water. During the seasonal outbreaks in Bangladesh, the bacteria are amplified by humans' who excrete high concentrations of the bacteria near local ponds (Huq et al., 2005).

[11] *Vibrio cholerae* can also be transported to non-endemic areas by infected persons or contaminated food sources, but the bacteria will not survive indefinitely outside human hosts.

Beginning in 2005, a group of epidemiologists and geographers re-examined the cholera vaccine efficacy data from the 1985 trial (Ali et al., 2005; Emch et al., 2006; Ali et al., 2008; Longini Jr. et al., 2007). They found strong evidence of herd protection effects, which were ignored in the original efficacy calculations. Indirect protection was modeled based on coverage rates in the areas surrounding individual neighborhood clusters of about 5-15 households, locally referred to as *baris*. Coverage rates and incidences are averaged across overlapping circles of area with 0.5 km or 2 km radii centered on each *bari*. The incidence for unvaccinated persons was inversely correlated with coverage rates across these overlapping circles. Children less than 2 years of age were excluded from the trial, but also experienced herd protection. This is important because young children typically experience higher incidence rates compared to other age groups. For young children, herd protection effects are significantly correlated with the coverage of adult women, but not with the coverage of other children. The authors do not report if the coverage of women is also disproportionately important for other age groups (Ali et al., 2008).

Since cholera vaccines are less than 100% effective, both vaccinated and unvaccinated persons benefit from herd protection. Indirect protection for both vaccinated and unvaccinated persons depends on vaccine coverage rates. As the vaccine coverage rate increases, the number of susceptible persons in the community decreases, retarding disease spread. As a result, exposure to infected persons and their associated disease vectors decreases and incidence rates decline for the vaccinated and unvaccinated subpopulations.

Longini et al. (2007) expanded the analysis by Ali et al. (2005; 2008) to estimate empirically the relationship between coverage and vaccine protection in Matlab. The results from their analysis are summarized in 5 data points from 10-90% coverage. I fit an exponential function to these data points for the vaccinated and unvaccinated subgroups, as shown in Figure 3.2. The expected percentage reduction in incidence for vaccinated and unvaccinated persons is plotted relative to a baseline in which nobody is vaccinated. I note that the authors extrapolate

herd protection effects for adult males who were excluded from the trial. They do not report if adult males are treated differently than females in the epidemiological model.

According to Longini's model, the total effectiveness of vaccination is the total impact of the indirect protection resulting from herd protection and direct protection of vaccinated individuals. Unvaccinated persons only experience indirect protection, while vaccinated persons benefit from both indirect and direct protection. The direct protection for vaccinated persons reduces incidence by 65% relative to the unvaccinated group at any coverage rate. The indirect protection varies with the coverage rate, and is demonstrated by the increase in protection for unvaccinated persons. Indirect protection for unvaccinated persons increases quickly from zero when nobody is vaccinated to 30% protection at 10% coverage to 90% protection at 50% coverage. The total protection for vaccinated persons is the product of indirect protection and direct protection (i.e. 65%). The difference in the magnitude of risk reduction for vaccinated versus unvaccinated persons becomes smaller and smaller as coverage increases and the incidence in unvaccinated persons decreases. These vertical lines labeled $MPrB_{10}$, $MPrB_{30}$, and $MPrB_{50}$ in Figure 3.2 demonstrate the magnitude of differences in incidences between vaccinated and unvaccinated subgroups at 10%, 30%, and 50% coverage rates respectively. The magnitude of the change in incidence, MPrB, is correlated with the private value of vaccination to the last person vaccinated (i.e. the marginal private benefit of vaccination).

Similarly, I assume that the marginal change in indirect protection benefits is represented by MPuB in Figure 3.2. Thus, the marginal value of indirect protection is correlated with the slopes of the incidence curves. As coverage increases, the marginal value of indirect protection per vaccine decreases from $MPuB_{10}$ to $MPuB_{30}$ to $MPuB_{50}$. Indirect protection benefits accrue to the entire community, while the private benefit of direct protection only accrues to vaccine purchasers.

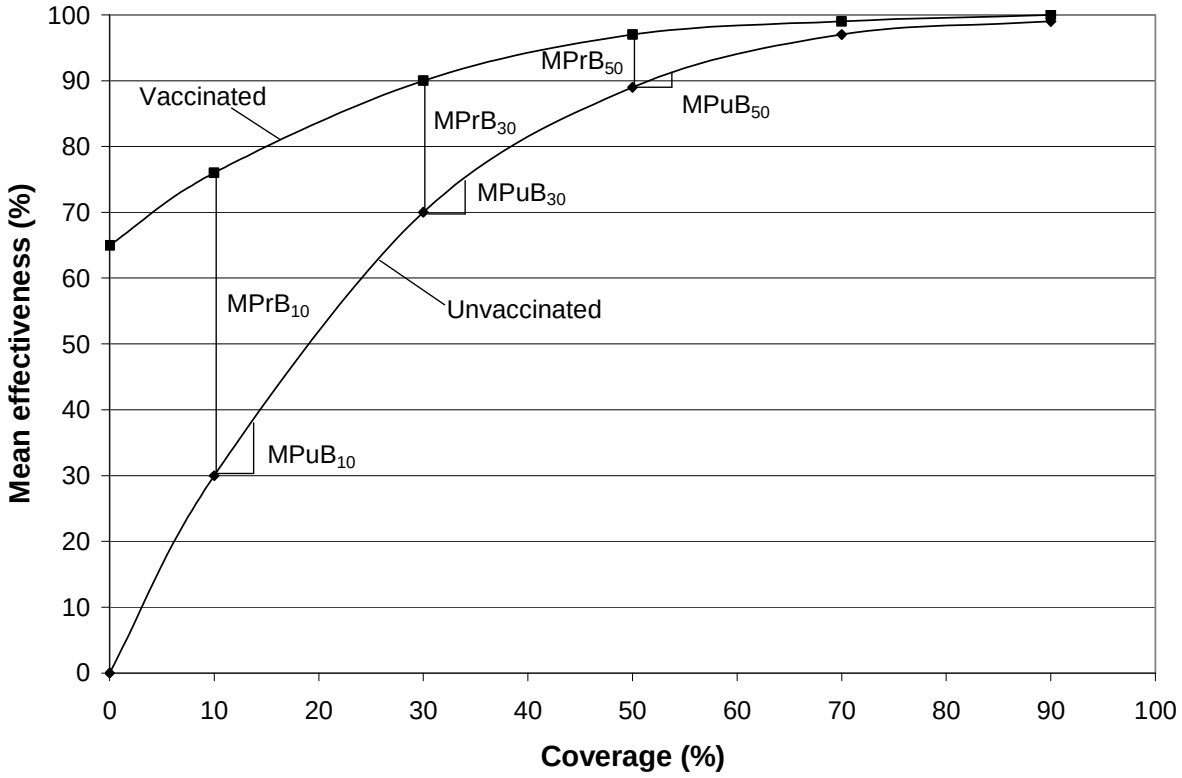


Figure 3.2. Direct and indirect protection as a function of coverage (extrapolated from Longini et al. 2007)

Longini et al. (2007) also report the expected number of cases avoided per 1,000 vaccines delivered, which is shown in 3.3.[12] The number of cases avoided per 1,000 vaccines decreases as a function of coverage from 40 cases avoided per 1,000 vaccines at 10% coverage to 13 cases per 1,000 vaccines at 90% coverage. If the cost per vaccine delivered is assumed to be constant, the cost per case avoided would be an increasing function of coverage.

[12]This figure is based on cholera epidemiology observed in 1985. Cholera incidence estimates are currently much lower, which may result in different epidemiology.

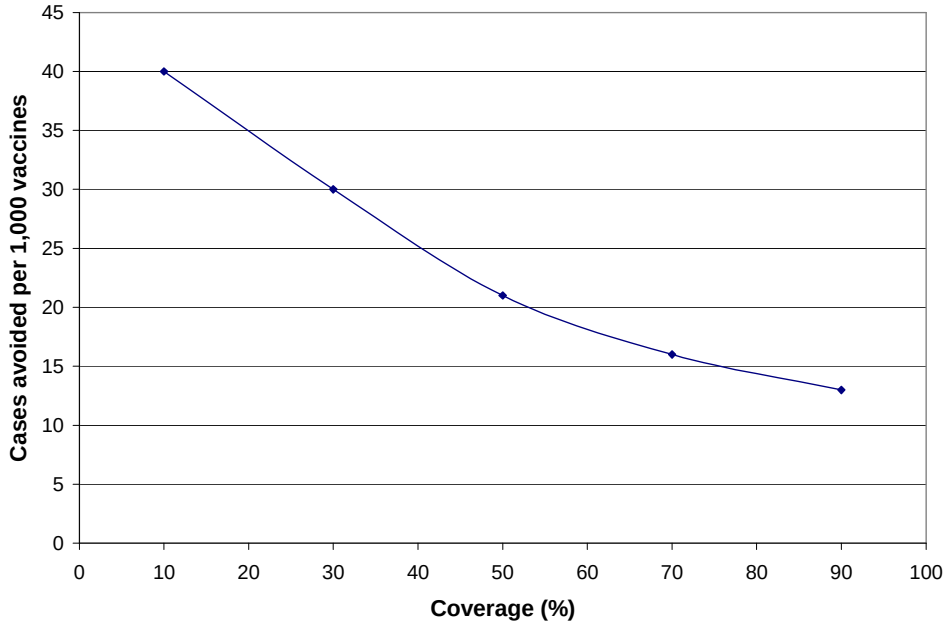


Figure 3.3. Cases avoided per 1,000 vaccines

Emch et al. (2009) examined the relationship between herd protection and coverage at smaller scales. Specifically, they examined relationships across environmentally connected baris, i.e. baris connected by common water bodies. Thus, unvaccinated persons that are environmentally connected to neighbors with high coverage rates are much less likely to contract cholera than unvaccinated persons connected to neighbors with low coverage rates. The authors report that their revised methodology is more precise than their earlier efforts reported in Ali et al. (2005). This suggests that discrete localized coverage rates are more important for calculating herd protection effects than an overall population average. In the extreme case, more cases would be avoided if 50% of each bari is vaccinated than if half of the baris achieved 100% coverage and the other half achieved zero coverage.

3.6 Economic epidemiology research

In the previous sections, I separately examine the economics and epidemiology of cholera vaccination. In this section, I first review how herd protection has been applied to cost utility analysis. Next, I review how epidemiologists would optimize vaccination programs without

consideration for private demand. Finally, I summarize how other researchers have attempted to integrate economics and epidemiology into a more comprehensive analysis of health interventions.

Many cost utility analyses have omitted herd immunity effects (Beutels et al., 2002; Beutels et al., 2007; Cook et al., 2008; Kim et al., 2009). Other analyses incorporate herd protection data from other sites for a pre-specified coverage rate, often between 70% and 90% for a targeted group (Welte et al., 2004; Armstrong et al., 2007; Lee et al., 2007; Lloyd et al., 2007).[13] A majority of vaccination analyses are undertaken for infant vaccination programs. In these cases, population coverage rates increase over time as successive cohorts of infants participate. Herd protection effects are then estimated as population coverage rates gradually increase with time from the initiation of the vaccination program. Vaccination benefits are aggregated based on incidence reductions for both vaccine recipients and for non-recipients. Notably, it is almost always assumed that more than 70% of eligible infants would be vaccinated under the newly implemented vaccination program. The accounting for herd protection effects can reduce the cost per DALY saved considerably, especially when incidence is indirectly reduced for elderly age groups who are most at risk from disease mortality (Lee et al., 2007; Lloyd et al., 2007).

While cost utility analysis is useful to prioritize projects and to identify low-value projects, it typically assumes that coverage rates are predetermined. When accounting for herd protection, it is useful to examine how coverage rates would affect cost utility metrics. Thus, this dissertation focuses on more flexible applications of cost utility analysis that may be used in comparison with cost benefit analysis.

Epidemiologists have examined how to optimally distribute a limited number of vaccines throughout a community. Epidemiological optimization models often assume that the initial supply of vaccines is limited, and that everyone would want to receive a vaccine if available. The

[13]Both the Jeuland et al. and Cook et al. analyses examine three scenarios in which different groups receive vaccinations: 1) young children less than 5 years of age, 2) all children less than 14 years of age, and 3) universal vaccination of all age groups.

optimal allocation depends on the epidemiology of the disease; there is no single approach that would apply to all vaccines (i.e. optimal influenza vaccination policy is likely to differ from optimal cholera vaccination policy). In one of the first epidemiology-based optimization analyses, Longini et al. (1978) examine how to allocate influenza vaccines during an epidemic. More recent examinations have considered the optimal distribution of vaccines in the aftermath of a bio-terror attack (Becker and Starczak, 1997; Longini Jr. et al., 2004) or if vaccine supply is insufficient due to production issues (Patel et al., 2005). In the aftermath of a terrorist attack, Longini et al. (2004) find that it is important to target the vaccine to people that have already come into direct contact with infected individuals (or are likely to have direct contact). If influenza vaccine supply is limited by production problems, Patel et al. (2005) find that it is optimal to prioritize school children before other age groups because the influenza reproductive rate for school children tends to be much greater than for other age groups. Even though elderly adults are more susceptible to influenza mortality, the prioritization of school children has a greater impact on elderly mortality rates because influenza vaccines are considerably less than 100% effective. Another study examines the optimal distribution of vaccines for an illness that is primarily spread through intra-household contacts (rather than inter-household contacts) (Becker and Starczak, 1997). They conclude that the optimal distribution should leave the same number of susceptible individuals in every household, regardless of household size (i.e. coverage rates should be greater in households with more members).

Finally, I examine published articles that merge private demand considerations with epidemiological modeling. The joint application of economics and epidemiology theory to public health problems is commonly referred to as epidemiological economics. This is a relatively new discipline; most of the seminal articles were written in the 1990s (e.g., Geoffard and Philipson, 1996; Philipson, 1996; Gersovitz and Hammer, 2003). The DOMI economic studies of cholera vaccination that were presented in Section 3.4 would also qualify as epidemiological economics.

The inclusion of herd protection effects into economic models of vaccination programs has been examined by a number of authors (e.g., (Brito et al., 1991; Francis, 1997; Francis, 2004; Boulier et al., 2007). Brito et al. (1991) examine the optimal tax or subsidy required to achieve the socially optimal vaccine coverage rate. They assume that 1) vaccines are 100% effective, 2) benefits are homogenous across the community, and 3) that costs vary across the community. They also prove that compulsory vaccination is always non-optimal compared to a tax/subsidy scheme. Francis (1997; 2004) expands upon this work by incorporating a common mathematical model of epidemic disease spread, the susceptible-infected-recovered model (see the box model in Figure 3.1). This dynamic model is applicable to epidemic disease spread, for which prevalence increases until the number of susceptible individuals is offset by the number of recovered (i.e. immune) individuals. At this point, prevalence begins to decline back to zero. Unlike Brito, Francis assumes that both vaccine costs and benefits are homogenous across the community. Francis solves for a threshold prevalence such that 1) when prevalence is below the threshold, no one is vaccinated and 2) when prevalence is above the threshold, everyone is vaccinated. Francis also examines a static equilibrium for which an optimal price is derived. Boulier et al. (2007) also employ the SIR model, but focus on how SIR parameters affect the optimal coverage rates. They also assume homogenous vaccine benefits and costs in the community. The optimal coverage rate depends primarily on the infectiousness of disease.

While Francis and Boulier et al. clarify how common epidemiological parameters affect optimal vaccination coverage for different diseases, their methodology does not show how to incorporate heterogeneous demand data into the model. My model is one of the first to include empirical vaccine demand data into a herd protection policy model (i.e. heterogeneous benefits). Since I assume that benefits are heterogeneous, only those with the greatest WTP choose to purchase vaccines as prices increase.

Other authors have examined how demand for preventative health products changes relative to changes in disease prevalence. This relationship is defined as prevalence elasticity or

incidence elasticity (Gersovitz and Hammer, 2003). Prevalence elasticity is typically measured based on survey panel data in conjunction with disease prevalence data. The survey data are used to estimate private usage of vaccines or other preventative products. The health data includes disease incidence or disease mortality rates. Researchers have examined the cross-sectional and longitudinal usage of condoms in response to changes in AIDS prevalence by county in the United States. They find that even small changes in risk can increase condom use substantially and suggest that epidemiologists should account for behavioral changes in their models of disease spread (Ahituv et al., 1996). Geoffard and Philipson (1996) use a mathematical epidemiology model in connection with behavioral response assumptions to identify a threshold prevalence for HIV; people would engage in permissive behavior below this threshold prevalence and protective behavior above this threshold. This threshold prevalence increases with the cost of protection and the discount rate, and decreases with the cost of infection and the probability of transmission upon exposure.

Philipson (1996) examines how long parents would wait to vaccinate their children with a measles, mumps, and rubella vaccine as a function of measles prevalence.[14] Around 1989-1990 a large measles outbreak occurred in the United States, the extent of which varied from state to state. At the time different states had promoted different levels of subsidies and other efforts to encourage early vaccination. Philipson reports that the public efforts to promote vaccination had very little effect on the age of uptake, while local prevalence of measles had an extremely large effect. The AIDS and measles studies suggest that subsidies and other public health efforts are limited in their ability to affect private behavior, at least in the United States context. There needs to be a strong private incentive to pursue preventative activities. A lack of private incentives to pursue vaccination in low-prevalence communities has often been cited as a limiting factor in

[14]MMR is required for students entering formal education. Thus, all children would eventually be vaccinated.

disease eradication efforts (Geoffard and Philipson, 1996; Geoffard and Philipson, 1997). With low prevalence, there is almost zero private benefit to vaccination.

The measles and HIV examples from the United States are likely not very useful for guiding cholera vaccination policy in Matlab. HIV has no cure and is spread primarily through voluntary sexual interactions or intravenous drug needle sharing. Thus, protective activities require endogenous changes in the frequency and/or intensity[15] of pleasurable activities rather than simply pursuing a vaccination. In the American measles example, vaccination is mandated for public schooling and the disease incidence is already very low. There is no mandate for cholera vaccination in Matlab, and prevalence is significantly greater. In addition, the measles vaccine provides long term protection at a much higher efficacy than the currently available cholera vaccine.

Other studies examine influenza and pneumococcal cross-sectional and longitudinal vaccine demand in response to changes in disease mortality in the United States (Li et al., 2004) and Japan (Ohkusa, 2001). In the United States, vaccine demand is correlated with mortality in the previous year, but cross-sectional correlation to demand was less significant. For Japan, Ohkusa (2005) develops a cost-benefit analysis after researching the price elasticity based on recipient co-pays and the probability that the elderly would be vaccinated in 12 large Japanese cities. Ohkusa finds that an US$8 reduction in the vaccination co-pay would increase vaccination rates enough to prevent approximately 400 deaths per year in the average large city. Influenza vaccine studies are a better analog for cholera vaccination because influenza vaccination is not mandated and because those vaccines confer limited protection (40-80% depending on age of recipient) and duration (about one year) (Coleman et al., 2006).

Finally, I summarize a typhoid vaccination cross-subsidy article to which I contributed (Lauria et al., 2009). This article examines how to maximize the number of cases avoided by

[15]It is assumed that condom use may be seen as decreasing the utility of sexual interactions by some individuals.

setting adult and child vaccine prices. It is assumed that adult and child prices are the only choice variables, and that the program must be cost neutral from the vaccine provider's prospective. In addition to the revenues collected from user fees, it is assumed that the vaccine provider could offset costs with some percentage of expected savings in future public treatment costs. We use average data from a number studies conducted in Asia and find that child incidence is typically greater than adult incidence and that household private demand for child vaccinations is greater than adult vaccinations. We examine both deterministic and stochastic models. The results from the deterministic model suggest that it is optimal to provide free vaccines for children and to offset revenue shortfalls by charging higher prices for adults. However, the increase in cases avoided from the cross-subsidy approach is relatively modest compared to the outcome from a program in which adult and child vaccinations cost the same amount. The results from the stochastic model are less clear cut and suggest that policy makers are likely to be better off charging both adults and children the full cost of vaccination because the greater incidences typically experienced by children are offset by the reduced vaccination demand for adults.

4 Research Design and Data Collection

In this chapter, I summarize data collection methods including the research designs for two stated preference scenarios that were included in a survey to support this dissertation. A number of studies have been conducted in Matlab, Bangladesh over the last 20 years. The ICDDR,B hospital has been collecting data regarding the number and types of cholera cases each year since the 1960s. Recent studies have estimated cholera incidence (Deen et al., 2008) and the public and private costs per cholera case (Poulos et al., 2008). The chapter also contains a detailed description of the two contingent valuation scenarios conducted in support of this dissertation: 1) household willingness-to-pay for cholera vaccines and 2) willingness-to-pay to reduce mortality risk for children. The economic and statistical models used to evaluate these scenarios are summarized in Chapter 5.

4.1 Historical cholera incidence data

Accurate estimates of disease incidence are rare, but the ICDDR,B has conducted ongoing surveillance of the area since 1966 (Longini Jr. et al., 2002). This surveillance is based on the number of patients treated at the ICDDR,B hospital, but does not include cases treated at other clinics or hospitals. All patients that presented at the clinic with cholera symptoms provided stool samples that identified the serogroup, biotype, and serotype. The number of cases treated at the hospital from 1963 to 1998 is shown in Figure 4.7 (originally created by Longini et al. 2000). The number of cases is highly variable from year to year, with an approximate range of 100 to 1,200 cases. The dominant serogroup shifted back and forth between the classical and El Tor serogroups until the classical group disappeared around 1993. At the same time, the 0139

serogroup first appeared. Longini et al. performed autocorrelation analysis, which showed that both Inaba and Ogawa outbreaks were followed 12 months later by outbreaks of the same serotype. Ogawa outbreaks were also followed by additional Ogawa outbreaks only 6 months later. Thus, population-level immunity for Inaba may be longer lasting than for Ogawa infection (Longini et al., 2002).

The ICDDR,B surveillance area is large, and includes more than 220,000 people. The people living in the most distant sectors of the surveillance area would have to devote up to 5 hours to travel to the ICDDR,B hospital via traditional methods. Since the ICDDR,B hospital is very well regarded and provides free treatment, it is expected that most residents of the service would choose to pursue treatment there. However, some of the cholera patients from distant northern villages may seek treatment from closer clinics or hospitals. It would take at least 4 hours for these residents to reach the ICDDR,B hospital via traditional transportation methods (rickshaw and country boat). In addition, these residents have easier access to the main road to Dhaka (Emch 2009).

Using data from ICDDR,B's hospital surveillance records, the annual incidence of cholera ranges from 1 to 5 cases per 1,000 persons. Sack (2003) reported that if the annual ICDDR,B hospital incidence were about 1 to 5 cases per 1,000 persons, the actual incidence could be about 4 to 20 cases per 1,000 persons in the surveillance area. A recent analysis of cholera and dysentery treatment at the hospital demonstrated that incidence in 1994 decreased sharply for villages located more than 10 km from the hospital. Annual cholera incidence was about 3 to 6 cases per 1,000 persons for villages within 8 km of the hospital compared to less than 1 case per 1,000 persons for villages located more than 10 km from the hospital (Ali et al., 2006). Thus, cholera incidence may be underestimated for areas located far from the ICDDR,B hospital.

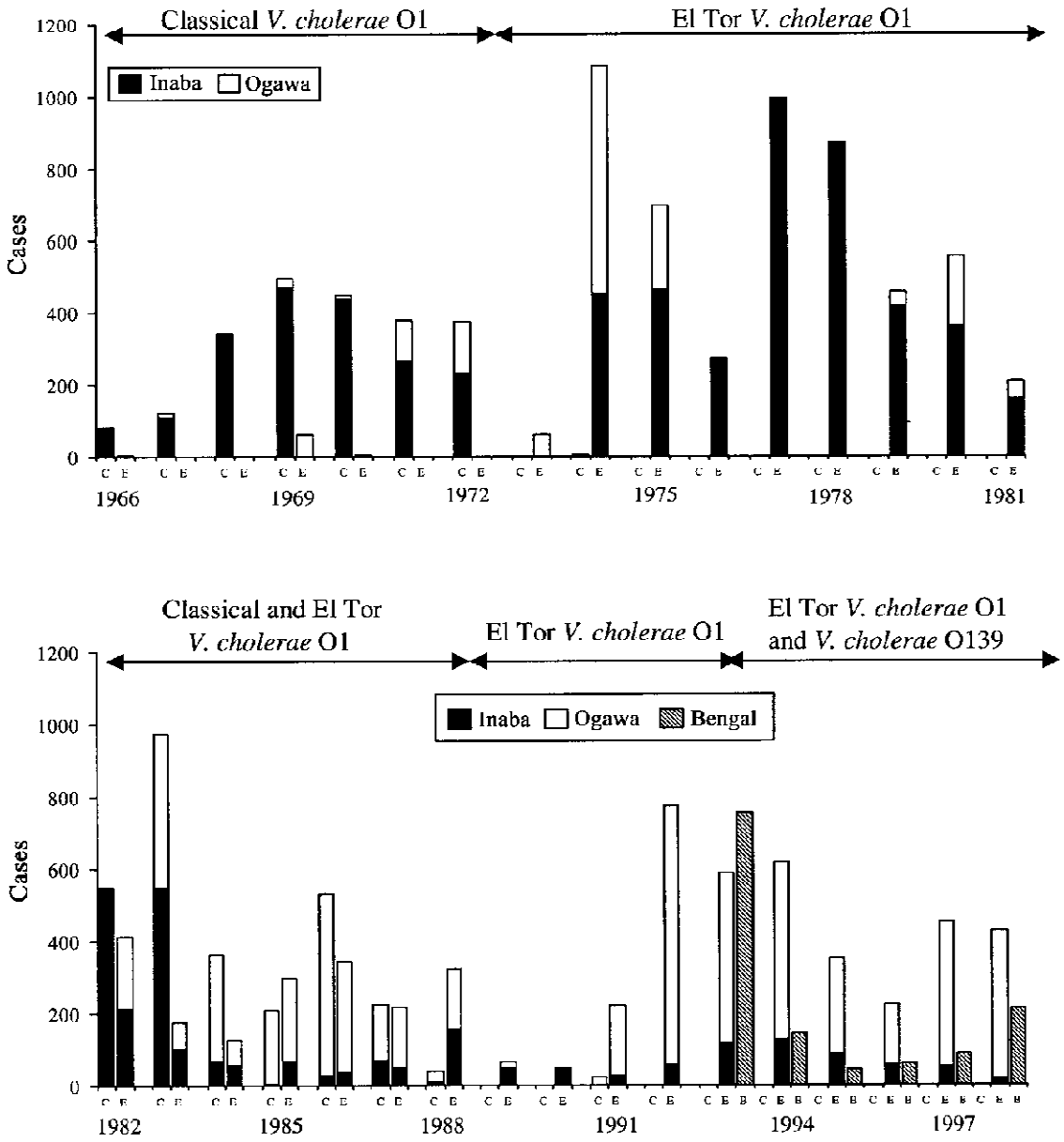


Figure 4.1. Yearly reported number of cholera cases, by Vibrio cholerae biotype and serotype, for the period 1966–1998, in Matlab, Bangladesh. Arrows indicate the periods of various dominant serogroups and biotypes. B, Bengal; C, classical; E, El Tor. taken from Longini Jr. et al (2002).

I obtained hospital surveillance records of cholera patients treated at the ICDDR,B hospital over the period from 1985-2007. Table 5.1 summarizes incidence by village over four overlapping time periods: the latest 3 years (2005-2007), the latest 5 years (2003-2007), the latest 10 years (1998-2007), and the full 23 years (1985-2007). There is large variation in both village size and the annual incidence of cases treated at the ICDDR,B hospital. The range in village size

is 55 to 9,400. The range of incidence rates varies from zero from 2005 to 2007 for a number of villages to almost 35 cases per 1,000 persons over the full period in one of the villages. It appears that there has been a dramatic decline in the number of cholera cases treated at the hospital over the previous 22 years; however, the literature does not report a reason for this decline. Figure 5.2 summarizes the annual number of cases treated at the hospital from 1983 through 2007. The figure includes the annual number and five-year rolling averages of cases treated at the hospital. There is great fluctuation in the yearly number of cases, which is smoothed by the 5-year rolling average.

There was a large drop in cases treated following the 1985 vaccination trial. Incidence remained low until 1992 when the 0139 strain was introduced and the number of cases treated increased rapidly, exceeding the rates reported prior to the vaccination trial. After a peak of 1,100 in 1993, the number of cases treated has declined steadily over the past 15 years. The hospital treated about 5,000 cases during the 10 year period from 1985-2004 compared to just 2,000 cases during the 10-year period from 1998-2007 and 350 cases over the last three years. Thus, it appears that the community may have made some progress in reducing the cholera burden over the past 22 years. As a result, a cholera vaccination program may be considered less important to the community in the present relative to the time of the last vaccination trial in 1985.

Table 4.1. Incidence by village over the last 3 years, 5 years, 10 years, and 22 years (annual cases per 1,000 incidence)

Village code	Village name	Village population	3 yr incidence	5 yr incidence	10 yr incidence	All yr incidence
A00	Uddamdi	3251	0.92	0.98	1.23	2.85
B00	Charmasua	2038	0.49	0.69	1.47	3.35
C00	Sarderkandi	3987	1.00	1.00	1.15	3.41
D00	Charmukundi	2484	0.67	1.13	1.21	2.45
D28	Bazarkhola	1128	0.00	0.00	0.18	0.28
D29	Kirtonkhola	209	0.00	0.00	0.00	0.00
D30	Banuakandi	791	0.00	0.00	0.13	0.06
D31	Harina Bazarkhola	1099	0.30	0.36	0.36	0.29
D32	Khalisha	789	0.85	0.51	0.38	0.29
D33	Nayanagar	1087	0.00	0.00	0.09	0.17

Village code	Village name	Village population	3 yr incidence	5 yr incidence	10 yr incidence	All yr incidence
D34	Saidkharkandi	1389	0.00	0.14	0.22	0.16
D35	Mollah Kandi	627	0.00	0.00	0.00	0.07
D88	Sankibhanga	1490	0.00	0.00	0.47	1.68
D89	Sankibhanga Namapara	1143	0.58	1.40	1.49	3.86
D90	Zahirabad	958	0.00	0.21	0.73	3.94
D93	Maizkandi	1334	1.00	0.60	1.20	3.85
D94	Hazipur	1504	2.22	1.46	1.99	3.78
D95	Tapaderpara	563	0.59	0.36	0.89	1.21
D96	Sakharipara	1116	0.90	0.54	0.90	1.26
D97	Nayakandi	738	1.81	1.08	0.54	2.53
D98	Bara Haldia	3379	0.79	0.71	0.74	2.35
D99	Mandertoli	2028	0.82	0.69	0.79	1.73
DX0	Barogaon	3655	0.00	0.11	0.16	0.20
DX1	Naojan	1376	0.00	0.00	0.00	0.23
F00	Sepoykandi	1464	0.91	1.23	1.23	3.23
G00	Thatalia	2970	1.01	1.28	1.31	2.60
H00	Lamchari	1239	0.27	0.65	0.40	1.65
J00	Char Harigope	745	0.00	1.07	2.42	2.44
K00	Shahpur	954	0.00	0.00	0.00	0.10
L00	Tatkhana	587	0.00	1.70	0.85	0.70
M00	Char Nayergaon	203	0.00	0.00	0.49	0.22
N00	Aswinpur	2199	0.00	0.00	0.09	0.39
O00	Nayergaon	1952	0.17	0.10	0.10	0.14
P00	Titerkandi	2137	0.16	0.28	0.14	0.17
Q00	Char Shibpur	261	0.00	0.00	0.00	0.00
R00	Nandalalpur	1449	0.69	0.55	0.62	0.66
S00	Tatua	939	0.00	0.00	0.00	0.58
T00	Amuakanda	1676	1.19	3.70	2.15	2.47
U00	Baispur	8830	0.49	0.86	1.25	3.17
V01	Kadamtali	379	0.88	0.53	2.64	6.36
V02	Nilokhi	503	0.66	0.80	1.19	3.34
V03	Char Nilokhi	623	0.54	0.32	0.48	2.85
V04	Char Pathalia	338	1.97	1.18	2.37	3.50
V05	Gazipur	3333	0.60	1.14	1.68	4.24
V06	Fatepur	2438	0.41	1.15	1.19	2.54
V07	Nayakandi	300	0.00	0.00	0.00	3.79
V08	Goalbhar	1174	0.00	0.68	1.28	2.56
V09	Naburkandi	1209	0.28	0.33	0.66	1.43
V10	Dhakirgaon	1798	1.30	1.11	1.45	3.31
V11	Nabakalash	2665	1.13	1.35	1.73	2.54
V12	Bhangerpar	674	0.49	0.89	2.08	4.52
V13	Baburpara	710	0.47	1.13	1.13	4.10
V14	Enayetnagar	771	0.86	2.85	1.43	4.42
V15	Bhati Rasulpur	761	0.00	0.26	0.53	1.73
V16	Binandapur	868	0.00	0.23	0.46	3.09
V17	Hatighata	1079	0.31	0.37	0.93	2.23
V18	Torkey	3953	0.34	1.21	1.06	1.90
V19	Lakshmipur	2934	0.68	0.95	1.43	2.39

Village code	Village name	Village population	3 yr incidence	5 yr incidence	10 yr incidence	All yr incidence
V20	Dagorpur	1332	0.75	0.60	0.90	2.66
V21	Khadergaon	552	3.62	2.90	1.63	2.31
V22	Beloti	634	0.00	0.63	0.47	1.79
V23	Baluchar	635	0.00	1.26	1.10	2.15
V24	Machuakhal	2942	0.91	1.02	1.02	2.27
V25	Char Pathalia	1361	0.24	0.73	0.73	0.90
V26	Narayanpur	3052	0.33	1.51	1.41	1.34
V27	Panchghoria	974	0.68	1.03	0.51	0.89
V28	Khidirpur	1559	0.00	0.26	0.19	0.90
V29	Shibpur (South)	491	0.00	0.41	0.00	0.28
V30	Harion	546	0.00	0.00	0.18	0.17
V31	Dighaldi	9433	0.95	1.08	1.14	2.67
V32	Mobarakdi	3332	0.40	1.08	1.29	2.51
V33	Shibpur (North)	447	0.00	0.00	0.45	0.61
V34	Satparia	810	0.00	0.00	0.25	0.51
V35	Durgapur	3731	0.00	0.21	0.32	0.38
V36	Ludhua	5605	0.36	0.36	1.05	2.59
V38	Galimkha	1571	0.64	0.51	0.45	0.61
V39	Gobindapur	346	0.00	0.00	0.00	0.00
V40	Masunda	802	0.00	0.00	0.25	0.17
V41	Paton	1857	0.00	0.00	0.32	0.24
V42	Adhara (South)	765	0.00	0.00	0.00	0.00
V43	Kanachak	1031	0.00	0.00	0.10	0.26
V44	Panchdona	623	0.00	0.00	0.00	0.22
V45	Bakchar	1101	0.00	0.00	0.00	0.25
V46	Silinda	403	0.00	0.00	0.25	0.23
V47	Tulatali	1795	0.00	0.00	0.06	0.20
V48	Gangkanda	568	0.00	0.00	0.35	0.32
V49	Harina Bhabanipur	1245	0.00	0.00	0.16	0.22
V50	Bakharpur	55	0.00	0.00	0.00	34.71
V51	Induriakandi	525	0.63	0.38	1.71	7.71
V52	Nayakandi	216	0.00	0.00	0.00	3.16
V53	Chhoto Haldia	3040	0.77	0.92	1.32	3.05
V54	Balairkandi	600	1.67	1.00	1.33	1.82
V55	Induria	533	0.63	1.50	1.69	2.39
V56	Pailpara	1511	0.44	0.53	1.13	2.74
V57	Baluchar	1066	0.00	0.00	0.09	0.17
V59	Doshpara	1702	2.15	1.29	1.65	2.24
V60	Suvankardi	987	0.68	0.81	1.01	3.18
V61	Munsabdi	678	2.95	2.06	1.62	3.29
V62	Shilmondi	924	0.36	0.22	0.54	2.66
V63	Islamabad (East)	2114	0.00	0.00	0.09	0.84
V64	Kawadi	4619	0.00	0.00	0.04	0.11
V65	Nayachar	804	0.00	0.00	0.37	0.17
V66	Thatalia	846	0.00	0.00	0.00	0.38
V67	Majlishpur	604	0.00	0.00	0.33	1.58
V68	Sobahan	1041	0.00	0.00	0.00	0.13
V71	Khamarpara	505	1.32	0.79	0.40	0.27
V72	Upadi	6342	1.21	1.73	1.69	2.59

Village code	Village name	Village population	3 yr incidence	5 yr incidence	10 yr incidence	All yr incidence
V73	Sadardia	844	0.00	0.00	0.00	0.05
V74	Ketundi	1434	0.00	0.00	0.21	0.29
V75	Mukundi	323	0.00	0.00	0.00	0.28
V76	Chosoi	1843	0.00	0.00	0.05	0.12
V78	Soladana	237	0.00	0.00	0.00	0.77
V79	Pitambordi	363	0.00	0.00	0.55	0.50
V80	Daribond	1258	0.00	0.00	0.08	0.04
V81	Sonaterkandi	703	1.90	2.28	1.28	2.59
V82	Dhanarpar	1748	0.38	0.69	0.97	2.73
V83	Padmapal	613	0.00	0.00	0.65	2.89
V84	Shahbajkandi	2323	0.57	1.55	1.46	2.60
V85	Bhanurpara	516	1.29	1.16	0.78	1.85
V86	Adhara	946	0.00	1.27	0.95	1.11
V87	Hurmaisha	689	0.48	0.58	3.05	3.50
V88	Datikara	531	0.00	0.00	0.38	0.94
V89	Islamabad (Middle)	1467	0.23	0.41	0.48	1.61
V90	Narinda	1249	0.00	0.00	0.00	0.25
V95	Baluchar	2275	0.15	0.62	1.93	2.76
V96	Rampur	669	0.50	0.60	0.75	3.06
V97	Dhanagoda	338	0.00	0.00	0.00	0.40
V98	Santoshpur	125	0.00	0.00	0.00	0.00
V99	Baluakandi	520	0.00	0.00	0.19	0.70
VB0	South Rampur	2792	0.84	0.72	1.90	3.29
VB1	Taltoli	1059	0.00	0.00	0.00	0.17
VB2	Sree Rayerchar	1156	0.29	0.17	0.35	0.31
VB3	Rayerkandi	3015	0.00	0.00	0.27	0.32
VB4	Ramdaspur	3610	0.65	0.66	1.11	2.53
VB5	Thakurpara	834	1.20	1.44	2.28	3.32
VB6	Sarkerpara	530	0.00	0.38	1.13	2.66
VB7	Mirpur	313	0.00	0.00	4.47	5.81
VB8	Farazikandi	1347	0.74	0.89	1.41	2.09
VBA	Mehron	2483	1.34	0.97	0.72	0.84
VBB	Nagda	4556	0.37	1.49	1.21	2.78
VBC	Naogaon	4925	1.22	1.42	1.40	2.45
W00	Kaladi	6371	0.68	1.13	1.04	1.18
Average		1580	0.45	0.59	0.79	1.95
Minimum		55	0.00	0.00	0.00	0.00
10 percentile		381	0.00	0.00	0.00	0.16
25 percentile		624	0.00	0.00	0.16	0.28
50 percentile		381	0.24	0.39	0.59	1.7
75 percentile		1066	0.68	1.0	1.2	2.7
90 percentile		3333	1.2	1.4	1.7	3.5
Maximum		9433	3.6	3.7	4.5	35

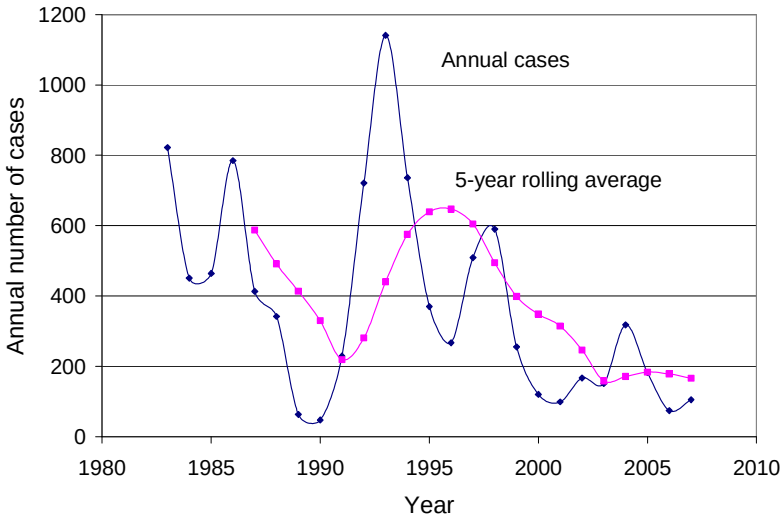


Figure 4.2. Annual and 5-year rolling average of hospital-treated cases

Estimates of cholera incidence by age group are obtained from a recent DOMI study that estimated incidence rates and cost of illness in multiple countries (Deen et al., 2008; Poulos et al., 2008). These incidence estimates are summarized in Table 5.2. Incidence was highest for younger children less than 5 years of age, followed by school age children, and adults. The average across age groups is 1.6 cases per 1,000 persons. These estimates are split into a high incidence group, which represents the 10% of villages with the highest incidence over the previous 10 years and the remaining 90% of villages. On average, the high incidence villages' incidence rates were about four times greater than the remaining 90% (see Table 5.1). This is based on historical incidence rates by village. Although some of these village-by-village differences result from the distance to the hospital, this is still the best estimate available.

Emch (1999) examined the risk factors for hospitalization with cholera and non-cholera watery diarrhea at the ICDDR,B hospital. He found cholera incidence was significantly correlated with environmental and socioeconomic variables (e.g., baris in which multiple households use open latrines, more households sharing a tube well, households with less land, population in a bari is high, population density surrounding a bari is high, living in flood controlled areas. Thus,

use of improved water and sanitation has a positive impact on cholera transmission as expected. Cholera transmission is also more prominent in densely populated baris and households. It is unclear why cholera transmission is greater in the flood-controlled region. While households with less land were more likely to contract cholera, household income and assets were not correlated to cholera transmission. It may be that the amount of land available to households is a better indicator of wealth than income or asset measurements in a rural community. It is important to note that most all of the households in the Matlab area are poor. Thus, differences in income are smaller than what may be found in urban areas.

Table 4.2. Average annual incidence by age group

Age group	Annual incidence (cases per 1,000 persons)		
	All	Highest 10% of villages	Remaining 90% of villages
Infants (age < 1 year)	4.6	14	3.5
Young children (age 1-4 years)	3.8	12	2.9
School-age children (age 5-14 years)	1.6	4.9	1.2
Adults (age >14 years)	1.0	3.1	0.8
All ages	1.6	4.9	1.2

4.2 Cholera cost of illness

The public and private costs of illness were recently estimated by another DOMI study, for which I am a co-author (Poulos et al., 2008). The public cost of illness is estimated based on the ICDDR,B hospital's operating records using a standardized micro-costing approach (Drummond et al., 2005). Estimates are calculated based on 1) the length of patients' stays, 2) the type and amount of medication dispensed, and 3) the type of diagnostic tests performed. Each test performed is multiplied by an estimated unit cost for that test. Medicine costs are similarly estimated by multiplying the amount dispensed by an average unit cost. The overnight stay costs are more complicated because it is necessary to account for non-cholera-specific staff, operating

and capital costs. These costs include 1) material costs such as maintenance, electricity, telephone, meals, and security, 2) labor costs, and 3) capital costs which are estimated as a percentage of operating costs based on studies performed in Thailand (Riewpaiboon et al., 2005; Riewpaiboon et al., 2007a; Riewpaiboon et al., 2007b; Riewpaiboon et al., 2007c). Because the hospital provides treatment for a number of different diseases, it is necessary to determine how to allocate administrative and other overhead costs across diseases. For a particular department, the ratio of services rendered for one type of disease is calculated relative to the total number of services produced by that department. In total, the average public cost of a cholera episode was about US$20, and is roughly equivalent for children and adults.

Private COI is estimated based on in-home interviews conducted with cholera patients or the caretakers of child patients. Cholera patients were interviewed at 7 days and 14 days after they were tested at the outpost or hospital. The survey instrument includes specific questions about direct and indirect costs. The direct COI questions include private expenditure for medication, diagnostic tests, and general clinic costs. Other direct non-medical costs include non-medical expenditure for transportation; special foods and drinks purchased for patients; and food and lodging requirements for caretakers that accompanied hospitalized patients.

The indirect costs of illness measure the lost productivity of the patients, substitute laborers, caretakers, and travel companions. If the patient, their caretaker or their substitute laborer missed time at work, the indirect COI is simply calculated as their wage rate multiplied by the number of work days missed.[16] Time lost from household activities, school, or leisure are calculated as a fraction of the average wage: 50% for housework or school time; 30% for leisure. The value of lost time for children who could not perform housework or school work is further reduced by 25% for teenagers and by 50% for children between 5 and 12 years of age. We do not

[16]If a patient reported a substitute laborer for some or all days, the substitute laborer is assumed to make up for the missed work of the patient, although the substitute's personal lost productivity is accounted for in place of time spent on substitute labor. If a caretaker or substitute laborer would have worked for a wage that was unknown to the respondent, the average wage was used in its place.

value time lost by children under 5. The average private COI varies by age group as shown in Table 4.3.

Table 4.3. Public and private cost per cholera episode and *ex ante* COI

		Children	Adults	All ages
Public COI per case (*ex post*)	Provider treatment costs (US$)	21	19	20
	Private payments to public facilities (US$)	1	1	1
	Net public treatment costs (US$)	20	18	19
Private COI per case (*ex post*)	Direct treatment costs (US$)	4	7	5
	Indirect treatment costs (US$)	4	11	7
	Total private treatment costs (US$)	8	18	12
Total COI per case (ex ante)		*28*	*36*	*31*
Annual Incidence (cases per 1,000)		2.2	1.0	1.6
Annual ex ante public COI	(US$)	0.04	0.02	0.03
Annual ex ante private COI	(US$)	0.02	0.02	0.02

The average private direct COI is about US$4 for children and US$7 for adults. Private indirect COI is much greater for adults (US$11) than for children (US$4). It is not surprising that indirect COI is greater for adults, because they are more likely to miss time at work. In addition, we assume there is no productivity loss for children less than 5 years old. The sum of direct and indirect private COI is about twice as great for adults relative to children. The annual *ex ante* private COI is roughly equal for children and adults. While children's incidence is about twice as large as adults', the private cost per case is about double. Thus, the difference in incidence is balanced by the difference in cost per case. The *ex ante* public COI is greater for children, because the cost per case estimates are roughly equal (while the child incidence is larger).

4.3 Survey research design

Household cholera vaccine demand and willingness-to-pay for mortality risk reduction of the household's youngest child were evaluated in separate sections of a single interview. Thus, all of the respondents received both sets of questions. I begin this section with a brief summary of

the sample protocol used to select households. Then, I explain the time-to-think protocol used in a subset of the surveys. I conclude with discussions of the valuation scenarios used for the cholera vaccine demand and VSL scenarios.

4.3.1 Sampling

The Matlab area is generally homogenous in terms of its population, although the area nearest to the hospital is slightly less rural than the surrounding villages. Survey respondents were chosen randomly from the Health and Demographic Surveillance System database via a two-stage cluster sample without replacement. The first stage selected a total of 3,000 households, each with at least one child less than 18 years of age. Two-thirds of these households were located in the government service area, and one-third in the ICDDR,B service area. The sample list was subdivided into clusters of 22 to 28 households located in small areas ranging about 1 km^2 to 4 km^2 depending on population density. In the second stage I randomly selected clusters of households and assigned one each to enumerators. Enumerators were instructed to allot half their interviews to males and only to interview the primary caretaker of the children in the household, typically one of the parents.[17] The second stage sampling was implemented twice to coincide with staging of the interviews. In total, 591 households granted interviews and only two households refused. Another 160 households were dropped because the selected male parents lived and worked outside the village and were not available.

4.3.2 Survey instrument

The survey instrument was based on a questionnaire used in a DOMI WTP study in Kolkata, India and is included as Appendix 1. Two sets of 60 pretest interviews helped us to adapt the survey to local conditions in the Matlab area and to set an appropriate range of prices for the contingent valuation scenarios. The study employed 20 local enumerators to conduct the

[17]Two respondents were the grandparents of children.

interviews. These enumerators had experience working on other public health studies conducted by ICDDR,B, but they had not worked on a CV survey before. They received two weeks of training according to the guidelines recommended in Whittington's review of CV practices in developing countries (Whittington, 2002). Afterward the enumerators practiced implementing the questionnaire via field tests and pretests.

The survey instrument had six sections of questions. The first section recorded demographic information about the respondent and members of the household. The second section had questions regarding the respondent's perception of cholera. It also asked about the respondent's experience with cholera and about knowledge of other family members or friends having contracted the disease and/or having died from it. The third section discussed how cholera was contracted, spread, prevented, and treated; it also included questions about the respondent's previous experience with the oral cholera and TABC vaccines. This section also introduced the CV scenario of the hypothetical new cholera vaccine, described the vaccine's effectiveness, and then tested the respondents' understanding of the concept of vaccine effectiveness. The visual aid presented to respondents to help them understand vaccine effectiveness was adapted from Suraratdecha et al. (2005), and is presented as Figure 4.3. The fourth section contained the CV questions that were used to estimate WTP (described in Section 4.3.3). The fifth section included questions to determine the value of a reduction in the risk of death for the respondent's youngest child (described in Section 4.3.4). The sixth section included socioeconomic questions about education, income, housing characteristics, household assets, disease-averting behaviors, economic status, and access to credit. This section also had questions on access to and usage of electricity, water, and telephones.

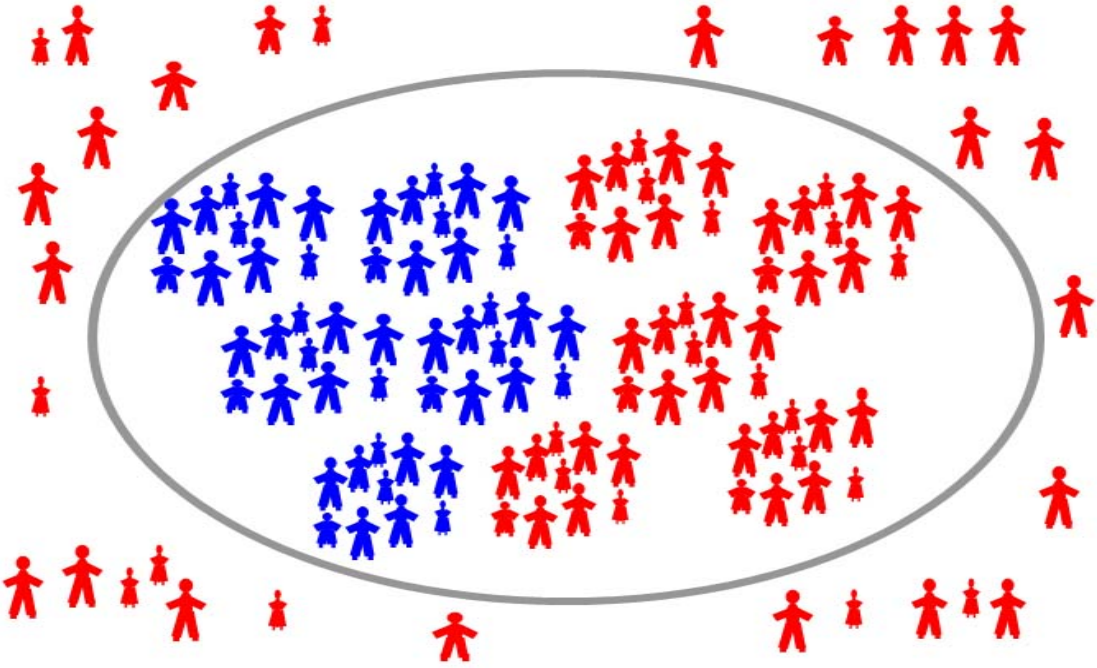


Figure 4.3. Vaccine effectiveness visual aid (Suraratdecha et al. (2005)

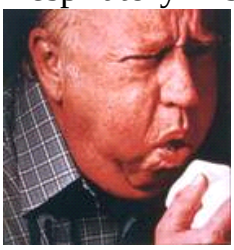
4.3.3 Contingent valuation scenario to estimate WTP for mortality risk reduction of the household's youngest child

This section includes more detail in the description of the information provided to respondents because valuation for mortality risk reduction is considerably more controversial and difficult to present to survey respondents, especially those in developing countries. The survey questionnaire informed respondents about children's risk of death, presented a hypothetical nutritional supplement that would reduce the risk, and elicited respondents' willingness-to-pay for such a supplement in terms of its efficacy (two levels) and price (from five possible sets of paired amounts). The average risk of death from a number of causes is summarized in Chapter 2 (Table 2.1). Although the primary causes and numerical risks of death are different for children younger than 5 years compared to older children, I used the same CV nutritional supplement scenario for all ages of children because of the length and complexity of the survey instrument, the distances traveled by interviewers to respondents' households, and other limitations of working in rural areas. For respondents with more than one child less than 18 years, the questions always referred

to the youngest child. Younger children were the focus because they are often targeted for vaccination and public health campaigns.

The entire nutritional supplement CV scenario is presented in Appendix 1. The first objective of this section was for respondents to consider all possible risks of death for children and the relative likelihood of each. Following Corso et al. (2001), I presented a scale that showed pictures of a number of different causes of death such that the most common causes appeared at the top of the scale and the least common at the bottom (Figure 4.4). Next, using techniques similar to Mahmud (2009), the enumerator instructed the respondent about probability using coin flips and die rolls as examples. The enumerator used Figure 4.5 to explain the expected outcomes for a single coin flip and for a series of 1,000 coin flips. After the coin flip example, the enumerator turned to an example based on die throws. She pointed out that the probability of getting a 5 in a single die throw was considerably less than getting a particular outcome from a single coin flip.

Respiratory Disease



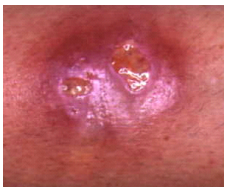
Drowning

Any diarrhea

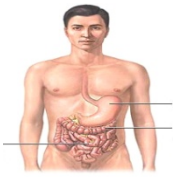
Cancer

Malnutrition

Infections



Murder



Lightning strike

Gastro-intestinal

death

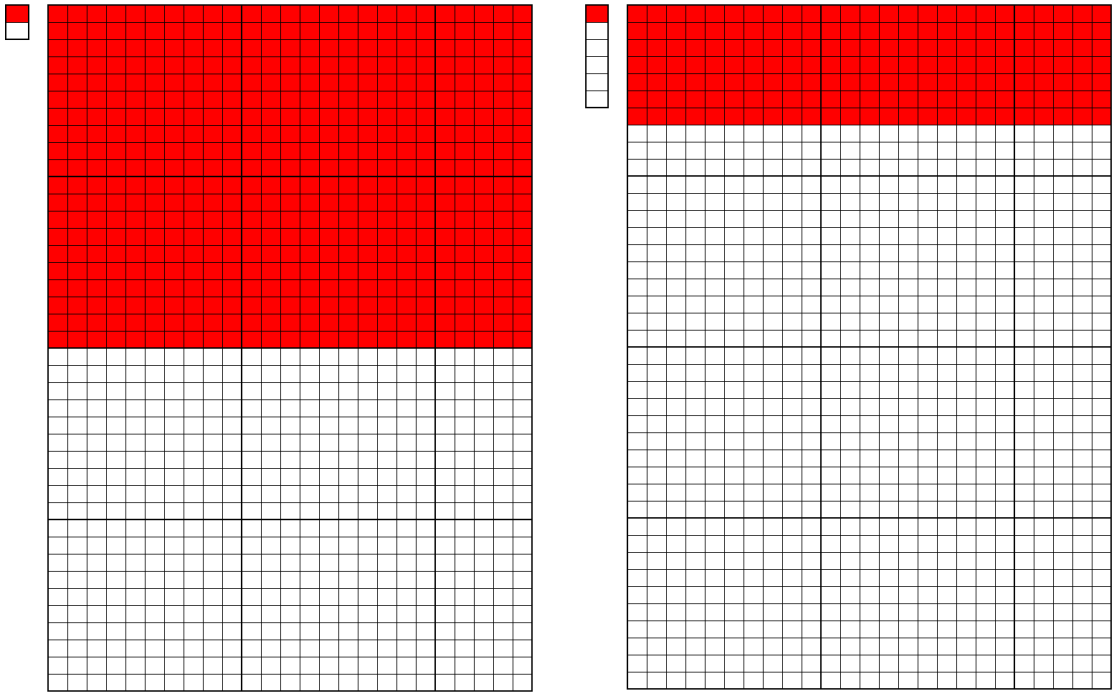


Figure 4.5 Visual aid for probability of coin flip and die roll

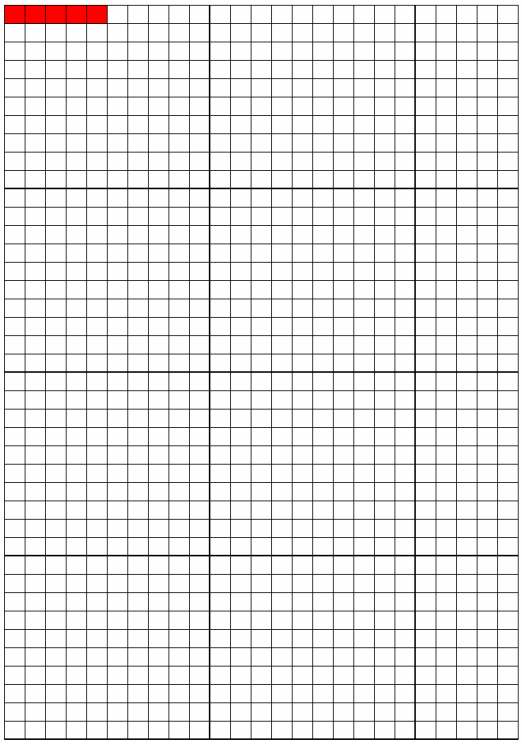


Figure 4.6. Visual aid representing the average risk of death for children in Matlab (adapted from Alberini et al., 2004a)

Next the enumerator introduced the hypothetical nutritional supplement that would reduce the child's risk of death. Each respondent received a randomly assigned scenario such that the supplement reduced the child's risk of death from disease from 5 in 1,000 to either (a) 2 in 1,000 or (b) 4 in 1,000 over 5 years. Respondents were shown another figure, which was adapted from a previous study by Alberini et al. (2004a) (Figure 4.7 or Figure 4.8). These figures helped respondents to visualize how the supplement would decrease the already small baseline risk for their child. I chose to use large risk reductions in the scenarios to improve respondent comprehension and because large changes in risk generate conservative VSL estimates. Most other VSL studies use smaller risk reductions relative to baseline. Prior to asking the valuation questions, respondents were told to assume that the cholera vaccine was not available and not to consider the vaccine cost in their hypothetical purchasing decision.

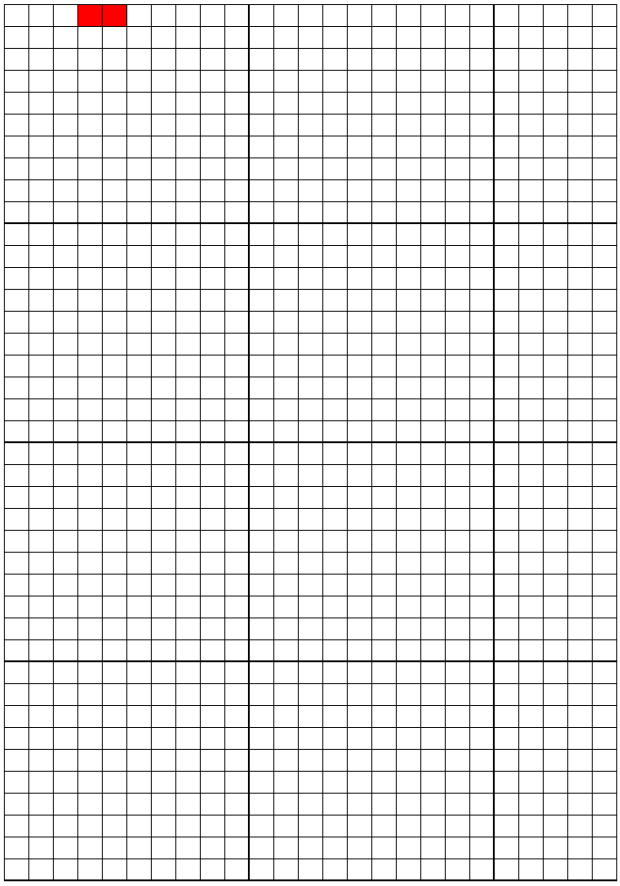


Figure 4.7. VSL hypothetical risk reduction- high effectiveness (adapted from Alberini et al., 2004a)

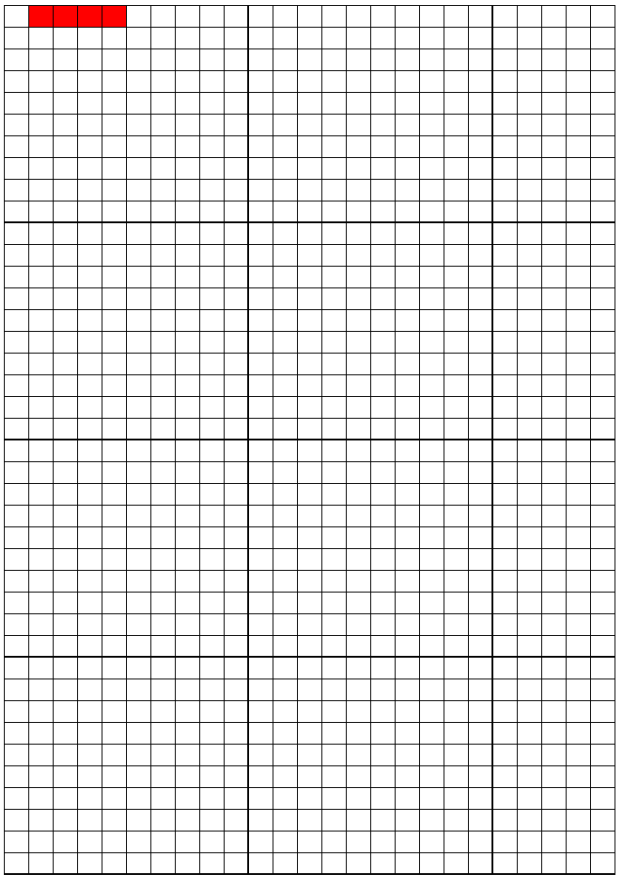


Figure 4.8. VSL hypothetical risk reduction- low effectiveness (adapted from Alberini et al., 2004a)

I chose a monthly payment mechanism because of Matlab's low average income and because many respondents were farmers and did not have large amounts of cash on hand. Thus, the enumerator explained that the parent would need to continue buying the supplement every month to maintain protection for the child. Each respondent was asked if they would purchase the hypothetical supplement at a monthly price that was randomly assigned from an array of five: US$0.15, $0.30, $0.75, $1.50, and $7.50. Next, the respondent was asked if they would purchase the supplement at a specified follow-up price, which was either higher or lower, depending upon whether the respondent agreed to the initial price. The respondents were again read a short cheap talk script to urge careful and honest responses to the purchasing question.

4.3.4 Time to think treatment

Before the interviews began, respondents were divided into two groups. NTTT (no time to think) respondents received the entire questionnaire in one sitting. TTT (time to think) respondents answered the first half of the survey, then were given overnight to consider the prospective "purchase" of the hypothetical vaccines for self and family and to discuss the decision with other family members; an interviewer returned the next day to finish the survey. The TTT treatment has previously resulted in lower estimates of willingness-to-pay (Cook et al., 2006; Lucas et al., 2007). It is possible that the TTT treatment would be more representative of actual vaccine purchasing decisions because households would have time to think about their decision, especially for vaccinations that must be purchased every three years to maintain efficacy.

Because the VSL section was always presented after the vaccine scenario, it always occurred in a single session—either in the single-day NTTT interview, or in the return-visit portion of the TTT interview. Although TTT considerations were not directly applied to the nutritional supplement purchase decision, TTT would have allowed respondents to carefully consider their budget constraints prior to hearing the supplement scenario. It is also possible that respondents could have overestimated the importance of cholera mortality relative to other risks.

5 Model formulation

The policy models are developed in a number of stages. Both models require examination of vaccination demand as a function of price, the epidemiology of cholera vaccination herd protection and the interaction between demand, coverage, herd protection, and vaccination program outcomes. These program outcomes include coverage rates, cases avoided, and DALYs saved, which can be converted to monetary estimates of benefits and costs.

The first section of this chapter includes a graphical summary of basic theoretical considerations. The second and third sections summarize the statistical estimation of the results from the Matlab in-home surveys for household cholera vaccination demand and VSL estimates for households' youngest children. The fourth and fifth sections develop the numerical optimization models for maximizing net societal benefits and total DALYs for a cholera vaccination program subject to a net revenue constraint.

5.1 Graphical model

The graphical model is used to demonstrate basic concepts. The relationships shown in this section may not necessarily represent cholera vaccination in Matlab. The equations and parameter estimates for Matlab are specified in later sections. This section starts with an examination of the simple relationships between price and coverage rates as well as between coverage rates and herd protection impacts. These relationships can be used to estimate public health outcomes, cases avoided and DALYs saved, as functions of price or coverage. Economic benefits can also be estimated from program outcomes. In the absence of herd protection, economic benefits can be estimated directly from vaccination demand curves. I begin with an examination of vaccination demand. The demand curves in Figure 5.1 subdivide demand into

adult, child, and total categories based on expected coverage rates as functions of price. It is important to note that it is possible that a large percentage of adults and children would not choose to pursue vaccinations even if vaccines are provided free of charge. In order to receive a vaccination, it is necessary to travel to and from a clinic or outpost and to wait in line for service. Since this dissertation examines policy in a developing country context, it is expected that coverage rates decline quickly as functions of price. However, it is possible that small groups of adults and children have relatively high WTP (i.e. fat tails in the demand distribution). If herd protection impacts are ignored, WTP benefits may be calculated directly from the integral of the demand curve.

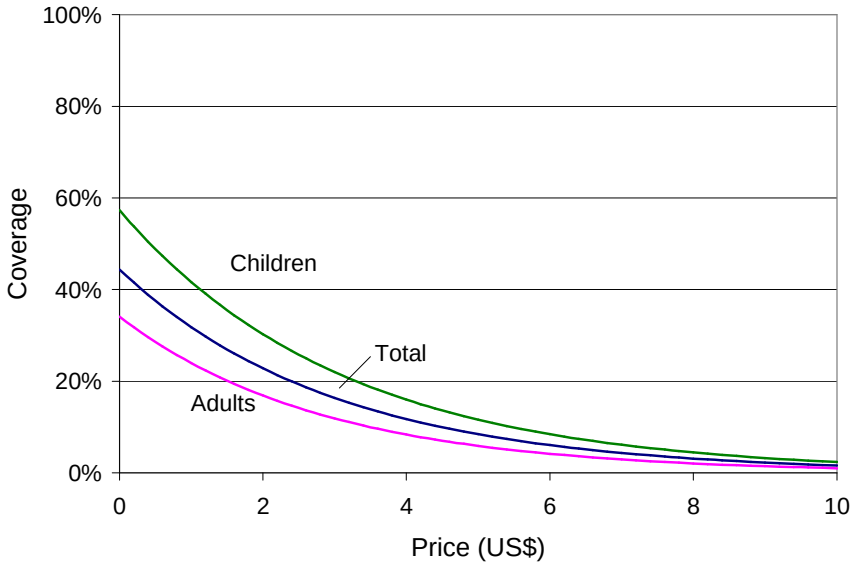


Figure 5.1. Adult and child vaccination demand as functions of price

The next figure (5.2) demonstrates a herd protection versus coverage relationship. The figure is similar to the cholera vaccination herd protection figure (3.2) presented in Chapter 3. In this figure, I demonstrate two distinct types of protection, assuming an average coverage rate of about 35%. The purple or darker rectangle represents the baseline direct protection benefits (65% reduction in baseline incidence) that would accrue to the 35% of the population that received

vaccines. The green or lighter rectangle represents the additional indirect protection experienced by both the vaccinated and unvaccinated populations. For vaccinated persons, there is an increase from the direct protection rate of 65% to the effective protection rate of 90%. Despite not receiving vaccinations, unvaccinated persons' effective risk of infection would decline by more than 70% if just 35% of the population were vaccinated. Thus, the expected indirect protection for unvaccinated persons would exceed the direct protection of vaccination in the absence of herd protection at low coverage rates. Total incidence reduction for the population would be calculated by dividing the colored area by the total area.

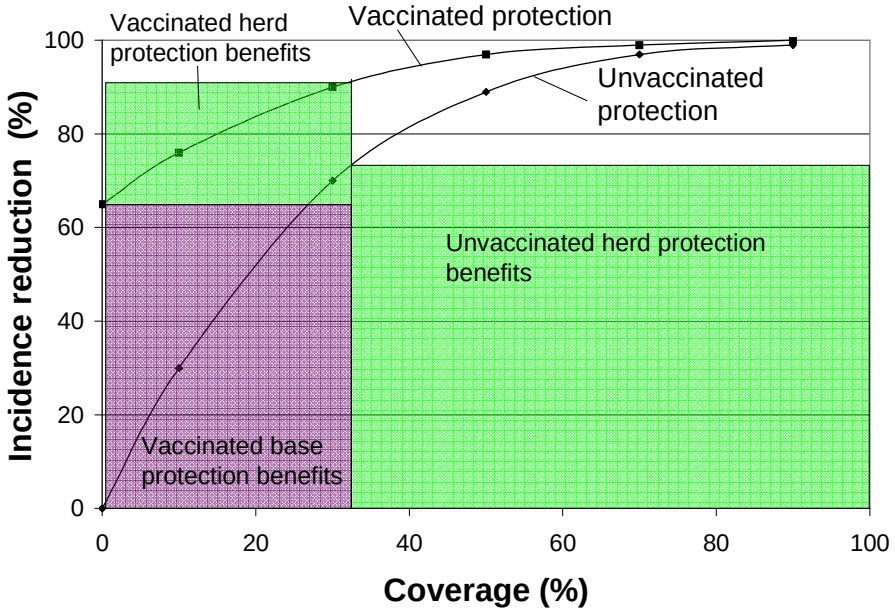


Figure 5.2. Delineation of direct versus indirect protection with consideration for herd protection

The total number of cases for a hypothetical vaccination scenario with and without consideration for herd protection is shown in Figure 5.3. Without consideration for herd protection, the number of cases avoided would be a linear function of the coverage rate. The linear relationship would depend on the baseline incidence, the direct effectiveness of vaccination, and the coverage rate. When herd protection is accounted for, the number of cases avoided is a nonlinear function of coverage, and the expected number of cases avoided is much

greater. This suggests that vaccination benefits may be considerably underestimated if herd protection benefits are unaccounted for.

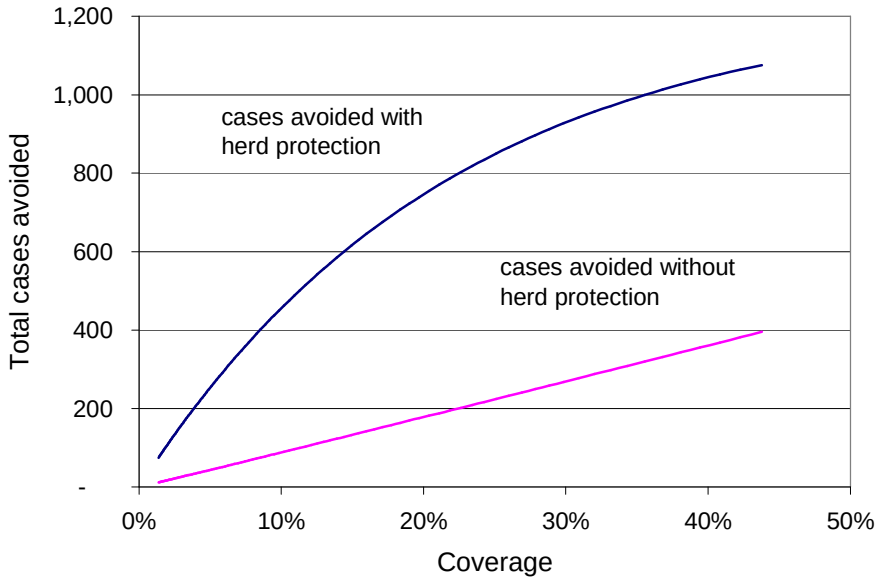


Figure 5.3. Cases avoided with and without consideration for herd protection

The next figure (5.4) examines how total monetary benefits, which should be a function of the number of cases avoided, and costs are influenced by herd protection. The total costs are assumed to be the sum of a fixed cost and a constant variable cost, resulting in a linear function of coverage. Monetary benefits can be estimated both with and without consideration of herd protection effects. The total private benefits function is calculated based on an integral of the demand curve shown in Figure 5.1 without consideration for herd protection. If herd protection benefits are ignored, the private benefit calculation is nonlinear because demand is heterogeneous. If coverage rates are assumed to be a function of price, it is expected that those with the greatest WTP would be covered at low coverage rates (i.e. low coverage rates would correspond with higher user fees, such that only those with high WTP would choose to purchase). As coverage rates increase (due to decreasing user fees), those with successively lower WTP would choose to pursue vaccinations. Thus, the private benefits would increase as coverage increases; however the rate of increase decreases across the entire range of coverage rates.

The total social benefits function incorporates both direct and indirect benefits that result from herd protection impacts. Because unvaccinated persons are also protected (and vaccinated persons are protected at a greater effective rate), the total societal benefits increase at a faster rate and societal benefits are greater than the private benefits of direct protection.

Net benefit calculations are the total benefits minus the total costs, as shown in Figure 5.5. Similarly, the maximum net benefits are significantly larger after accounting for herd protection impacts. In addition, the maximum net benefits occur at a higher coverage rate when herd protection benefits are incorporated. Thus, the optimal coverage rate from a societal perspective is greater when indirect protection benefits are properly accounted. In order to achieve this optimal coverage rate, it is necessary to use a Pigouvian subsidy to boost coverage from the optimal coverage that results from private vaccination decisions to the optimal coverage rate for societal benefits (i.e. from 20% to 25% in Figure 5.5)..

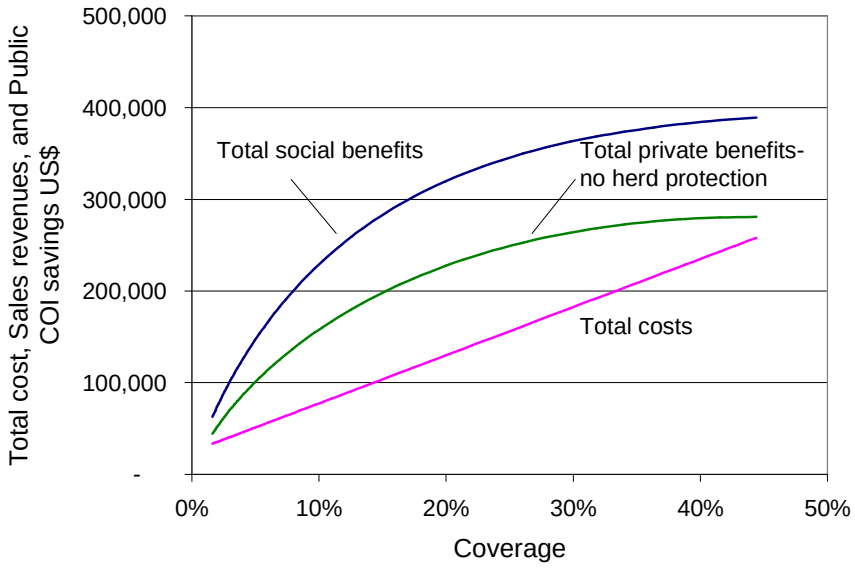


Figure 5.4. Total benefits and costs of a vaccination program

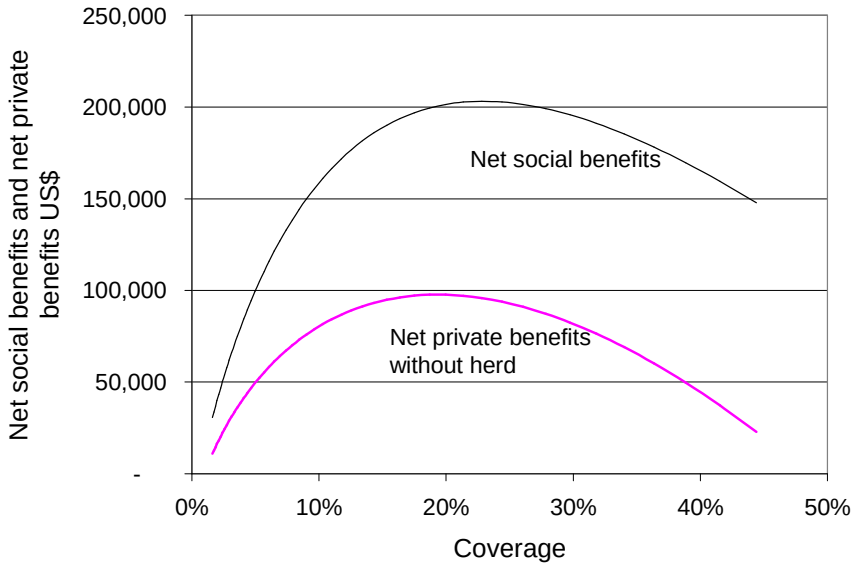


Figure 5.5. Net benefits of a vaccination program

Figures 5.4 and 5.5 examine hypothetical vaccination benefits and costs in monetary terms; however, public health professionals often prefer to consider public health outcomes. In Figure 5.6, I present cases avoided, DALYs saved, and total costs as functions of coverage (with consideration for herd protection). The total cost curve is again a linear function of coverage; however, the DALYs saved and cases avoided functions are both increasing functions; however, like, the benefit estimate curves, the rates of increase decline as coverage increases.

Returning to Figure 5.2, it appears that community incidence would decrease rapidly as coverage increases from low coverage rates. At higher coverage rates, incidence is already reduced to almost zero. Thus, further increases in coverage would have relatively modest impacts on incidence. The decreasing marginal changes in incidence are reflected in the average and marginal cost per DALY saved functions, as summarized in Figure 5.7. The average cost per DALY curve is u-shaped because of competing effects. At low coverage rates, the fixed component of cost may dominate the variable component of cost because these fixed costs would be spread across a small number of recipients. The average cost per vaccination declines as coverage increases. At high coverage rates, the variable cost component would dominate the

fixed cost component. However, at high coverage rates, the marginal change in cases avoided per change in coverage declines because most cases have already been avoided. Thus, the marginal cost per DALY is greater at high coverage rates. The marginal cost per DALY increases monotonically as a function of coverage because of diminishing herd protection effects and because fixed costs do not affect the marginal cost calculation. Overall, there is much more variation in the marginal cost per DALY than the average cost per DALY. The average cost per DALY varies from US$100-150 over a range of coverage rates from 10%-30%.

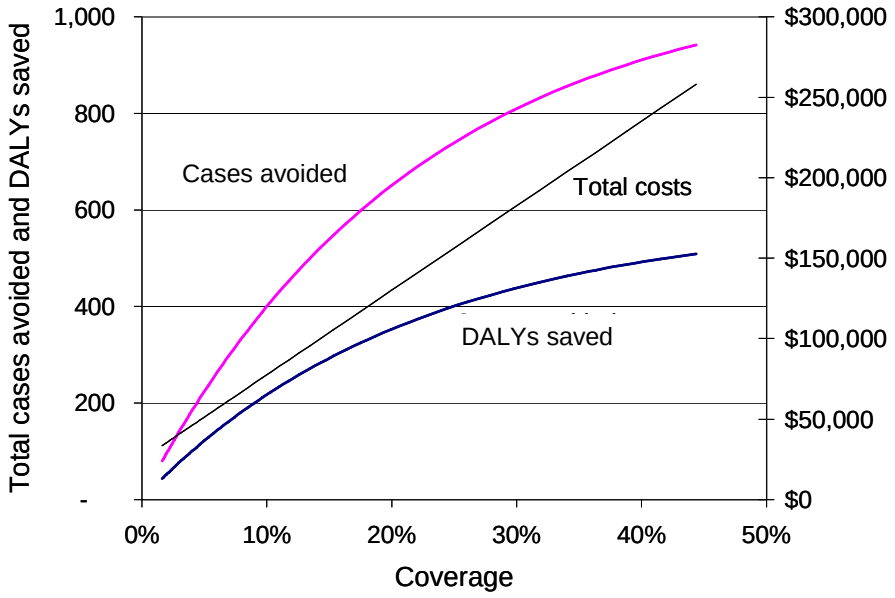


Figure 5.6. Total costs, cases avoided and DALYs saved as functions of price

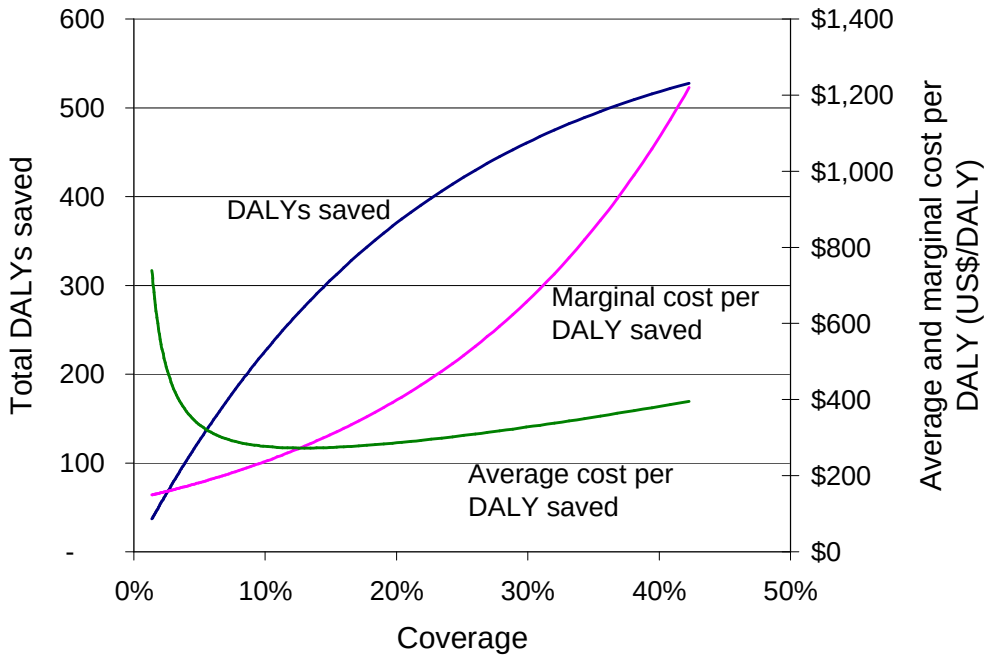


Figure 5.7. Average and marginal costs per DALY saved

In conclusion, a number of important insights are obtained from Figures 5.1 through 5.7. First, the omission of herd protection may lead to considerable underestimates of cases avoided, total societal benefits, and optimal coverage rates. In addition, the average cost per DALY may be overestimated. This could potentially lead to under-provision of vaccinations. These figures also demonstrate that it may not be optimal to provide free vaccinations. In Figure 5.5, the net societal benefit curves are downward-sloping over the range of coverage rates from 25-44%. Thus, it may be possible to collect some user fees to offset the cost of the program while still achieving socially optimal coverage rates for the example shown. Finally, I also show that the average and marginal costs per DALY are not constant and that single point estimates may not be sufficient for cost utility analysis.

These figures assume that an entire community would purchase vaccinations at the same price. However, it may be optimal to charge different prices to different subgroups (by age or by incidence). The rest of the chapter summarizes the mathematical models that can be used to develop similar figures using empirical data. I begin with a summary of the modeling approaches

that I use to estimate WTP for cholera vaccinations and for mortality risk reduction. The basic modeling approaches assume no herd protection effects. These models are then expanded to incorporate the herd protection effect.

5.2 Household demand for cholera vaccines (no herd protection)

This section demonstrates my models for estimating vaccination demand as function of household characteristics and an exogenously assigned user fee. Following the approaches of Cropper et al (2004), Canh et al (2006), and Cook (2007), 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 risk of becoming ill with a specific illness (S_i), and the expected treatment and productivity costs of illness imposed if a family member gets sick (COI_i). Assuming n family members, the utility function is:

$$U = u(X_1,\ldots,X_n, L_1,\ldots,L_n, S_1,\ldots,S_n, COI_1,\ldots COI_n) \quad (5.1)$$

The decision-maker maximizes utility subject to the household budget constraint, given in eq. 5.2[18].

$$I + \sum_{i=1}^{n} w_i(T - L_i) = \sum_{i=1}^{n} X_i + p_V \sum_{i=1}^{n} Q_i + p_m \sum_{i=1}^{n} M_i \quad (5.2)$$

The left-hand side of eq. 5.2 is the amount of income available to the household that can be used for the numeraire good and for prevention and treatment of disease. This is the sum of household non-earned income (I) and earned income, where w_i is the wage for family member i and the total time available is T. The right-hand side of the equality is the sum of household expenditure on the numeraire good, on prevention (p_v is the price of prevention and Q_i indexes the quantity of

[18]Note that I assume that lost productivity is incorporated into the cost of illness on the right hand side of the equation rather than the left hand side of the equation. For a disease like cholera, the time spent ill should be very small relative to work and leisure time.

prevention purchased for the i^{th} household member), and on treatment of the disease (p_m is treatment cost and M_i indexes the quantity of treatment purchased for household member i).

The head of household selects values of X, L, Q_i and M to maximize household utility subject to the budget constraint and to their health production functions (adapted from (Grossman, 1972). The solutions to q series of these maximization problems yields a demand function for preventive care

$$(5.3) \qquad q^* = \sum_{i=1}^{n} q_i \ ,$$

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; I assume the decision-maker takes into account the probabilities, mortality risks, and treatment costs of getting ill in arriving at q*. Rather than define household demand for prevention as an additive function of demand for individual members, I simplify household demand as a 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):

$$(5.4) \qquad q^* = g(p_v, p_m, I, w, Z, H) \ .$$

The total household willingness-to-pay (WTP) for vaccines (or other preventive measures) for n household members is calculated by integrating the inverse demand function $g^{-1}(\cdot)$ from 0 to n vaccines[19].

$$(5.5) \qquad WTP = \int_0^n g^{-1}(q, I, \mathbf{w}, \mathrm{Z}, \mathrm{H}) dq$$

The model requires some additional structure in order to estimate the parameters of the demand function g(·) in eq. 5.4 and to calculate WTP. First, combine the characteristics of

[19] As a Marshallian demand function, this assumes that the marginal utility of income is constant.

household *i*, the vaccine and prevention (including terms I, w, p_m, *Z* and *H* in eq. 5.4, as well as variables for the study like whether the respondent was given time-to-think and the respondent's neighborhood) into the vector X_i. Further define the bid price of the vaccine offered to respondents in the contingent valuation survey as *A*. Assuming an additive and separable utility function, the model I estimate statistically is:

(5.6) $g(X_i, A) = \exp(X_i\beta - A\beta p) + \varepsilon_i$

To estimate β and β_p from the observed data, I use the negative binomial regression model, a variant of the Poisson count model. The Poisson-distributed probability of observing the respondent buying vaccines for all *n* household members is[20]:

(5.7) $$P[q = n] = \frac{\exp(\exp(X_i\beta - A\beta_p)) \cdot \exp(X_i\beta - A\beta_p)^n}{n!}.$$

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 $X_i\beta$ to allow the two to differ. The predicted number of units $\hat{q}$ purchased by household *i* at price *A* is given by eq. 5.8. Notice that when the bid price is zero (i.e. there are no user charges), A=0, and $\hat{q}$ is simply $\exp(X_i\beta)$.

(5.8) $\hat{q} = \exp(X_i\beta - A\beta p)$

To calculate the percentage of the sample that would purchase a vaccine at a specific price, 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.

(5.9) Percent coverage $= \sum_{i=1}^{H} \exp(X_i\beta - A\beta p) \; / \; \sum_{i=1}^{H}$ (*Members in household i)*

[20]Because the sample was spread across a number of villages, I assigned each interviewer to a cluster of nearby households. Because there are likely to be unobserved similarities among neighboring households, I used a cluster correction for standard errors.

Again, willingness-to-pay[21] to vaccinate the entire household (not an individual person) is the area under the inverse household demand curve $g^{-1}(\cdot)$ and to the left of household size

$$(5.10) \quad WTP_i = \int_0^n g^{-1}(q, X)\, dq$$

Equivalently, I can also integrate the demand function $g(\cdot)$ over prices A.

$$(5.11) \quad WTP_i = \int_0^\infty \exp(X_i\beta - A\beta p)\, dA$$

$$= -1/\beta p \cdot \exp(X_i\beta - A\beta p) \Big|_0^\infty = [\exp(X_i\beta)] / -\beta p$$

WTP is simply the household consumer surplus calculated at price $A = 0$. Next, I define an average WTP per person in each household as WTP_i / n_i (i.e. the total household WTP divided by the number of household members). The population average WTP per person is simply $\sum_{i=1}^{H} WTP_i \; / \; \sum_{i=1}^{H} n_i$.

As price increases, the predicted number of vaccines purchased declines for each household. I would like to estimate the average WTP per vaccine purchased (rather than per person) as price increases and demand declines. When A is non-zero, the household's WTP per vaccine is comprised of the consumer surplus at price $A = p^*$ plus the expenditure on vaccines divided by the expected number of vaccines purchased (i.e. $\exp(X_i\beta - p^*\beta p)$). Eq. 5.12 characterizes the consumer surplus at price $A = p^*$, and eq. 5.13 characterizes household expenditures at $A = p^*$.

[21]The theoretically correct measure of WTP is the Hicksian compensating variation. Because we asked respondents how many vaccines they would buy at price A, I actually observe a Marshallian demand function; consumer surplus, not Hicksian compensating variation, is the area I calculate with eq. 5.11. This "uncompensated" demand should theoretically be adjusted for income in order to observe true Hicksian compensating variation, but I make the common assumption that the income effect is likely to be so small that the Marshallian consumer surplus which I observe is a reasonable approximation of Hicksian compensating variation (Willig, 1976)

(5.12) $CS = -1/\beta p \cdot \exp(X_i\beta - A\beta p) \Big|_{p^*}^{\infty} = 1/\beta p \cdot \exp(X_i\beta - p^*\beta p)$

(5.13) Expenditures $= p^* \cdot \exp(X_i\beta - p^*\beta p)$

and average WTP per vaccine is[22]:

(5.14) Average WTP/vaccine = (Expenditure + CS) / expected coverage

$$= \frac{(\exp(Xi\beta - p^*\beta_p)\cdot(p^* + 1/\beta_p)}{\exp(X_i\beta - p^*\beta_p)} = p^* - 1/\beta p$$

Thus, unlike the average WTP per person calculated from eq. 5.11, the WTP per vaccine is dependent only on the price coefficient and the price at which vaccines are offered for sale. Because my modeling approach uses the same price coefficient for every household, the WTP per vaccine is the same for all households (though the predicted number of vaccines purchased will vary by household). If vaccines are provided free of charge the average WTP per vaccine received is simply $-1/\beta p$. The average WTP per vaccine should not be considered analogous to the average WTP per person if a significant fraction of the population would choose not to receive free vaccines. The average WTP per person includes zero values for those predicted not to pursue free vaccines. In contrast, the WTP per vaccine only includes the fraction of the population that is predicted to purchase vaccines, which varies as a function of price. The WTP per vaccine is important for calculating the private benefits of vaccination as a function of the price charged.

Note that this framework 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) disease incidence should be less variable among family members of similar ages, and 3) the characteristics included

[22]Note that this derivation is only applicable for an additive, separable utility function with an exponential price-demand relationship. For example if I used log price in place of price in eq. 5.14, this derivation would no longer be correct.

in the vector $\mathbf{X_i}$ may differ somewhat. Note that my derivation does not assume a discontinuity in demand for free vaccines. In the survey results for respondents, I found that the fraction of respondents that said they would receive free vaccines (85%) was much greater than the estimated demand for free vaccines using the statistical models (35%)[23]. This suggests there may be a discontinuity in the demand function for free vaccinations.

5.3 Children's value of statistical life

Theoretical approaches for modeling parents' willingness-to-pay to reduce mortality risk for children turn on whether parents value mortality risk reductions for children due to altruistic intentions, or paternalistic intentions. As Jones-Lee (1991; 1992) explains, a purely altruistic concern would optimally result in a direct wealth transfer from giver(s) to receiver(s), who could then freely choose to purchase an optimal level of risk reduction without further involvement of the giver. A purely paternalistic approach assumes that the giver only values mortality risk reduction for the receiver, being indifferent to the preferences of the receiver. Of course parents' regards for children are somewhere between pure altruism and pure paternalism. Parents are concerned about a variety of aspects of their children's well-being besides their mortality risk. However, parents' interests in reducing their children's mortality risk is likely to be greater than that of the children themselves, owing to children's lack of experience with causes and risks of death (Cropper and Sussman, 1988; Jones-Lee, 1991; Jones-Lee, 1992).[24]

For the analysis, I simplified Jones-Lee's unitary decision maker approach (1992) to modeling familial WTP for a public good that reduced mortality risk for all family members

[23]Note that respondents were told respondents that vaccines would be available at a convenient clinic. Thus, there should be some travel and waiting time costs even for free vaccines. Given these costs, I might not expect a discontinuity for free vaccination.

[24]An additional complication is introduced when comparing a mother's and a father's separate valuations for a mortality risk reduction for one of their children. Some authors (e.g., Mount et al. 2001) have developed game theoretic constructs to explore how parents make joint decisions. Others (e.g., Cropper et al. 2004; Dickie and Gerking 2003) use a simpler unitary household model where a single decision-maker optimally allocates resources among family members.

simultaneously (as well as for the public at large). In the model, the household decision maker decides whether to purchase a private good that would reduce the mortality risk only for one member of the family. Unlike Jones-Lee's model, the hypothetical nutritional supplement used in my survey was a private good that would only affect the survival probability of the family member that used it, (i.e. the youngest child). I assume that the decision maker maximizes the household utility function, which includes the family's consumption of a numeraire good *w*, the probability of death for each of *n* family members prior to the next period (π_i), and a vector of socioeconomic characteristics of each family, *X*. The representative utility function is represented as

$$U = u(w, \pi_1, \pi_2, \ldots, \pi_n, X). \quad (5.15)$$

I assume that the utility function is increasing in *w* and decreasing for each π_i, and that the marginal willingness to trade off a decrease in current consumption, *w*, for a decrease in π_i, can be obtained by simple differentiation. The marginal rate of substitution between the numeraire good and a one-month risk reduction for one member can be considered as the VSL.

$$VSL_i = (\partial U / \partial \pi_i) / (\partial U / \partial w) = \partial w / \partial \pi_i . \quad (5.16)$$

This calculation assumes that VSL is constant regardless of the magnitude of mortality risk reduction. Given the large mortality risk reductions (20% or 60% of total health-related mortality risk) specified in the VSL scenario, the results may be limited by this assumption.

The econometric model is based on a stochastic utility function $v(h,y;X) + \varepsilon_h$, with $h = 1$ if the respondent wanted to purchase the supplement and $h = 0$ if not. The other components are household income *y* and a vector of socioeconomic variables *X* expected to influence preferences. The stochastic term ε_h is assumed to be independent and identically distributed. Similar to other studies (Alberini 1995; Alberini, Boyle, and Welsh 2003), I find that answers to the follow-up price question in the survey were influenced by presentation of the initial price, and suffer from

starting point bias issues.[25] As a result, I only use the first price to model the decision to purchase. The probability that an offer is accepted at price A_i is

$$(5.17)\quad \Pr(\text{yes}) = \Pr\left[\, v(1, y_i - A_i; X_i) - v(0, y_i; X_i) > e_0 - e_1 \,\right] = F(-\Delta v) = F(A_i, \theta)$$

5.4 Net societal benefit optimization

The calculation of economic benefits begins with equations 5.14 and 5.15 such that the private willingness-to-pay for direct protection, $WTPd_i$, as a function of price for subgroup *i* is

$$(5.18)\quad WTPd_i = (p_i^* - 1/\beta p_i) \cdot \exp(X_i\beta_i) + \beta p_i \cdot p_i^*) = (p_i^* - 1/\beta p_i) \cdot \alpha_i \cdot \exp(\beta p_i \cdot p_i^*),$$

where p_i^* is the optimal price for subgroup *i*, βp_i is the price coefficient for subgroup i, and α_i is the demand intercept for subgroup *i*, where α_i is expressed as the number of people vaccinated at price equal to zero (not the fraction of population expressed as a percentage).

Eq. 5.18 is maximized when price is set equal to zero and coverage rates are maximized. The maximum private WTP for direct protection, $WTPMAXd_i$, is

$$(5.19)\quad WTPMAXd_i = (-1/\beta p_i) \cdot \exp(X_i\beta_i) = (-\alpha_i / \beta p_i).$$

In the absence of herd protection, only vaccinated persons' risk of infection is reduced by a fraction representing the direct efficacy of vaccination. Unvaccinated persons' risk of infection would remain equal to the pre-vaccination baseline. Before defining economic benefits of herd protection, it is necessary to define functional forms for the coverage-incidence relationships effected by herd protection for both the vaccinated and unvaccinated subgroups. The variable COV_i is coverage for subgroup *i* and is based on the demand relationship: $COV_i = \alpha_i \cdot \exp(\beta p_i \cdot p_i^*)$. The coverage-incidence relationship for unvaccinated persons in subgroup *i* ($INCU_i$) is assumed to be the following exponential relationship

[25] A bivariate normal model was also used to jointly model the responses to the first and second prices. The coefficients estimates for the two questions were statistically different at the 1% level. I also estimated interval models based on normal, lognormal, and Weibull distributions. The Weibull distribution best fit the data and provided average WTP estimates that were very similar to those from the probit models. (Median WTP estimates from the Weibull interval model were smaller.)

(5.20) $INCU_i = INCU^0_i \cdot \exp(\gamma_i,1 \cdot COV1 + \gamma_i,2 \cdot COV2 + \ldots)$

where $INCU^0_i$ is the baseline incidence for group i and $\gamma i,1$ and $\gamma i,2$ are herd protection coefficients. The choice of an exponential function ensures that the magnitude of incidence reduction will be greatest at low coverage rates and that the rate of change will decrease as coverage increases. If COV_i represents the number of people vaccinated in each subgroup, the herd protection coefficients determine the impact increased coverage on indirect protection by subgroup, allowing for differential rates of impact by subgroup. Thus, an increase in coverage for subgroup 1 may have a greater impact on herd protection than an increase in coverage for subgroup 2.

Next, I assume that the direct efficacy of vaccination, *Eff*, is constant such that the vaccinated subgroup incidence is a fraction of the unvaccinated incidence rate, specifically 1 - *Eff*. Thus, the expected incidence rate for vaccinated persons in subgroup i ($INCV_i$) is

(5.21) $INCV_i = (1\text{-}Eff) \cdot INCU_i$.

These $INCU_i$ and $INCV_i$ relationships can be used in combination with the willingness-to-pay for direct protection functions to estimate the value of indirect protection. The estimated benefits for vaccinated persons can be calculated based on eq. 5.19 for $WTPd_i$ and the difference in incidence reduction with and without consideration for herd protection. This difference can be calculated from $(1\text{-}Eff) \cdot (INCU^0_i - INCU_i)$. I assume that vaccinated persons would value the reduced risk of infection due to herd protection; however, I do not have any empirical data on the prevalence elasticity of demand. In the absence of data, I assume that vaccinated persons' willingness-to-pay for indirect protection, $WTPvi_i$, are proportional to the magnitude of $(1\text{-}Eff) \cdot (INCU^0_i - INCU_i)$ according to

(5.22) $WTPvi_i = \pi v \cdot Eff \cdot (INCU^0_i - INCU_i) / (Eff \cdot INCU^0_i) \cdot WTPd_i$

where πv is a correction factor for the value of indirect versus direct protection for vaccinated persons. The fraction, $Eff \cdot (INCU^0_i - INCU_i) / (Eff \cdot INCU^0_i)$, represents the ratio of the magnitude of indirect protection to the magnitude of direct protection without herd protection.

For example, assume that the baseline incidence, $INCU^0_i$, is 1 case per 1,000 persons, vaccination efficacy, *Eff*, is 65% and that the incidence for unvaccinated persons, $INCU_i$, is 0.50 cases per 1,000. Without herd protection, the incidence of vaccinated persons would be $(1 - Eff) \cdot INCU^0_i$ = 0.35 cases per 1,000 persons. With herd protection incidence declines to $(1 - Eff) \cdot INCU^0_i$ = 0.175 cases per 1,000 persons. Thus, the ratio of indirect to direct protection would be 0.175/0.65 = 0.27, indicating that the additional indirect protection is about a quarter of the expected direct vaccine protection without regard for herd protection. This is multiplied by a correction factor, πv, such that the sum of willingness-to-pay for direct and indirect protection for vaccination persons is $(1 + 0.75 \cdot 0.27) \cdot WTPd_i$ or $1.20 \cdot WTPd_i$

Next, I develop an expression to estimate unvaccinated persons' WTP for indirect protection. Recall that α_i is the fraction of the population that would receive a free vaccination. For now, I assume that the rest of the population, $POP_i - \alpha_i$, has no value for indirect protection. Thus, I focus on the remaining portion of the population that would accept a free vaccination, but would not purchase a vaccination at price p_i*. Recall from eq. 5.19 that the total WTP for a free vaccination program without consideration of herd protection is $WTPMAXd_i$ or $-\alpha_i / \beta p_i$ for subgroup *i*. Next, I define the change in WTP benefits in moving from a program that offers vaccines at price *pi** to a free program.

(5.23) $WTPMAXd_i - WTPd_i = (-\alpha_i / \beta p_i) - (p_i^* - 1/\beta p_i) \cdot \alpha_i \cdot \exp(\beta p_i \cdot p_i^*)$

This would represent the potential value of protection for the unvaccinated if their incidence were reduced to exactly $INCU_i = (1\text{-}Eff) \cdot INCU^0_i$, i.e. the expected direct protection from vaccination without herd protection. Of course, it is unlikely that the unvaccinated incidence would be exactly $(1\text{-}Eff) \cdot INCU^0_i$. I set up a second ratio that relates the unvaccinated incidence reduction due to herd protection relative to the direct-protection-induced incidence reduction effected by vaccination in the absence of herd protection: $(INCU^0_i - INCU_i) / (Eff \cdot INCU^0_i)$. Using this ratio, the estimated willingness-to-pay for indirect protection for the unvaccinated, $WTPui_i$ is

(5.24) $WTPui_i = \pi u \cdot (INCU^0_i - INCU_i) / (Eff \cdot INCU^0_i) \cdot (WTPMAXd_i - WTPd_i)$

where πu is a correction factor for the value of indirect versus direct protection for the unvaccinated subgroup. In the sensitivity analysis, I can also assume that persons unwilling to purchase vaccines would have some non-zero WTP for protection. This would occur if people were unwilling to spend time procuring vaccinations or if they were frightened of vaccination side effects. I again assume that WTP is proportional to the magnitude of protection, similar to eqs. 5.22 and 5.24. I have already accounted for the monetary benefits for those with non-zero willingness-to-pay, as represented by the demand function intercept, α_i. The remainder of the population is $POP_i - \alpha_i$. The willingness-to-pay for indirect protection for those with zero WTP for vaccinations is

$$(5.25) \quad \pi u \cdot (POP_i - \alpha_i) \cdot (INCU^0_i - INCU_i) \,/\, (Eff \cdot INCU^0_i) \cdot TIME \cdot MED\_WAGE \cdot CORR.$$

where *TIME* is the average time required to receive two doses of cholera vaccine, *MED_WAGE* is median hourly wage rate, and *CORR* is a correction factor that relates the value time required for vaccination and the median wage rate. This assumes that the maximum willingness-to-pay for indirect protection by those unwilling to receive a free vaccination is equal to the opportunity cost of time required to pursue a free vaccination.

Next, I examine the public cost of illness avoided. This is equal to the number of cases avoided multiplied by the average public COI per case. I discount these savings over three years at 8% interest using a present worth function, *PWF*. The following expression summarizes the public COI savings, $PUBSAV_i$, for group *i*.

$$(5.26) \quad PUBSAV_i = PUBCOI_i \cdot PWF \cdot (POP_i \cdot (INCU^0_i - INCU_i) + COV_i \cdot (INCU_i - INCV_i)$$

The cost function is simply assumed to be a fixed cost plus a constant variable cost multiplied by the coverage for each group *i*.

$$(5.27) \quad \text{Total costs} = F + C \cdot (COV1 + COV2 + \dots)$$

Now, I am prepared to calculate the set of optimal prices that maximize societal net benefits via unconstrained optimization. I exclude the unvaccinated benefits for those with zero WTP for vaccinations, eq. 5.25. I revisit these benefits in the sensitivity analysis. Without these benefits, net societal benefits are calculated from the sum of eqs. 5.18, 5.22, 5.24 and 5.26 less eq. 5.27. If I assume that there are four subgroups, the complete expression would be

$$(5.28)\quad \sum_{i=1}^{4} [(1 + \pi v \cdot Eff \cdot (INCU^{0}_{i} - INCU_i) / (Eff \cdot INCU^{0}_{i})) \cdot (p_i^* - 1/\beta p_i) \cdot \alpha_i \cdot \exp(\beta p_i \cdot p_i^*) + \pi u \cdot (INCU^{0}_{i} - INCU_i) / (Eff \cdot INCU^{0}_{i}) \cdot ((-\alpha_i / \beta p_i) - (p_i^* - 1/\beta p_i) \cdot \alpha_i \cdot \exp(\beta p_i \cdot p_i^*)) + PUBCOI_i \cdot PWF \cdot (POP_i \cdot (INCU^{0}_{i} - INCU_i) + COV_i \cdot (INCU_i - INCV_i)] - F - C \cdot (COV_1 + COV_2 + COV_3 + COV_4)$$

$$= \sum_{i=1}^{4} [WTPd_i + WTPvi_i + WTPui_i + PUBSAV_i] - F - C \cdot (COV_1 + COV_2 + COV_3 + COV_4)$$

An optimal set of prices, *p1**, *p2**, *p3**, *p4**, can be solved for via Lagrangian analysis or similar numerical methods. If public COI benefits are small relative to WTP benefits and herd protection benefits are minimal, the optimal solution would set price equal to the marginal cost of vaccination. Eq. 5.28 assumes that either the public health ministry or an external donor would be willing to pay the difference between socially optimal prices and revenue neutral prices. However, the program may be constrained to be revenue neutral. The net revenue constraint is program revenues plus public COI savings less program costs as shown in eq. 5.29.

$$(5.29)\quad \sum_{i=1}^{4} [COV_i \cdot p_i^* + PUBSAV_i] - F - C \cdot (COV_1 + COV_2 + COV_3 + COV_4) \geq Z$$

where $COV_i \cdot p_i^*$ represents the revenue generate through vaccination sales to subgroup *i* at price p_i^* and Z is a fixed external contribution which may be zero. The maximum societal net benefits subject to a revenue constraint can be solved via a Lagrange multiplier approach using the following equation

(5.30) $L_1 = \sum_{i=1}^{4} [WTPd_i + WTPvi_i + WTPui_i + PUBSAV_i] - F - C \cdot (COV_1 + COV_2 + COV_3 + COV_4) - \lambda_1 \cdot (\sum_{i=1}^{4} [COV_i \cdot p_i^* + PUBSAV_i] - F - C \cdot (COV_1 + COV_2 + COV_3 + COV_4) - Z)$

where λ_1 is the undetermined Lagrangian multiplier, which denotes the marginal change in the net societal benefits per unit change in present value net revenue. The optimal prices p_i^* can be found numerically or by using calculus to solve for i = 1 to 4, $\partial L_1/\partial(p_i) = \partial L_1/\partial(\pi)=0$.

In summary, the net societal benefit maximization equations contain many variables despite a number of simplifying assumptions, including the following:

- I assume that demand is independent of herd protection effects. While this is reasonable for the first vaccination period, it seems likely that prospective purchasers would change their behavior in subsequent periods as they become aware of herd protection impacts.
- I model demand based on an average uptake of vaccinations for each subgroup. However, there may be spatial differences in uptake rates within subgroups.
- I assume that indirect protection benefits can be calculated based on simple fractional incidence reduction relationships because I do not have any data regarding valuation of indirect protection.
- I assume that the population can be modeled based on relatively simplistic subdivisions of the population. I assume four subdivisions based on the subdivisions I use in the empirical models in Chapter 7.
- I assume a linear marginal cost function.

5.5 Public health outcome (DALY) optimization

The analysis in Section 5.4 requires monetization of the economic costs and benefits of vaccination. In this section, I reexamine vaccination programs in terms of public health outcomes,

specifically, cases avoided and DALYs saved. I already estimated cases avoided in the estimation of public COI savings. In order to calculate the number of DALYs saved, it is necessary to estimate disutility units per case. The disutility depends on the degree of incapacitation experienced during the illness, the duration of illness, the case fatality rate, and the expected number of life years lost per case (Jeuland et al., 2008).

The average number of DALYs saved per case avoided is calculated for each of i groups over the duration of the program. The total number of DALYs incorporate both reductions in morbidity (years of life lost to disability, *YLD*) and mortality (years of life lost, *YLL*). I used uniform age weights that apply the same value to an extra year of life regardless of the age of the recipient. I also use country-specific life expectancies, *LE,* based on ICDDR,B life tables for the Matlab area ((ICDDRB), 2005). The numbers of life years saved for each age group are discounted using a 3% real discount rate.

(5.31) YLD_i saved per case = $(1 - CFR_i) \cdot DUR_i \cdot$ *DALY weight*

(5.32) YLL_i saved per case = $(CFR_i / 0.03 \cdot (1 - \exp(-0.03 \cdot LE_i))$

(5.33) $DALY_i$ saved per case avoided = $YLL_i + YLD_i / (1 + 0.03)^t$

where *CFRi* is the case fatality rate, *DURi* is the disease's average duration, and *t* is the time span of vaccination protection, *DALYweight* is a weight that compares the disutility of living with the disease to death. The total number of DALYs saved is equal to the number of DALYs saved per case multiplied by the number of cases avoided. The objective function for DALY maximization is thus

(5.34) $\sum_{i=1}^{4} DALY_i \cdot (POP_i \cdot (INCU^0_i - INCU_i) + COV_i \cdot (INCU_i - INCV_i))$

Without a revenue constraint, the maximum number of DALYs saved would result from a free vaccination program. For comparison with the net societal benefit optimization, it is again necessary to include a net revenue constraint. This net revenue constraint is the sum of

vaccination sales revenue and public treatment cost savings less program cost. The full Lagrangian equation for DALY maximization with a net revenue constraint is thus

$$(5.35)\quad L_2 = \sum_{i=1}^{4} [DALY_i \cdot (POP_i \cdot (INCU^0_i - INCU_i) + COV_i \cdot (INCU_i - INCV_i))] -$$

$$\lambda_2 \cdot \sum_{i=1}^{4} [COV_i \cdot p_i^* + PUBSAV_i] - F - C \cdot (COV_1 + COV_2 + COV_3 + COV_4) - Z]$$

where λ_2 is the undetermined Lagrangian multiplier, which denotes the marginal change in the DALYs saved per unit change in present value net revenue. The optimal prices p_i^* can be found numerically or by using calculus to solve for i = 1 to 4, $\partial L_2/\partial(p_i) = \partial L_2/\partial(\pi)=0$.

I am not aware of any published articles that examine how to maximize DALYs saved subject to a revenue constraint. This may be used when considering how to set prices across subgroups for a single intervention or it may be possible to expand this analysis to consider how to set prices for multiple interventions given a single revenue constraint. It is necessary to understand the price-coverage and coverage-herd protection relationships to employ this analysis. These data are not commonly available, which would preclude the widespread use of this approach.

For locations where data are available, it is useful to compare approaches that maximize societal net benefits with those that maximize DALYs. When comparing eq. 5.30 with eq. 5.35, the net revenue constraints are the same. Thus, differences arise from the marginal change in the DALYs saved per unit change in present value net revenue compared to the marginal change in the societal net benefits per unit change in present value net revenue. The herd protection effects should be similar for both the societal net benefit calculation and for the DALY calculations. All else equal, the subgroups with greater impacts on herd protection should be charged lower user fees. For example, since school-age children have a greater impact on influenza vaccine herd protection than other age groups, they should be charged lower user fees since herd protection effects may be experienced across subgroups.

When comparing one subgroup to another, differences in baseline incidence rates and DALYs saved per case would influence optimal prices such that, all else equal, subgroups with higher baseline incidence rates, $INCU^0_i$, and more DALYs saved per case avoided, $DALY_i$, should be charged smaller user fees. In contrast, if public COI savings are small in comparison to program costs, net societal benefits are maximized when all groups were charged the same price (i.e. a price similar to the marginal cost of vaccination). In fact, incidence rates may not have much influence on WTP benefits. For example, in Kolkata, private WTP for cholera vaccines was higher in a average incidence, middle class neighborhood than in a high incidence, low income neighborhood (Whittington et al., 2009). If public treatment cost savings are large compared to program costs, subgroups with higher incidence rates and higher public COI per case estimates, $PUBCOI_i$ should be charged lower prices.

6 Contingent valuation survey results for household cholera vaccination demand and children's value of statistical life

This chapter presents the estimates of household cholera vaccine demand and estimates of children's VSL based on results from my contingent valuation studies. Section 6.1 summarizes respondent and household characteristics of survey participants. Section 6.2 presents a statistical analysis of household cholera vaccine demand. Section 6.3 presents a statistical analysis of VSL estimates for the youngest children of households based on the nutritional supplement scenario. Finally, Section 6.4 presents a comparison of implicit VSL estimates generated from a combination of cholera vaccine WTP data and cholera COI data with the VSL estimates generated from the nutritional supplement scenario. The article published in *Health Policy* summarizing the household cholera vaccination demand is included at Appendix 2. The children's VSL study is formatted as an article for submission and is included as Appendix 3.

6.1 Household sample characteristics

Prior to examining household demand for cholera vaccinations, I summarize socioeconomic and other characteristics of the sample. Since the optimization models subdivide populations into high and average incidence subgroups, summary statistics are provided by these subgroups in Table 6.1. The high incidence group represents households located in the villages with the highest incidence (top 10% based on cases treated at the ICDDR,B hospital over the previous 10 years). The average incidence group represents households in the remaining 90% of villages. Incidence rates were not a sampling criterion; thus, these groupings were created after data were collected. In my sample, the top 10% of villages experienced incidence rates that were twice as large as the remaining 90% of villages. Note that estimates for the entire Matlab area

would indicate that the top 10% of villages experience about four times greater incidence than the remaining villages (See Table 4.1). In addition, the incidence rates observed for villages in my sample are about twice as high as for surveillance area as a whole in Table 4.1. This suggests that incidence rates for all of the villages in my sample may be greater than for the remainder of the surveillance area. Recall that I was unable to sample from the entire ICDDR,B surveillance area due to travel time constraints. It is notable that ratio of high-to-average incidence villages is larger for shorter observation periods (i.e. using a 3-year observation period instead of a 10-year period).

Some of the overall average characteristics were summarized in Chapter 2. The average respondent was about 40 years old with less than five years of education. The average household had about 3 adults, 2 school-age children and 0.7 children less than five years of age. These households had average household incomes of about US$75 and monthly per capita incomes of about US$21 after adjusting household sizes by OECD equivalency scales. Education rates were slightly higher in the average incidence villages, but differences were generally not significant. Respondents in the high incidence areas were significantly more likely to be unable to read a newspaper. The differences in educational achievement did not appear to influence income as the average household per capita incomes were exactly the same across groups. Emch (1999) also found that neither household income, nor household assets were correlated with cholera incidence based on a study of patients treated at the ICDDR,B hospital.

Descriptive statistics of experience with and attitudes towards cholera and vaccines are summarized in Table 6.2. Households in the average incidence villages were significantly more likely to treat drinking water, although very few households treated water in either group. In addition, most of the high incidence villages were located in the government service area. This is not surprising because there have been fewer health related research studies conducted in the government service area. In the high incidence villages, a larger fraction of respondents reported that they had experienced a case of cholera within the household. However, more respondents in

the average incidence villages reported that they knew someone outside the household that experienced cholera. Respondents from average incidence villages were also more likely to believe that cholera is common in their community, that their children are likely to contract cholera and that cholera is serious or very serious for adults. Thus, it appears that the fear of cholera may actually be lessened in villages where the disease is more common. The differences in attitudinal variables are not large, but they are significant.

Importantly, the average travel time from village to hospital is not statistically different between average incidence and high incidence villages. This suggests that differences in incidence rates are not caused by differences in hospital accessibility across villages. It is also important to note that residents of high incidence villages were significantly less likely to be selected for the time-to-think treatment.

Table 6.1. Variable definition and descriptive statistics (Respondent and household characteristics)

		Average incidence	High incidence
Variable name	Description	Mean (SD)	Mean (SD)
		(*N* = 524)	(*N* = 67)
Respondent characteristics			
Male respndent	Gender =1 if male, = 0 if female	0.50 (0.50)	0.43 (0.50)
Age	Age (yrs), continuous	40 (10)	40 (9.0)
Practice Hinduism	Religion = 1 if Hindu, 0 = else	0.07** (0.26)	0** (0)
Education 1–5 years	= 1 if respondent completed 1–5 years of school, 0 = else	0.36 (0.48)	0.33 (0.47)
Education 5–10 years, vocational	= 1 if respondent completed 5–10 years of school, vocational school, or madrassa, 0 = else	0.18* (0.39)	0.13* (0.34)
Education more than 10 years	= 1 if respondent completed university, postgraduate or professional course, 0 = else	0.13 (0.33)	0.04 (0.21)
Unable to read	= 1 if respondent is not able to read a newspaper,	0.51***	0.69***

		Average incidence	High incidence
Variable name	Description	Mean (SD)	Mean (SD)
		(*N* = 524)	(*N* = 67)
	0 = else	(0.50)	(0.47)
Household characteristics			
Infants	number of infants (<1 year), continuous	0.12 (0.34)	0.16 (0.37)
Young children	number of children age 1–5, continuous	0.75 (0.72)	0.66 (0.69)
School-aged children	number of children 6–17, continuous	1.7** (1.1)	2.0** (1.3)
Adults	number of adults age 18–65, continuous	3.1 (1.5)	3.2 (1.6)
Monthly income per capita	hh income divided by number of hh members (US$ per month), continuous	14 (11)	14 (12)
Log income per capita	Natural log of hh income divided by number of hh members, continuous	7.3 (0.7)	7.3 (0.72)
Gender of hh's youngest child	=1 if male, =0 if female	0.52 (0.5)	0.45 (0.5)
Age of hh's youngest child	Age (yrs), continuous	6.5 (4.9)	5.6 (3.9)
Household income quartile 2[b]	=1 if hh income is between about 25th and 50th percentiles	0.15 (0.36)	0.07 (0.26)
Household income quartile 3[b]	=1 if hh income is between about 50th and 75th percentiles	0.23 (0.42)	0.16 (0.37)
Household income quartile 4[b]	=1 if hh income is between about 75th and 99th percentiles	0.27 (0.45)	0.27 (0.45)

[a] This corresponds to an average household monthly income of US$75 (Tk. 5000).

[b] The household income could not be divided into exact quartiles because a number of households often reported the same income. For example, about 17% of the population reported an income of Tk 100 per day. For these duplicate values, households were assigned to the lower income quartile. As a result, the lowest income quartile included 32% of the households.

Table 6.2. Variable definition and descriptive statistics (Perceptions of disease, vaccine history and characteristics of research design)

		Average incidence	High incidence
Risk behavior, perceptions of disease, vaccination history		Average (SD)	Average (SD)
Treat drinking water	= 1 if household treats water for drinking, 0 = else	0.20** (0.40)	0.07** (0.26)
Someone in household has had cholera	= 1 if someone in household has had cholera, 0 = else	0.36* (0.48)	0.46* (0.50)
Know person who has had cholera (outside hh)	= 1 if knows someone outside hh who has had cholera, but not some in hh, 0 = else	0.29** (0.45)	0.13** (0.34)
Cholera is very serious for adults	= 1 if respondent believes cholera is (very) serious for adults, 0 = else	0.65* (0.48)	0.54* (0.50)
Cholera is serious for children	= 1 if cholera (very) serious for children, 0 = else	0.84 (0.37)	0.85 (0.35)
Cholera likely for respondent	= 1 if respondent believes he or she is likely or very likely to contract cholera in next 5 years, 0 = else	0.21 (0.41)	0.18 (0.38)
Cholera likely for respondent's child	= 1 if respondent believes his or her child will likely contract cholera in next 5 years, 0 = else	0.42** (0.49)	0.25** (0.43)
Believes cholera is common in community	= 1 if respondent believes cholera is common in his or her community, 0 = else	0.24** (0.43)	0.13** (0.34)
Respondent believes vaccine is still working	= 1 if respondent had oral cholera vaccine and believes that it is still effective, 0 = else	0.24 (0.43)	0.27 (0.44)
Respondent unsatisfied with vaccine	= 1 if respondent was not satisfied with previous vaccine for self or family member, 0 = else	0.025 (0.16)	0.015 (0.12)
Average annual incidence in villages over previous 10 years	=average annual cases per 1000 persons	1.0*** (0.5)	2.1*** (0.2)
Average travel time to village by traditional methods	=minutes to travel to village reported by enumerators	72 (31)	82 (26)
Characteristics of research design			
Time to think (TTT)	= 1 if given time to think overnight, =0 else	0.49** (0.50)	0.34** (0.47)
ICDDR,B	Health service area; = 1 if ICDDR,B, = 0 if government	0.40*** (0.49)	0.05*** (0.20)

6.2 Household cholera vaccination demand

Next, I summarize household cholera vaccination demand results from the contingent valuation survey. The average fraction of household members vaccinated decreases as the price increases and for respondents given time to think (TTT). In the raw data, I find that many respondents (74%) either decide to purchase vaccines for all family members or for none of their family members. Relatively fewer respondents (26%) choose to purchase vaccines for some, but not all of their family members.

Negative binomial regression results for the household demand model are summarized in Table 6.3. Average marginal effects, which reflect the change in population average demand for a unit change in a single variable, are summarized in Table 6.4. Statistically significant variable coefficients typically correspond to statistically significant marginal effects. Price is highly significant and there is an average marginal decrease in stated demand of 0.12 adult vaccines and 0.20 child vaccines per family for a price increase from US$1.00 to US$1.50. The change in vaccine demand is larger for children because the demand intercept for children is greater. Note that the adult and child price coefficients are similar in magnitude.

Village incidence rates appear to be negatively correlated with demand; however, coefficient estimates are not statistically significant for either adult or child models. While it might be expected that higher incidence villages should have higher WTP, it appears that the discrepancy in incidence rates were not large enough across the sampled villages to result in statistically significant differences in WTP. In addition, attitudinal data suggests that households in high incidence villages tend to believe cholera is less serious than households in other villages. Generally, respondents residing in the ICDDR,B service area and TTT respondents state that they would purchase fewer vaccines for both age groups; average marginal decreases are about 0.34 adult vaccines and 0.48 child vaccines if given TTT and 0.21 adult vaccines and 0.18 child vaccines for the ICDDR,B service area. Male respondents and respondents from wealthier families purchase significantly more vaccines; average marginal demand increases by 0.16 adult

vaccines and 0.30 child vaccines per 1 log unit increase in monthly per capita income. Average marginal demand decreases by 0.003 adult vaccines and 0.012 child vaccines as respondent age increases by one year. As expected, respondents with larger families are shown to purchase more vaccines. This is true for all age groups.

Table 6.3. Household cholera vaccine demand negative binomial regression results

Model	Adults (n=582)	Children age 1-17 (n=582)
Price (Tk)	–0.0049***	–0.0054***
	(–9.1)	(–11)
Average annual incidence over last 10 years	-116	-91
	(-1.25)	(-1.21)
Time to think	–0.47***	–0.44***
	(–4.4)	(–5.2)
Male respondent	0.33***	0.077
	(2.76)	(0.80)
Resident from ICDDR,B service area	–0.29*	–0.17*
	(2.44)	(–1.80)
Age	0.054	–0.011**
	(0.84)	(–2.0)
Education 1–5 yrs.	0.16	0.10
	(1.23)	(0.98)
Education 6–10 yrs.	0.38**	0.24**
	(2.39)	(1.97)
Education >10 yrs.	0.11	0.09
	(0.57)	(0.62)
Log income per capita	0.25***	0.29***
	(2.74)	(3.9)

Model	Adults (n=582)	Children age 1-17 (n=582)
No. of infants < age 1	-0.055	0.02
	(-0.37)	(0.17)
No. of children age 1–5	-0.038	0.40***
	(-0.53)	(6.9)
No. of children age 6–17	-0.088	0.39***
	(-1.64)	(8.9)
No. of adults age >18	0.35***	0.02
	(11.2)	(0.65)
Practice Hinduism	0.31	0.04
	(1.59)	(0.23)
Serious or very serious for children	-0.16	-0.15
	(-1.1)	(–1.4)
Serious or very serious for adults	0.28**	0.26***
	(2.46)	(2.93)
Cholera likely for respondent	0.24*	0.18*
	(1.84)	(1.65)
Cholera likely for children	0.15	0.02
	(1.34)	(0.26)
Someone in hh has had cholera	0.05	-0.028
	(0.43)	-(0.30)
Know someone other than hh member that has had cholera	-0.25*	-0.11
	(-1.77)	(–1.03)
Resp had prior vaccine; was satisfied and thinks vaccine still works	0.19	0.19**
	(0.92)	(2.07)
Resp. had prior vaccine; not satisfied	-0.57*	-0.06

Model	Adults (n=582)	Children age 1-17 (n=582)
	(-1.22)	(-0.19)
Treats water	-0.021	0.15
	(-0.16)	(1.54)
Constant	–2.67***	–1.87***
	(–2.9)	(–3.29)
Pseudo-R^2	0.020	0.19

* indicates significance at the 10% level
** at the 5% level
*** at the 1% level
T–statistic in parentheses

Table 6.4. Average marginal effects for household negative binomial regression

Price (US$; 1 unit US$0.50)	-0.12*** (-8.0)	-0.20*** (-10.2)
Average annual incidence over last 10 years	-81 (-1.2)	-98 (-1.22)
Time to think	-0.34*** (-4.3)	-0.48*** (-5.2)
Male	0.22** (2.5)	0.083 (0.80)
Resident from ICDDR,B service area	-0.21** (-2.53	-0.18* (-1.85)
Age (yrs)	0.0032 (0.67)	-0.012** (-1.95)
Education (category- 0, 1—5, 6—10, >10)	0.056 (1.3)	0.062 (1.27)
Log income per capita (log Tk per cap)	0.16* (2.5)	0.30*** (3.81)
No. of infants < age 1	-0.044 (-0.39)	0.015 (0.11)
No. of children age 1–5	-0.026 (-0.49)	0.43*** (7.1)
No. of children age 6–17	-0.064 (-1.6)	0.42*** (9.4)
No. of adults age >18	0.25 (11)	0.017 (0.60)
Practice Hinduism	0.26 (1.4)	0.054 (0.27)
Cholera likely for respondent	0.22* (1.9)	0.23* (1.7)
Cholera likely for children	0.10 (1.2)	0.01 (0.10)

Someone in household has had cholera	0.031 (0.34)	-0.03 (-0.30)
Unsatisfied with previous vaccine	-0.35* (-1.9)	-0.11 (-1.0)
Treats water	-0.013 (-0.14)	0.17 (1.44)

* indicates significance at the 10% level
** at the 5% level
*** at the 1% level
T–statistic in parentheses

The number of vaccines purchased increases significantly for respondents who believe that cholera is a serious disease for adults or who believe that adults are likely to contract cholera. The average marginal increase in demand if respondents believed that cholera is likely for adults is about 0.22 for both adult and child vaccines. The difference is much smaller and not significant for the same belief for children. This discrepancy in the importance of attitudes for adults compared to children might result if parents are more risk averse about their children's health than their own. Respondents who had previously received a cholera vaccine generally stated that they would purchase more vaccines for their families, unless they were not satisfied with the first vaccine. Previous recipients wanted additional vaccines despite the widespread belief that their previous vaccine was still effective in reducing risk. I find that respondents who treat their drinking water purchase more vaccines for children, but the difference is of borderline significance. The possible correlation between vaccine demand and water treatment would suggest common preferences for risk averting behaviors. I present a single model in Table 6.3, but I tested a number of different models. For example, I also estimated models to separately predict demand for high incidence and average incidence subgroups. The results from these models could be used to fit separate demand functions for high incidence villages. However, these models had fewer significant variables and likelihood ratio tests suggested that combined models performed better. In addition, since incidence rates did not significantly influence demand, I chose to use the same demand functions for high incidence and average incidence villages in the optimization models.

Figure 6.1 shows raw and predicted household demand for adult and child vaccines as functions of price. Comparing the raw data to the predicted data, it appears that the predictions may underestimate demand at low prices and overestimate demand at higher prices. It is important to note that the raw data do not account for non-price variables used in the multivariate predictions. Figure 6.1 shows that the predicted fraction of children vaccinated is higher than that for adults at any price. These findings suggest that respondents place precedence on vaccinating children over adults. This is consistent with my findings that cholera incidence and diarrhea mortality are greater for children, especially young children. My best WTP estimates are about US$1.0 per adult and US$1.6 per child age 1-17 years. The median WTP corresponds to the price in Figure 6.1 at which 50% of an age group population is vaccinated. The median WTP is about US$0.35 for children and it would be necessary to pay adults to achieve a 50% coverage rate. The large differences between mean and median WTP estimates indicate that there is great variation in WTP for cholera vaccines among households. In other words, there is a large portion of the population that is only willing to pay small amounts of money if any for cholera vaccines, while there is also a small fraction of the population with high WTP. Specifically, although the estimated average adult WTP is about US$1, I predict that only 25% of the adult population would choose to purchase a US$1 vaccine. The remaining 75% of adults would choose not to be vaccinated if price were set at the average WTP estimate.

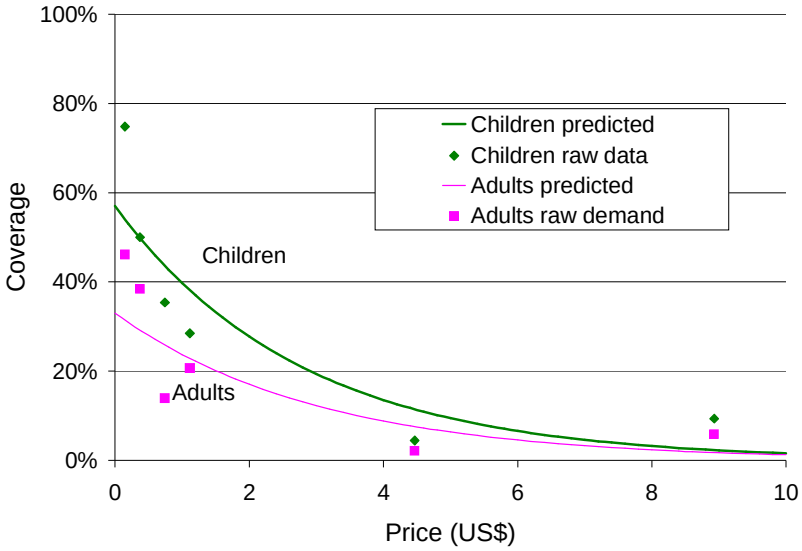


Figure 6.1. Predicted and raw coverage rates as functions of price by age

In summary, vaccine demand is strongly influenced by price, income, self-perceived risk and severity of disease, and whether respondents received time to think about their decision. While self perceived risk tended to be significant, estimates of actual incidence by village are not statistically significant for adults or children. In fact the coefficient estimate is negative, which would indicate that, all else equal, households that experience greater incidence would be less likely to purchase a vaccine. While this may seem illogical, I did find that risk perceptions were generally less in the high incidence villages. The residents of high incidence villages were less likely to think cholera was serious or that their family members would likely contract the disease. Thus, fear of the disease may have been greater in the average incidence villages.

However, there is a caveat for this finding. Note that incidence measurements are confounded by distance to the ICDDR,B hospital (i.e. villages further from hospital are more likely to self-treat or visit other health facilities). The distance from village to hospital has a negative correlation with incidence at the 25% significance level (the sample was restricted to villages located within 2 hours travel distance of hospital. The correlation would likely have been greater if I had included all villages.) Ali et al. (2006) also found a strong negative correlation

between incidence of cases treated at the hospital and distance from the hospital. However, on average for my sample, the travel times from high incidence villages are not statistically significantly different than for the remaining 90% of villages. Thus, while travel distance is important, it is not the only driver of variation in incidence.

There is likely to be less incidence variation from one village to the next in the Matlab area than between slum, middle class and affluent neighborhoods in urban areas (e.g., in Matlab). In those situations, it is likely that proper accounting for incidence would have a greater effect on vaccine demand and policy analysis in general.

6.3 VSL estimate for children

The results from the VSL study are discussed in more detail in Appendix 3. For this study, parents were asked if they would be willing to purchase a nutritional supplement that would reduce their youngest child's risk of death from all disease-related causes by an exogenously assigned 20% or 60%. Parents were only asked about their youngest child and would have to pay for the supplement every month to maintain protection. I summarize the raw demand data by age and percentage risk reduction in Table 6.5. I do not include results for children less than one year of age because their baseline risk is much greater than other ages and because I am not sure how breast-feeding mothers would interpret the usability of the hypothetical nutritional supplement. Households in which the youngest child is less than a year old are omitted from all analyses. As shown in Table 2.1, the annual baseline risks of non-accident mortality are about $2.1x10^{-3}$ for the children between 1 and at 2.9 years, $1.1x10^{-3}$ for children between 3 and 4.9 years and about $0.5x10^{-3}$ for children older than 5. The effective risk reduction is the baseline risk for that age group multiplied by the percentage risk reduction that was randomly assigned, either 20% or 60%. With four different baseline mortality risk rates for each of the four age groups and two exogenously assigned percentage risk reduction scenarios, there are eight different effective risk reduction values faced by survey respondents as shown in

Table 6.5. Since sampling was not stratified by age, some of sample sizes by price are quite small. As a result, there would appear to be some kinks in the demand curve; however, these disappear when results are aggregated over the whole sample. Generally, the fraction of the parents willing to purchase monthly supplements for their youngest child is greater at lower prices and for larger effective risk reductions.

It is easier to visualize trends by combining these data into two subgroups: a large risk reduction group and a small risk reduction group. I use an annual risk cutoff of 4×10^{-4} to define the high and low risk groups and plot raw demand as a function of price in Figure 5.4. This figure shows that the distribution of WTP for the large risk reduction may have a large tail, which indicates that a small fraction of the population would purchase the supplement at very high prices. The tail appears to be much smaller for the lower effective risk reduction group. Although stated demand is greater for the group that received the larger risk reduction, the difference in demand is smaller than would be expected if WTP were linearly correlated with risk reduction magnitude.

Nonparametric Turnbull lower-bound estimators (Haab and McConnell 2002), can be calculated based on the raw demand reported in Table 6.5. The average WTP per month varies between US$0.6 and US$3, and generally decreases as the effective risk reduction increases. It should be noted that these estimates are very sensitive to uptake at the highest price. Given the small sample sizes associated with each cell, a single affirmative response to the highest price has a large impact on the Turnbull estimator. These Turnbull estimates can be converted into VSL estimates for each subgroup by dividing the average monthly WTP by the monthly mortality risk reduction. Because the data per cell are limited, I average the VSL estimates across the large and small percentage change scenarios for each age group. The average VSL estimate is smaller for children between 1 and 2.9 years, but relatively constant for children older than 3. It is not surprising that VSL estimates are smallest for the youngest age group because their baseline risk is twice that for children between 3 and 4.9 years of age and four times greater than children older

than 5 years. In order to observe equivalent VSL estimates across age groups, the young children's WTP would have to twice as great relative to 3-4.9 year olds, and four times greater than older children to balance the difference in mortality rates.

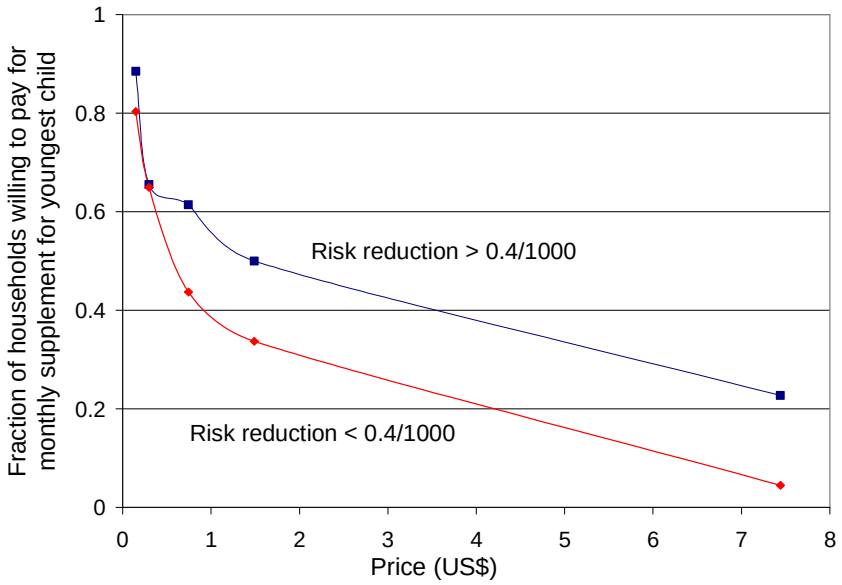


Figure 6.2. Raw demand for hypothetical mortality risk reduction

Table 6.5. Raw demand data and Turnbull estimates by age

Age group	Baseline annual risk ($1x10^{-3}$)	% risk change	Effective annual risk change ($1x10^{-3}$)	Coverage at US$0.15	Coverage at US$0.30	Coverage at US$0.74	Coverage at US$1.49	Coverage at US$7.44	Turnbull Avg. WTP per month	Turnbull Avg. VSL
1-2.9 yr	2.1	20%	0.42	0.9 (n=9)	0.7 (n=17)	0.8 (n=16)	0.4 (n=21)	0.2 (n=6)	$2.0	$40,000
		60%	1.26	0.9 (n=10)	0.6 (n=22)	0.7 (n=13)	0.6 (n=16)	0.1 (n=8)	$1.5	
3-4.9 yr	1.1	20%	0.22	1 (n=9)	0.6 (n=14)	0.4 (n=8)	0.6 (n=8)	0.1 (n=11)	$1.3	$60,000
		60%	0.66	0.9 (n=7)	0.7 (n=16)	0.4 (n=15)	0.4 (n=5)	0.4 (n=8)	$3.1	
5-9.9 yr	0.6	20%	0.12	0.6 (n=11)	0.8 (n=15)	0.5 (n=21)	0.3 (n=18)	0.1 (n=7)	$0.9	$60,000
		60%	0.36	0.8 (n=16)	0.7 (n=18)	0.6 (n=20)	0.2 (n=19)	0 (n=10)	$0.6	
> 10 yr	0.4	20%	0.08	0.7 (n=15)	0.6 (n=18)	0.3 (n=20)	0.3 (n=16)	0 (n=7)	$0.6	$60,000
		60%	0.24	1 (n=10)	0.6 (n=9)	0.4 (n=18)	0.4 (n=22)	0 (n=9)	$0.7	

Multivariate probit models are used to identify the socioeconomic determinants of demand for the nutritional supplement. The dependent variable is a binary representation of the decision to purchase the supplement and the independent variables include price, effective risk reduction and a series of socioeconomic variables. Coefficient estimates from three multivariate probit models with cluster corrected standard errors are included in Table 6.6. Table 6.7 shows the marginal changes in the probability of purchase for a 1-unit change in each variable after averaging over the sample. The first model, Model 1, omits respondent age and water treatment variables to avoid collineraity issues. Note that child age was omitted from the list of independent variables for all models because the effective risk change is a direct function of child age; thus, the inclusion of age would result in collinearity. Consistent with the raw data results, the analysis revealed that price and magnitude of risk reduction are strongly correlated with the decision to purchase the supplement. The probability of purchase decreases by about 5% for a US$0.50 price increase and increases by about 2% for a 1/10,000 change in annual risk. When respondent age is added to the model, the coefficient for effective risk reduction becomes smaller but remains significant. The coefficient for male respondents is positive and the average marginal effect (4-7%) is quite large; however, these findings are highly uncertain and not significant at the 10% level. There is no difference in demand among respondents living inside versus outside the ICDDR,B service area. All models show that respondents with more education and higher income are significantly more likely to purchase the supplement. Average marginal probability of purchase increases by about 10% for a one-category increase in education compared to 5% increase for a one-income-quartile increase.[26]

Respondents who are given time to think overnight about the hypothetical cholera vaccine are significantly less likely to agree to purchase the hypothetical nutritional supplement for their youngest child. The 16% average marginal decrease might result from the additional

[26]For marginal effects, I had to estimate a model that combined dummy categorical variables into a single ordered categorical variable for income quartiles and education categories.

time that they could have used to consider budgetary constraints prior to approaching the supplement section of the interview. Parents are about 7% more likely to purchase the hypothetical supplement for male children, but this difference is of borderline significance. When the youngest child is the only son, the difference is significant at the 5% level. Respondents' estimates of baseline risk of death for children in their villages are not included in the multivariate analysis because so many respondents were unable to provide estimates. In addition, I learned that respondent estimates of mortality risk are compromised by the way the question is presented. Our respondents provided estimates of the number of children that lived in their village (mean 2,300, SD 22,000) and then estimated how many might die from disease in the next 5 years (mean 62, SD 500). Many respondents (22%) were unable to answer one or both of the questions, despite encouragement to venture a "best guess". The median estimated risk of death based on these answers was 10 in 1,000, which is about 25% higher than the actual risk of death from disease for children age 1 to 4 years and about 400% higher than the risk of death from disease for older children. We discovered than another 40% of the respondents reported that there were 500 or fewer children in their village. These small estimates of the child population would limit the resolution in respondents' estimates because the expected number of children that would die was always an integer.

Table 6.6. Multivariate regression of parental demand for nutritional supplements for their households' youngest children

Model	1	2	3
T-statistic in parentheses			
Supplement price	-0.0036***	-0.0036***	-0.0036***
	(-6.9)	(-6.8)	(-6.9)
Male respondent	0.11	0.20	0.12
	(0.75)	(1.3)	(0.76)
Resident from ICDDR,B service area	-0.036	-0.041	-0.04
	(-0.21)	(-0.20)	(-0.20)

Model	1	2	3
Received time to think for	-0.41***	-0.41***	-0.40***
Cholera vaccine experiment	(-3.7)	(-3.4)	(-3.4)
Respondent age		-0.011	
		(-1.5)	
Respondent older than 55 years			-0.25*
			(-1.7)
Risk reduction (annual*1000)	0.45**	0.32*	0.39**
	(2.6)	(1.9)	(2.3)
Education 1-5 yrs.	0.36**	0.35**	0.33**
	(2.2)	(2.1)	(2.0)
Education 6-10 yrs.	0.61***	0.53**	0.60***
	(3.0)	(2.5)	(2.8)
Education >10 yrs.	0.77***	0.71***	0.82***
	(3.0)	(2.7)	(2.9)
Log income per capita	0.31***	0.31***	
	(4.6)	(4.4)	
HH income quartile 2			0.30
			(1.6)
HH income quartile 3			0.36***
			(2.8)
HH income quartile 4			0.37**
			(2.0)
Youngest child is male	0.17	0.17	0.15
	(1.6)	(1.5)	(1.4)
Treats water		0.15	0.16
		(0.65)	(0.77)

Model	1	2	3
Hindu respondent	-0.55*	-0.58**	-0.57**
	(-1.8)	(-2.0)	(-2.0)
Constant	-2.1***	-1.6**	-0.21
	(-4.7)	(-2.5)	(-1.2)
Log likelihood	-296	-297	-297
Average WTP per month	US$1.50	US$1.50	US$1.50
VSL estimate	US$22,000	US$16,000	US$19,000

* indicates significance at the 10% level
** at the 5% level
*** at the 1% level

Table 6.7. Average marginal effects estimated from determinants of parental demand for nutritional supplements

Model	1	2	3
Supplement price (increment $0.50)	-0.048 (.0071)	-0.049 (.0071)	-0.0048 (0.0072)
Male respondent (yes/no)	0.040 (0.059)	0.074 (0.059)	0.051 (0.059)
Resident from ICDDR,B service area (yes/no)	-0.012 (0.081)	-0.0014 (0.082)	-0.0038 (0.082)
Received time to think for cholera vaccine experiment (yes/no)	-0.16 (0.043)	-0.16 (0.046)	-0.16 (0.046)
Respondent age (increment 1 year)		-0.0047 (0.0032)	
Respondent older than 55 years (yes/no)			-0.094 (0.058)
Estimated risk reduction (1/10,000 annually)	0.018 (0.69)	0.0013 (0.068)	0.16 (0.068)
Education (increment 1 education category)	0.11 (0.035)	0.10 (0.035)	0.11 (0.037)
Log income per capita (increment 1 log unit)	0.12 (0.027)	0.12 (0.028)	
HH (increment 1 income quartile)			0.053 (0.22)
Youngest child is male (yes/no)	0.066 (0.042)	0.069 (0.045)	0.061 (0.044)
Hindu respondent	-0.21 (0.10)	-0.22 (0.10)	-0.22 (0.10)
Treats water (yes/no)		0.058 (0.090)	0.063 (0.085)

T-statistic in parentheses

Average willingness-to-pay for a nutritional supplement is estimated from the parameter estimates for each of three probit models. The population average WTP for supplements for households' youngest children is about US$1.50 per month for all three models. This estimate is within the range of Turnbull estimates presented in Table 6.5. The probit WTP estimate is an average across all age groups and effective risk reduction scenarios, and is not directly comparable to any of the Turnbull estimates. Note that age groups are based on the different ages for each household's youngest child not for all children in all households. Approximate VSL estimates can be calculated by dividing the coefficient for risk reduction by the price coefficient. Although the average WTP per month was constant across models, VSL estimates varied from

US$16,000 to US$22,000 because the coefficient for risk reduction varied across the model specifications depending on whether respondent age was included and how respondent age was specified.

These VSL estimates represent the average tradeoff between mortality risk reduction and price in the demand equation. As demonstrated in Table 6.5, it is likely that WTP for a nutritional supplement would not be a linearly function of the magnitude of risk reduction. Rather, VSL estimates depend on the magnitude of risk reduction presented. I believe this is generally the case for this population. Thus, parents appear to be more willing to purchase the supplement for younger children that face greater baseline risks of death. However, they are still willing to purchase the product for older children with much smaller risks of death as long as the price is reasonable. The VSL to annual income ratio is about 18-25, which is at the low end of the values reported in Table 3.2. It is important that the ratios in Table 3.2 refer to adult VSL. I am not aware of any estimate of parents' VSL for their children.

6.4 Comparison between cholera vaccine WTP estimates and nutritional supplement VSL estimates

I can now compare my nutritional supplement VSL results with cholera vaccine WTP estimates. In general, vaccines should reduce 1) *ex ante* private expenditure on treatment, 2) *ex ante* productivity losses for sick patients and their caretakers, 3) reduced risk of pain and suffering from cholera symptoms, and 4) reduced risk of cholera mortality. *Ex ante* private cost of illness (COI) estimates are inclusive of the first two types of benefits, while generic mortality risk reduction valuation[27] would cover the fourth type of benefit.

[27]Generally, I think that the value of generic mortality risk reduction multiplied by the magnitude of vaccine risk reduction plus the expected private treatment cost savings would be approximately equal to vaccine WTP. Recovered cholera patients are unlikely to experience long term disability, which would complicate comparisons between generic mortality risk reductions and vaccine WTP.

I expect that vaccine WTP estimates from my CV surveys should be inclusive of all four of these benefits. Cholera vaccine mortality risk benefits can be calculated based on the product of vaccine effectiveness, VSL estimates, and cholera mortality rates. These mortality risk reduction benefits can then be added to *ex ante* private COI (also multiplied by vaccine effectiveness) for comparison with WTP estimates. These calculations for VSL + COI benefits are summarized in Table 6.8.

Because the ICDDR,B diarrhea hospital provides free treatment for cholera patients, the patients' *ex ante* private COI are modest. I do not have explicit data for cholera mortality, though I do have estimates for diarrhea mortality. I know that cholera patients comprise about 10-25% of all diarrhea patients treated at the ICDDR,B hospital (personal communication with hospital staff). I also know that less than 1% of cholera patients will die if treated properly (Ryan et al., 2000). I presume that mortality rates for other types of diarrhea treated at the ICDDR,B would also be quite low, but I do not have that data. For the upper and lower bounds of cholera mortality risk estimates, I assume that 10% to 50% of all diarrhea deaths are caused by cholera. My best estimate is that 20% of diarrheal deaths are due to cholera. This is based on the facts that 1) cholera is a virulent form of diarrheal disease and 2) cholera cases comprise 10-25% of all patients with diarrhea presenting at ICDDR,B hospital.

For this comparison, I assume that the cholera vaccine will be 50% effective for 3 years to allow for a direct comparison to the cholera vaccine WTP study. (Note that recent herd protection research suggests that 65% is a better effectiveness estimate for the direct protection of vaccination.) The COI and mortality risk reduction benefits are summed and discounted at an 8% financial rate over a 3-year period.[28] My best estimates of VSL are US$15,000 for both age groups. The lower bound for both groups is US$10,000. The upper bound for young children is

[28]The financial discount rate (8%) is greater than the DALY discount rate (3%) used to discount future life years. The larger value is more representative of an interest rate that might be necessary to procure a loan to pay the upfront costs of a vaccination program in which future public treatment cost savings are expected. This financial discount rate should be different than a discount rate for future life years.

assumed to be US$25,000, while the upper bound for older children is US$50,000. I chose a higher upper bound for older children because their VSL estimates in Table 6.5 appear to be greater.

The overall average WTP per fully-vaccinated child (i.e. 2 doses of cholera vaccine) is US$1.6. If children are split into two groups, the average WTP for vaccinations for 1-5 year olds is US$2.4 compared to US$1.2 for older children age 5-17 years (Islam et al., 2008). Thus, WTP is considerably greater for younger children who also face a higher baseline risk of death from diarrhea. For sensitivity analysis, I assume that lower bound estimates are about half of these values and that upper bound estimates are twice as great. Similarly, I assume that the lower bound and upper bound estimates of private COI are about half and double the values reported in Table 4.3. The lower bound and base estimates of WTP are based on estimates for respondents given time to think. The upper bound estimates correspond to values for respondents who were not given time to think.

Vaccine WTP benefits should be inclusive of all three of *ex ante* private treatment savings, *ex ante* mortality risk reduction benefits, and *ex ante* reduced pain and suffering benefits. I cannot separately evaluate the value of reduced pain and suffering, so I assume it should be the difference between WTP benefits and the other types of benefits as shown in Figure 6.3. This figure shows the relative contributions of each type of discrete benefit to the overall private WTP estimate. The expected private COI savings for 3 years of vaccine protection are about US$0.04 for young children and US$0.02 for school-age children. These values are about 1-2% of the estimated private WTP per vaccinated young child, US$2.4, or per vaccinated school-age child, US$1.20, as estimated from my CV survey. This suggests that private COI savings in isolation are a poor estimate of the private benefits of vaccination. *Ex ante* mortality risk reduction benefits are estimated to be US$1.70 for young children and US$0.24 for older children. These are equivalent to 70% of WTP estimates for young children and 20% of WTP estimates for school-age children. The remaining benefits are reduced pain and suffering, the value of which can be

back-calculated from the other types of benefits as shown in Figure 6.3. The back-calculated value of reduced pain and suffering is about US$0.70 for young children and about US$0.95 for older children. These would represent 28% of total WTP benefits for young and 80% of total WTP benefits for school-age children.

In the CV survey, respondents were asked to identify the most important benefit of a cholera vaccination. Most respondents stated that the most important benefit was either to prevent pain and suffering (51%) or to reduce risk of death (24%). Very few respondents (8%) cited avoided treatment costs or lost wages as the primary benefit. These stated beliefs are consistent with my comparison between *ex ante* COI, *ex ante* mortality risk reduction benefits, and WTP for vaccination estimates. For older children, my best estimate of WTP for vaccination (US$1.20) is much greater than my best estimate of COI + VSL estimates (US$0.25). I speculate that parents may have overestimated the risk of death from cholera for older children, who actually have a very small diarrhea mortality risk. Alternatively, the value of reduced risk of pain and suffering might be a more important consideration relative to mortality risk for this age group. Similar to the nutritional supplement results, I find that parents are less willing to purchase vaccines for older children (i.e. WTP is lower); however, the ratio of vaccine WTP to vaccine mortality risk reduction is still greater for older children because their risk of death was much less than for younger children. Notably, the value of reduced pain and suffering is very similar for young children (US$0.70) and older children (US$0.95) are very similar.

Table 6.8. Summary of incidence, COI, VSL, and vaccine WTP by age

		Young Children			School-age children		
Upper/ Lower bound		Best	Lower	Upper	Best	Lower	Upper
Private COI per case (*ex post*)	Direct treatment costs, US$	$4	$2	$8	$4	$2	$8
	Indirect treatment costs, US$	$4	$2	$8	$4	$2	$8
	Total private treatment costs, US$	$8	$4	$16	$8	$4	$16
Annual Incidence (cases per 1,000)		3.8	1.9	7.2	1.6	0.8	3.2
Estimated cholera fatality rate (20%/10%/50% of diarrhea deaths)		8.8E-05	4.4E-05	2.2E-04	1.2E-05	5.8E-06	2.9E-05
VSL, US$ per statistical death		$15,000	$10,000	$25,000	$15,000	$10,000	$50,000
Annual *ex ante* private COI		$0.03	$0.01	$0.12	$0.01	$0.00	$0.05
Annual *ex ante* mortality cost		$1.30	$0.44	$5.50	$0.18	$0.06	$1.50
Discounted vaccine benefits for 50% effective – 3 year vaccine[a]							
Discounted private COI benefits, US$ per vaccine		$0.04	$0.01	$0.15	$0.02	$0.00	$0.07
Discounted mortality risk reduction benefits, US$ per vaccine		$1.70	$0.57	$7.10	$0.23	$0.07	$1.87
Discounted total benefits (COI + mortality), US$ per vaccine		$1.70	$0.57	$7.20	$0.24	$0.08	$1.90
Stated WTP for cholera vaccination from CV survey, US$		$2.40	$2.40	$3.80	$1.20	$1.20	$2.30

[a] Benefits are discounted using 8% annual discount rate- PWF for 3 years=2.58

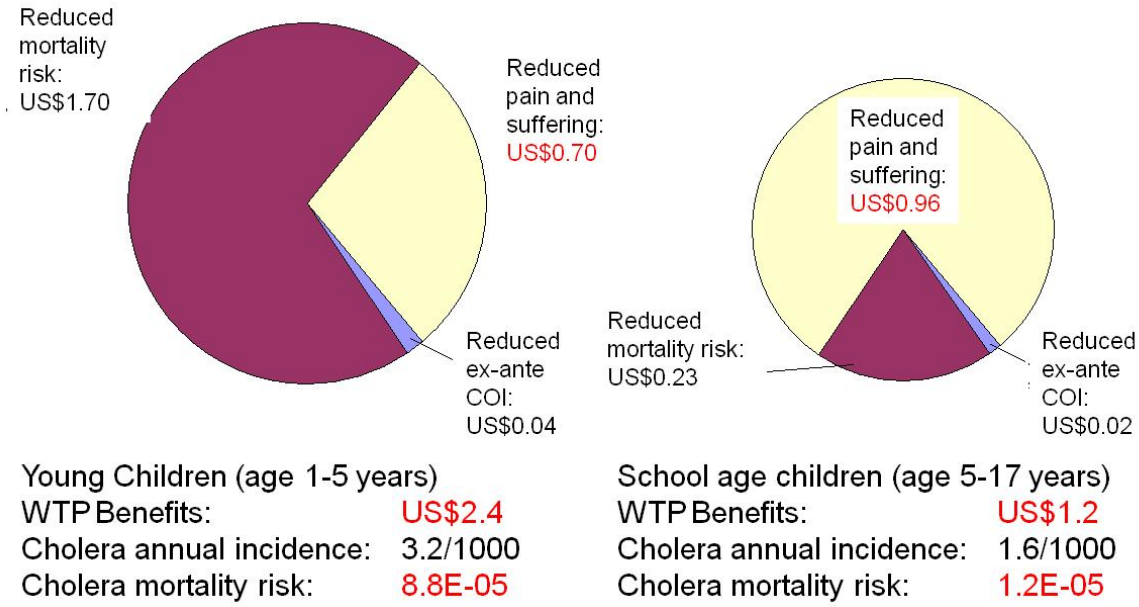


Figure 6.3. Graphical presentation of *ex ante* benefits

The lower bound COI + VSL benefits tend to be smaller than the lower bound WTP estimates, while the upper bound COI + VSL estimates tend to be greater. The difference between lower bound and upper bound COI + VSL estimates are greater than for WTP benefits, because the uncertainty in mortality rate and VSL estimates are multiplied together. Overall, the COI + VSL estimates appear to be consistent with the WTP estimates after accounting for the uncertainty. This might seem somewhat surprising because the number of deaths due to cholera comprise a relatively small fraction of the total number of child deaths in the Matlab area. As demonstrated in Table 3.2, scenarios with larger risk reductions usually generate smaller VSL estimates (within the same population). However, the valuation scenario for the cholera vaccine required an up-front payment of the entire cost of the vaccine, which was then effective for 3 years. As a result, the mortality risk reduction from a one-month supply of the nutritional supplement is similar to the protection provided by the cholera vaccine over a 3 year period (i.e. the risk of death from cholera was about 1/36 of the total risk of death from disease for young children).

7 Matlab policy model

7.1 Policy model input parameters

This chapter incorporates the Matlab-specific data from the previous chapter into an integrated economic model that summarizes the costs and benefits of cholera vaccination. In addition to these data, I need to make a number of assumptions. Model input parameters are summarized in Table 7.1. This table includes my best estimate for each parameter in addition to a range of possible low and high values. I split the Matlab area into four different subgroups: children in high incidence villages, children in average incidence villages, adults in high incidence villages, and adults in average incidence villages. The population is split such that 10% of the population resides in high incidence villages and the remaining 90% live outside these villages. Based on Table 4.1, it appears that villages with the top 10% of incidence experience about four times greater incidence than the rest of the villages. This represents the maximum potential difference between the highest incidence villages compared to the rest of the Matlab area. It is possible that incidence is underestimated in many villages because patients seek treatment at other facilities besides the ICDDR,B hospital, especially patients that live in villages located farther from the hospital in the northern part of the surveillance area. In personal conversations with hospital doctors, they stated that they believed that certain areas are more prone to cholera than others. However, it is possible that these doctors are somewhat biased by their experience of working at the hospital. Alternatively, differences may occur at geographical areas smaller than villages, such that differences are small after averaging across entire village populations. Among the villages in my CV survey sample, which included the majority of those located within two hours of the hospital, the top 10% of villages experienced twice the incidence

of the remaining 90% of villages over 10 years. If I restrict the observation period to 3 years instead of 10 years, the top 10% experience more than 4 times the incidence of the remaining 90%. I explore this maximum difference (i.e. 4 times greater incidence in the top 10%) to understand whether it is useful to attempt to target high incidence geographical areas in Matlab. Thus, the baseline scenario represents an upper bound difference in incidence rates between high and average incidence villages. Smaller differences are explored in the sensitivity analysis. If it is not useful to target prices assuming a larger discrepancy in incidence, it definitely would also not be useful for smaller discrepancies.

Thus, I adjusted my estimates of population average incidence rates for the high incidence villages to be four times greater than the remaining 90%. This adjustment is made such that the expected number of cases remains constant. Relative to the population average incidence, the risk of infection is almost four times greater in the high incidence villages and slightly less than average in the remaining 90% of villages where most of the population resides. The ranges of low-to-high incidence values used in the sensitivity analysis are one half and double the best estimates. Incidence may be less than the best estimate if the recent trend of declining incidence rates continues into the future. In contrast, incidence may be higher than expected if a large fraction of the population seeks treatment at alternative locations or if the recent downward trend in incidence were to be reversed.

I use the same demand equations for both low and high incidence groups because incidence rates were not significant in any of the demand models that I evaluated. Vaccination demand function parameters are taken from the previous chapter. The range in child demand intercepts is based on an assumption that between 50% and 80% of children would be willing to pursue free vaccinations if these were available. The adult intercept bounds are assumed to be smaller than the child bounds, 25% to 60% of the adult population.

This basic herd protection relationship is shown in Figure 3.2 and is the basis of the estimates in Table 7.1. As discussed in Section 3.5, Emch et al. (2009) found a strong correlation

between herd protection effects and environmental connectivity, specifically baris collocated with water bodies. These findings suggest that herd protection effects are highly localized. Thus, I assume that herd protection occurs primarily within village groups rather than between village groups. Specifically, I assume that coverage rates in high incidence villages have no impact on herd protection for average incidence villages. Similarly, I assume that coverage rates in average incidence villages have no impact on high incidence villages.

In the absence of age-group-specific herd protection effects, I assume that adult and child coverage rates have the same impact on herd protection effects within a village grouping. Because I express coverage rates in terms of the number of people vaccinated rather than as percentages, the coefficients for the average incidence villages must be smaller to account for the larger population. Specifically, the coefficients for high incidence villages are nine times greater to account for the fact that total population of the high incidence villages is nine times smaller than for the average incidence villages. The coefficients are determined by fitting an exponential expression to the data reported in Longini et al.'s (2007) model of herd protection observed during the 1985 vaccination trial. In the sensitivity analysis, I allow herd protection coefficients to vary separately for adults and children. The range of herd protection coefficients is 50% to 150% of the baseline values. For the lower bound, this is analogous to assuming that functional form remains the same, but twice as many people must be vaccinated to achieve the same herd protection effect. The herd protection results are based on the first year after vaccination and effects may diminish in years two and three (Longini et al., 2007).

Table 7.1. Population, herd protection and other model input parameters

Variable	Children high incidence (ch subscript)	Adults high incidence (ah subscript)	Children average incidence (cl subscript)	Adults average incidence (al subscript)
Values from literature				
Population, POP_{xx}	9,800	12,300	89,000	109,000
Demand intercept, α_{xx}	5,300 [4,600 – 7,100]	3,900 [3,000 – 7,400]	47,000 [34,000 – 68,000]	35,000 [26,000 – 62,000]
Price coefficient, β_{xx}	-0.36 [-0.20 – -0.50]	-0.33 [-0.20 – -0.75]	-0.36 [-0.20 – -0.50]	-0.33 [-0.20 – -0.75]
Baseline annual incidence, $INCU^0_{xx}$, cases per 1,000 persons	8.9 [2.9 – 18]	3.2 [1.0 – 6.3]	2.2 [1.1 – 4.4]	0.80 [0.4 – 2.0]
Herd protection coefficient for coverage γ_{xx}	-1.8E-04 [-8.9E-05 – -2.7E-04]	-1.8E-04 [-8.9E-05 – -2.7E-04]	-2.0E-05 [-1.0E-05 – -3.0E-05]	-2.0E-05 [-1.0E-05 – -3.0E-05]
Fixed cost, *F*, US$	22,000 [10,000 -50,000]			
Variable cost, *C*, US$	2.0 [1.5 – 4.0]			
Public COI per case-*PUBCOI*, US$	20 [10 - 30]	20 [10 – 30]	20 [10 - 30]	20 [10 - 30]
Vaccine efficacy, *Eff*,	65% [50 - 75]			
Duration of vaccine protection, *t* (years)	3 [2 - 4]			
Present worth factor, *PWF*	2.58			
DALY weight, *DALYweight*	0.105 [0.08 - 0.4]			
Case fatality rate, CFR_{xx} (%)	1 [0.5 – 3]			
Expected remaining life years, LE_{xx}	65	35 [10-35]	65	35 [10-35]

Variable	Children high incidence (ch subscript)	Adults high incidence (ah subscript)	Children average incidence (cl subscript)	Adults average incidence (al subscript)
Length of illness, *DUR* (days)		3 [1 – 7]		
Financial discount rate (%)		8		
DALY discount rate (%)		3		
Indirect protection valuation correction coefficient for vaccinated, πv		0.75 [0.5 – 1.0]		
Herd protection valuation coefficient- indirect protection for unvaccinated, πu		0.75 [0.5 – 1.0]		

The fixed cost is assumed to be US$22,000, which is equivalent to US$0.10 per person. This is similar to the amount used in a recent optimization study for typhoid vaccination programs in Asia (Lauria et al., 2009). The uncertainty range for fixed cost is US$10,000 to US$50,000, which corresponds to per person costs of US$0.05 to about US$0.25. The variable cost of vaccination is assumed to be US$2.2 for two doses of the cholera vaccination. Following Jeuland et al. (2009), this assumes a procurement cost per dose, inclusive of wastage, would be US$0.60 and that the delivery cost per dose would also be about US$0.50. The delivery costs are based on a study of delivery costs in low income countries (Lauria and Stewart, 2007). Overall, the uncertainty range is US$1.5 to US$4. The upper bound delivery cost may be greater than the average for low income countries if estimates are based on rural (rather than urban) areas.

The public treatment cost savings per case avoided is estimated to be US$20 as reported in Section 5.2. The uncertainty range (US$10 to US$30) is small because ICDDR,B keeps precise records of operations. Vaccination direct efficacy is assumed to be 65% based on Longini's reanalysis of vaccination efficacy (Longini et al., 2007). This is greater than the 50% direct

efficacy reported in the original analysis (Clemens et al., 1990b) because that study did not account for herd protection effects. Thus, at any coverage rate, vaccinated persons' risk of contracting cholera is 65% less than unvaccinated persons. I estimated that the duration of vaccine protection is 3 years based on a recent oral cholera vaccination effort in Vietnam (Thiem et al., 2006) with an uncertainty range of 2 to 4 years.

I estimate that the average duration of cholera illness is seven days and that the DALY disutility weight is 0.105 for those that survive the illness. This weight is based on the World Health Organization's standard for diarrheal disease ((WHO), 2003). For the sensitivity analysis, I assume DALY disutility weights range from 0.08 to 0.40 because cholera is an especially virulent form of diarrheal disease and patients are often unable to perform any other tasks during the short duration of symptoms. The case fatality rate is estimated at 1% based on personal communications with epidemiologists from the International Vaccine Institute. The range for case fatality rate is 0.5% to 3%. I would expect that the Matlab rate is at the low end of the range because of the high quality treatment facilities available at the ICDDR,B hospital. These estimates and ranges are consistent with those reported in a recent multicountry cost utility study of cholera vaccination (Jeuland et al., 2009).

The remaining life years per cholera death are 65 for children and 36 for adults based on life tables developed from ICDDR,B's surveillance efforts. I used the average adult age to calculate adult life expectancy. However, Table 2.1 suggests that elderly adults are considerably more likely to die from diarrheal disease than younger adults. Thus, I include a range of 10 to 36 years for adult life expectancy in the sensitivity analysis. There is little uncertainty for children because life expectancies are similar across all child ages. Overall, I estimate that 0.22 DALYs are saved per adult case prevented and 0.29 are saved per child case prevented. Most of the DALYs saved result from avoided mortality rather than avoided morbidity. Thus, case fatality rate would be especially important to estimate for an accurate DALY measure.

In the absence of data, I assume that πu and πv are equal to 0.75. This would indicate that indirect protection is less valuable than direct protection. It also indicates that WTP decreases per additional unit of protection. Indirect protection may be less valuable than direct protection for at least two reasons: 1) people are not protected when they spend time outside of the Matlab area or 2) estimates of indirect protection are much more uncertain than estimates of direct efficacy. I assume that the uncertainty ranges for πu and πv are 0.5 to 1.0.

7.2 Policy model results

The input parameters in Table 7.1 can be used to estimate outcomes of different types of vaccination programs. The baseline disease burden without a vaccination program is summarized in Table 7.2. The population and incidence rates are the same as the reported best estimates in Table 7.1. Over three years, the Matlab area is expected to experience about 1,200 cholera cases with about 30% occurring in the high incidence areas. The numbers of child cases are expected to more than double the numbers of adult cases. These cases would correspond to more than 330 lost DALYs and would cost the public treatment system about US$21,000. It is instructive to note that the maximum possible public treatment savings are approximately equal to the expected fixed cost of the vaccination program, US$22,000. Thus, these savings are unlikely to have much of an impact in offsetting total program costs, i.e. fixed + variable costs.

Prior to solving for optimal prices using the models developed in Chapter 5, I examine outcomes for some basic programs. In these basic programs, vaccinations will be provided either 1) free of cost or 2) at my best estimate of the variable cost of vaccination, US$2.2. The basic programs under consideration include: 1) free vaccinations for all groups; 2) free vaccinations for adults and children in high incidence villages, charging US$2.2 for vaccinations of adults and children in average incidence villages; 3) free vaccinations only for children in high incidence villages, charging US$2.2 for the other three groups; and 4) charging US$2.2 for all groups. Outcomes from each of these programs are summarized in Table 7.3.

Table 7.2. Cholera disease burden in Matlab in the absence of a vaccination program

	Children in high incidence villages	Adults in high incidence villages	Children in average incidence villages	Adults in average incidence villages	Total
Population	9,800	12,300	89,000	109,000	220,000
Baseline annual incidence, cases per 1000 persons	8.9	3.2	2.2	0.80	1.6
Number of cases over three years	260	120	590	260	1,200
DALYs lost	75	27	170	60	330
Discounted Public treatment savings	$4,400	$2,000	$10,000	$4,500	$21,000

Moving from left to right in Table 7.3, the total number of vaccinations delivered decreases as additional groups are required to pay the variable cost of vaccination. Because the adult and child price coefficients are similar, the percentage changes in coverage are approximately the same for both groups. In fact, coverage rates for both groups decline by slightly more than 50% as price increases from free to US$2.2. As coverage decreases, the number of cases avoided and DALYs saved also decrease. However, the declines are less than 50% because of the nonlinear herd protection relationships. The number of cases avoided decreases from 1100 for a program in which everyone receives free vaccines to 750 for a program in which everyone is forced to pay US$2.2. The decline in DALYs saved is from 290 to 210. Relative to the pre-vaccination baseline, about 90% of the disease burden is alleviated via free vaccination (cases avoided or DALYs saved) and by about 60% via a program in which all recipients must pay the marginal cost of vaccination. Outcomes are very similar across the three programs in which residents of low income villages must pay the variable cost of vaccination, probably because most of the population resides in these villages.

All of the monetary measures (direct and indirect benefits, public COI savings, and total costs) decline as prices increase. Public COI savings are about 10% of program costs for each of the programs, ranging from US$13,000 to US$19,000. These savings are insufficient to cover even the fixed cost of the programs. As a result, all of the programs require contributions from the government or donors. Moving from left to right, as coverage declines by more than 50%, program direct and indirect benefits decline by much less than 50% because of the nonlinear demand function. The fat tails of the demand distributions, shown in Figure 6.1, indicate that there is a small fraction of the population with very high willingness-to-pay for cholera vaccinations. This small subset of the population would be willing purchase vaccines for US$2.2 or at even greater prices. Recall that the herd protection relationship is also nonlinear and that the rate of change in incidence is greatest at low coverage rates. Net societal benefits are about US$170,000 for the free vaccination program and about US$220,000 for each of the other three programs. Without consideration for herd protection or public COI savings, net societal benefits would be maximized if price was set equal to the marginal cost of vaccination. With consideration of these benefits, net societal benefits are still greatest when recipients are charged prices close to the marginal cost of vaccination. Notably, since net societal benefits are positive for each program, all would pass a cost-benefit test.

The net revenue row represents the vaccination program cost to government or donor, net of collected user fees and public COI savings. It would cost about US$220,000 to provide free vaccines to everyone. This government/donor cost would decline to US$20,000 if free vaccinations were limited to only children in high incidence villages and to US$9,000 if vaccines were provided at the marginal cost. If prices are set equal to the marginal cost of vaccination, the external contribution is needed to offset the fixed cost of vaccination (after adjusting for public COI savings).

Table 7.3. Outcomes for four non-optimized vaccination programs

	Free vaccination for all subgroups	Free vaccination for adults and children in high incidence villages, US$2.2 for others	Free vaccination for children in high incidence villages, US$2.2 for others	All groups are charged US$2.2
Price- children high incidence, US$	$0	$0	$0	$2.20
Price- adults high incidence, US$	$0	$0	$2.20	$2.20
Price- children average incidence, US$	$0	$2.20	$2.20	$2.20
Price- adults average incidence, US$	$0	$2.20	$2.20	$2.20
Coverage- children high incidence	57%	57%	57%	26%
Coverage- adults high incidence	33%	33%	16%	16%
Coverage- children average incidence	57%	26%	26%	26%
Coverage- adults average incidence	33%	16%	16%	16%
Total vaccinations	96,000	50,000	48,000	45,000
Direct private benefits, US$	$280,000	$230,000	$230,000	$230,000
Indirect private benefits, US$	$110,000	$98,000	$97,000	$95,000
Public COI savings, US$	$19,000	$15,000	$14,000	$13,000
Sales revenue, US$	$-	$89,000	$93,000	$99,000
Total costs, US$	$230,000	$130,000	$130,000	$120,000
Net societal benefits, US$	$170,000	$210,000	$220,000	$220,000
Net revenue, US$	$(220,000)	$(28,000)	$(20,000)	$(9,000)
Total cases avoided	1100	850	830	750
Total DALYs saved	290	230	230	210

	Free vaccination for all subgroups	Free vaccination for adults and children in high incidence villages, US$2.2 for others	Free vaccination for children in high incidence villages, US$2.2 for others	All groups are charged US$2.2
Cost per case avoided, US$ per case	$200	$140	$140	$150
Cost per DALY saved, US$ per DALY	$750	$520	$510	$540
Cost per life saved, US$ per life saved	$20,000	$14,000	$14,000	$14,000

The cost per DALY calculation subtracts public COI savings from the total cost of vaccination and divides by the number of DALYs saved. The cost per DALY is typically used for comparison with other types of health interventions. However, it is important to note that this measure is variable depending on how a vaccination program is administered. The cost per DALY saved is greatest when free vaccinations are provided for everyone, US$750. The cost per DALY saved is approximately the same, US$510 – US$540, for the other three programs in which user fees are charged. The higher cost per DALY from providing free vaccinations to all groups results because herd protection very effectively reduces incidence even at low coverage rates. The cost of providing free vaccinations to all subgroups is about double the cost of other programs. However, the number of cases avoided only increase by about 25-30% when free vaccinations are provided to all. The total cost of implementing a free vaccination program is US$110,000 (90%) greater than the cost of providing vaccines to all subgroups at a price of US$2.20. This is because it is necessary to deliver nearly twice as many vaccines. However, due to herd protection, the number of DALYs saved increases by only 80 (40%). Thus, the marginal cost per marginal DALY saved in moving from a program that charges US$2.20 to a free vaccination program is US$110,000 / 350 DALYs = US$1375. This is about 2.5 times greater than the average cost per DALY for the program that charges all groups about US$2.20. A more

thorough examination of the average and marginal costs per DALY saved as functions of coverage rates is provided in Appendix 4.

According to the World Bank, a 'very cost-effective' intervention has a net cost per DALY ratio less than per capita GDP. A 'cost-effective' intervention has a ratio less than three times per capita GDP (Jeuland et al., 2009). For Bangladesh, per capita GDP is about US$510. Thus, free vaccination would not be considered 'very cost-effective', but the ratios for the other three programs in Table 7.3 are very close to this threshold.

The average cost per life saved varies from about US$14,000 to US$20,000. Similar to the DALY calculations, the cost per life saved estimate is considerably larger when vaccinations are provided for free to all subgroups. The range of cost per life saved estimates is very similar to the estimates of parents' VSL for their youngest child US$10,000 to US$25,000. If *ex ante* mortality risk reduction benefits were evaluated in place of CV estimates for cholera vaccine WTP benefits, the programs would still pass a benefit-cost test. However, the net societal benefits would be reduced. Recall that in Table 6.8, I showed that vaccine WTP estimates are greater than *ex ante* private COI plus mortality risk reduction benefits.[29]

Table 7.4 summarizes program outcomes for both of the objective functions developed in Chapter 5: 1) maximization of societal net benefits (Net Benefit model) and 2) maximization of DALYs saved (DALY model). These are both maximized subject to net revenue constraints, which require that program revenue shortfalls do not exceed a pre-specified government or donor contribution. Both objective functions are subjected to two distinct revenue constraints. The first two columns of Table 7.4 assume that there is no external contribution; the cost of the program must be less than or equal to the sum of program revenues and public treatment cost savings. The two rightmost columns of Table 7.4 assume that an external contribution of US$50,000 is

[29]While the average cost per life saved is within the range of VSL estimates from Section 6.3, the marginal cost per life saved in moving from variable cost pricing (US$2.20) to free vaccination is about US$31,000 per statistical life.

available to help finance the program. Optimal prices are considerably different for the Net Benefit model than for the DALY model. This occurs because economic benefits are strongly tied to the shape of the demand functions, which do not vary between high incidence and average incidence villages. The range in optimal prices for the Net Benefit model is from US$1.90 for children in high incidence areas to US$2.60 for adults in average incidence areas. The estimated coverage rates at these prices are all quite low (14% to 29%) because prices must be sufficient to generate enough revenue to cover program costs. The optimal prices are slightly lower for children because they have greater incidence, which means that more cases are avoided per child vaccination delivered. This translates to greater public COI savings per vaccination for children (though public COI savings are small compared to direct protection and indirect protection benefits). This is also the reason for price differences between high incidence and average incidence villages.

In comparison to the Net Benefit model, there is greater variation in optimal prices for the revenue neutral DALY model. The optimal price for children in high incidence villages (US$0.10) is much less than optimal prices for other groups (US$0.40 – US$3.20). This makes sense because incidence is so much greater for that group. The optimal price for adults in high incidence villages is also substantially larger than the optimal price for adults in average incidence villages.

Table 7.4. Outcomes for revenue-neutral optimized vaccination programs

	Net Benefit model: revenue neutral	DALY model: revenue neutral	Net Benefit model: maximum external contribution of US$50,000	DALY model: maximum external contribution of US$50,000
Price- children high incidence, US$	$1.90	$0.40	$1.20	$-
Price- adults high incidence, US$	$2.20	$1.50	$1.50	$0.25
Price- children average incidence, US$	$2.40	$2.50	$1.80	$1.40
Price- adults average incidence, US$	$2.60	$3.20	$1.80	$2.30
Coverage- children high incidence	29%	49%	37%	57%
Coverage- adults high incidence	16%	20%	20%	30%
Coverage- children average incidence	24%	23%	30%	35%
Coverage- adults average incidence	14%	12%	18%	16%
Total vaccinations	41,000	40,000	53,000	57,000
Direct private benefits, US$	$220,000	$210,000	$240,000	$250,000
Indirect private benefits, US$	$93,000	$93,000	$98,000	$101,000
Public COI savings, US$	$13,000	$13,000	$15,000	$16,000
Sales revenue, US$	$101,000	$97,000	$91,000	$82,000
Total costs, US$	$110,000	$110,000	$140,000	$150,000
Net societal benefits, US$	$210,000	$210,000	$220,000	$210,000
Net revenue, US$	$-	$-	$(32,000)	$(50,000)
Total cases avoided	740	760	840	910
Total DALYs saved	200	210	230	250
Cost per case avoided, US$ per	$140	$130	$150	$150

	Net Benefit model: revenue neutral	DALY model: revenue neutral	Net Benefit model: maximum external contribution of US$50,000	DALY model: maximum external contribution of US$50,000
case				
Cost per DALY saved, US$ per DALY	$500	$470	$540	$530
Cost per life saved, US$ per life saved	$14,000	$13,000	$15,000	$15,000

Although there are large differences in the optimal prices across model specifications, differences in program outcomes are considerably smaller. Net societal benefits are only about 2% greater for the Net Benefit model compared to the DALY model. Similarly, the number of DALYs saved is only about 4% greater for the DALY model compared to the Net Benefit model. The total cost and total number of vaccinations delivered are also very similar for the two models. Because the total number of vaccinations is similar for both objective functions, the herd protection effects and numbers of cases avoided are very similar for both objective functions. Thus, net societal benefits and total DALYs saved are almost equal for the two objective functions.

There are slightly fewer total vaccinations delivered with the DALY model since that program targets vaccinations for the high incidence villages. As a result, higher prices are necessary in the average incidence villages where a majority of the population lives. In addition, since slightly more DALYs are avoided at a slightly lower cost, the cost per DALY is reduced with the DALY objective function. In summary, while the optimal prices are considerably different across types of models, differences in program outcomes are typically less than 5%.

Next, I consider programs in which government or donors are willing to provide a US$50,000 contribution to a potential vaccination program. The outcomes for these models are summarized in the two rightmost columns of Table 7.4. The additional capital allows for a

considerable reduction in the user fees charged relative to the revenue neutral models. In other words, the external contribution is like a transfer payment to vaccine purchasers. This lump sum transfer is used to reduce user fees by varying amounts for each subgroup. The optimal prices vary from about US$1.20 to US$1.80 for the Net Benefit model compared to free to US$2.30 for the DALY model. It is again optimal to charge the lowest prices to children in high incidence villages and the highest price to adults in the average incidence villages. The reduced user fees result in increases in the number of vaccinations by about 12,000 (30%) for the Net Benefit model and by 17,000 (43%) for the DALY model. These increases in total vaccinations boost total program costs by US$27,000 and US$37,000 respectively.

Notably, only about US$32,000 is required to maximize societal net benefits. If one tried to further reduce prices from those listed, the net societal benefits would decline. The US$32,000 contribution from government or donors allows a US$5,000 increase in net societal benefits (about 3%). Thus, there is a net increase in social welfare, but the external investment has a small effect on program outcomes.

For the DALY model, the entire US$50,000 in available extra funding is used to maximize the number of DALYs saved. This reduction in user fees made possible by this extra US$50,000 results in an increase of 40 DALYs saved (16%). In contrast to Net Benefit model, the extra funding has a substantial impact on the objective function (i.e. the number of DALYs saved). The total costs of the program increase by US$37,000 to save the additional 40 DALYs. Thus, the marginal cost per DALY saved is US$37,000 / 40 DALYs = US$930. This is substantially greater than the average cost per DALY estimate (US$470) for the revenue neutral program.

Prior to examining results from the sensitivity analysis, I examine a range of pricing options graphically. The results depicted in each graph are based on programs in which each of the four groups is charged the same price. I assume that US$10 would be the maximum price charged and that free vaccination would be the minimum price. When both groups are charged

the same price, child coverage rates are expected to be considerably greater than adult coverage rates. Since all graphs are 2-dimensional, it should be assumed that child coverage rates are disproportional to adult coverage rates within the population average coverage rates. Figure 7.1 summarizes total economic benefits, total costs, total cases avoided and total vaccinations as functions of coverage. Figure 7.2 summarizes the same outcomes as functions of price.

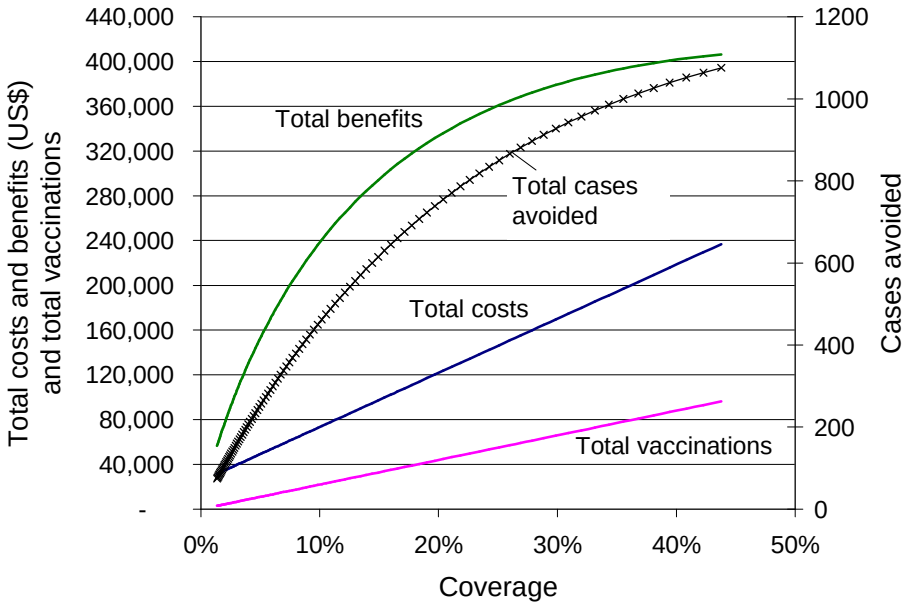


Figure 7.1. Total benefits, costs, vaccinations, and cases avoided as functions of coverage

Total costs and vaccinations are linear functions of coverage. The total benefits and cases avoided functions are nonlinear and the rate of change decreases as coverage increases. Total economic benefits include WTP estimates for direct and indirect protection in addition to public treatment cost savings. Total economic benefits are about US$290,000 at a 15% coverage rate; and the maximum total benefits are about US$410,000. Thus, about 70% of the maximum total benefits can be captured at a coverage rate of just 15%. The total cases avoided function does not level off as quickly as the total benefits function. At 15% coverage, there are about 630 cases avoided. The maximum 1,100 cases are avoided when vaccinations are provided for free and the

coverage rate is 44%. In contrast to total benefit calculation, only about 58% of the maximum cases are avoided at 15% coverage.

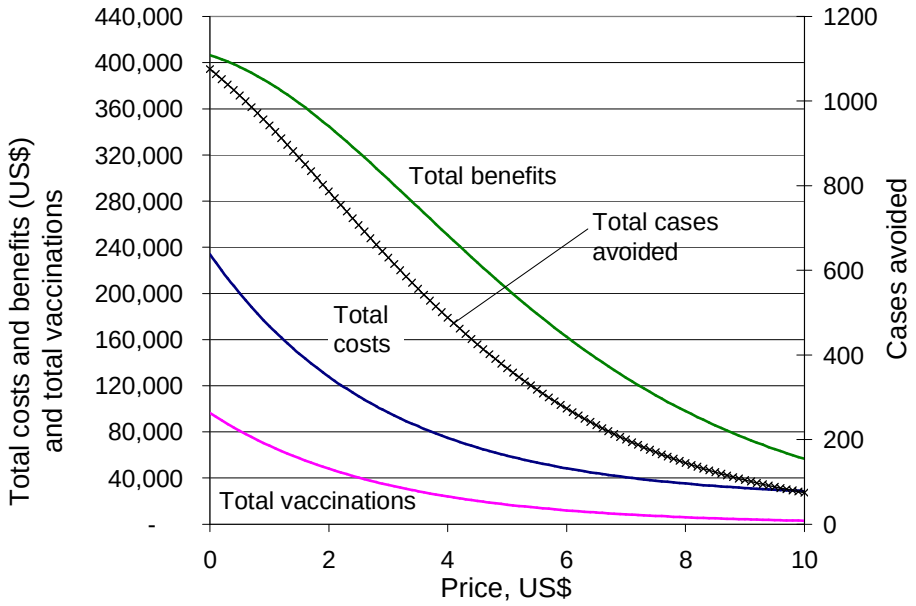


Figure 7.2. Total benefits, costs, vaccinations, and cases avoided as functions of price

Figure 7.2 is an inverted version of Figure 7.1, because cases avoided, vaccinations, total costs, and total benefits all decrease as functions of price. The number of cases avoided again declines at a faster rate than total benefits. There is a large drop (more than 50%) in total vaccinations as price increases from free to US$2. As price continues to increase from US$2, the number of vaccinations purchased appears to level off up to US$10 at which point a small fraction of the population would be willing to pay. The number of cases avoided decline at a faster rate than total economic benefits. Thus, changes in price are likely to have larger effects on cases avoided than on total economic benefits. These differences are caused by the shape of the demand functions, which are also nonlinear.

Figure 7.3 summarizes public revenues and costs from a potential vaccination program. The public sector earns income from vaccination sales and public COI savings, while paying for the fixed and variable costs of vaccination. It is clear that public COI savings are always quite

small relative to total costs. Thus, it is necessary to charge user fees to achieve revenue neutrality. Sales revenue increases quickly to a maximum at US$3, then decline slowly back toward zero. Net revenue is maximized at a price of about US$4.70. It would be illogical to charge a greater price; both because fewer cases would be avoided and because less net revenue would be earned.

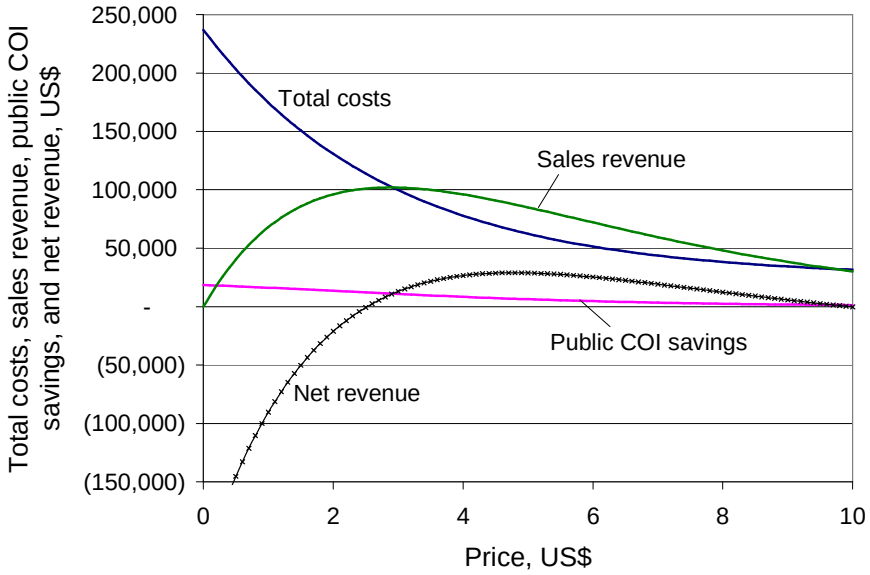


Figure 7.3. Total costs, sales revenue, public COI savings, and net revenue as functions of price

The individual components of benefits include direct private benefits, indirect private benefits, and public COI savings, which are summarized in Figure 7.4. All three types of benefits are maximized when vaccinations are free and decrease as price increases. Public COI benefits are quite small relative to other types of benefits, just as public COI is small relative to costs in the revenue graph. The percentage composition of benefits is summarized in Figure 7.5. Public COI savings are never more than 5% of the total benefits. The percentage of public COI savings relative to total benefits decrease from 5% at low coverage rates and high prices to 2% at high prices and low coverage. This is because the average WTP per vaccine increases as price increases and only those with the highest WTP are willing to purchase vaccinations.

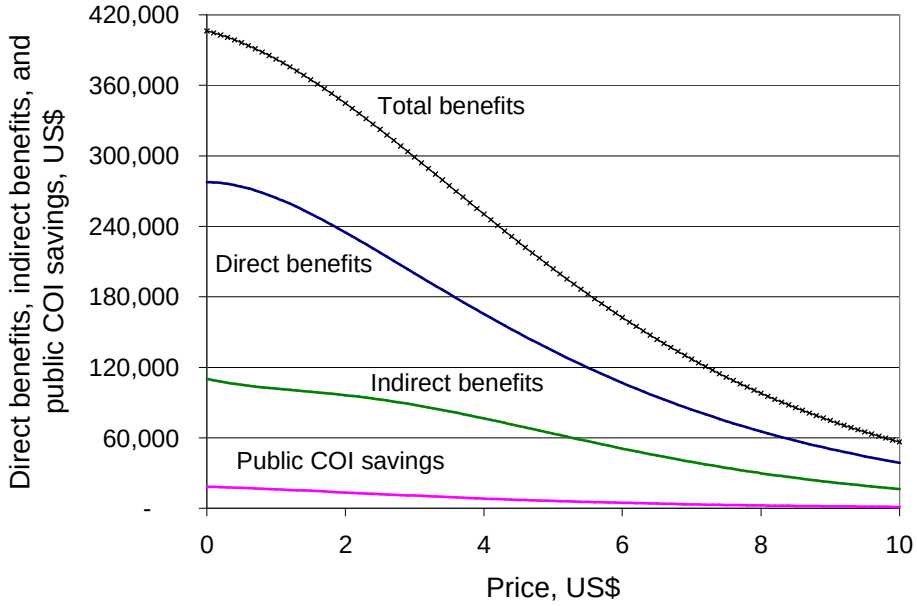


Figure 7.4. Individual components of total benefits

Indirect benefits decrease from a maximum of US$110,000 for free vaccination to a minimum of about US$15,000 when vaccinations cost US$10. The percentage of indirect benefits relative to total benefits remains between 26% and 31% across the entire range of prices. Direct benefits decrease from a maximum of about US$280,000 to a minimum of about US$37,000. The percentage of direct benefits also remains almost constant between 65% and 70%.

The composition of direct versus indirect benefits depends on the way that benefits are accounted for. There are competing factors for the percentage of direct versus indirect benefits. Recall that I assigned zero monetary benefits to the fraction of the population that I predicted would be unwilling to receive free vaccination. As price decreases, more people become vaccinated and the pool of unvaccinated persons who receive indirect benefits decreases. Concurrently, the magnitudes of indirect protection for both vaccinated and unvaccinated persons increase. Thus, the indirect benefit per person increases as coverage increases; however, the number of unvaccinated persons with non-zero WTP decreases. In addition, indirect protection is valued at 75% of direct protection. Thus, direct protection benefits are consistently larger than indirect benefits. In Figure 7.5, I show the fractional breakdown of benefits for a program with

free vaccination in comparison to a program in which all subgroups are charged US$2.20. The total indirect benefits decrease by about US$50,000 (16%), while the direct private benefits decrease by about US$50,000 (18%). Thus, the percentage composition of benefits remain almost constant across the likely pricing range.

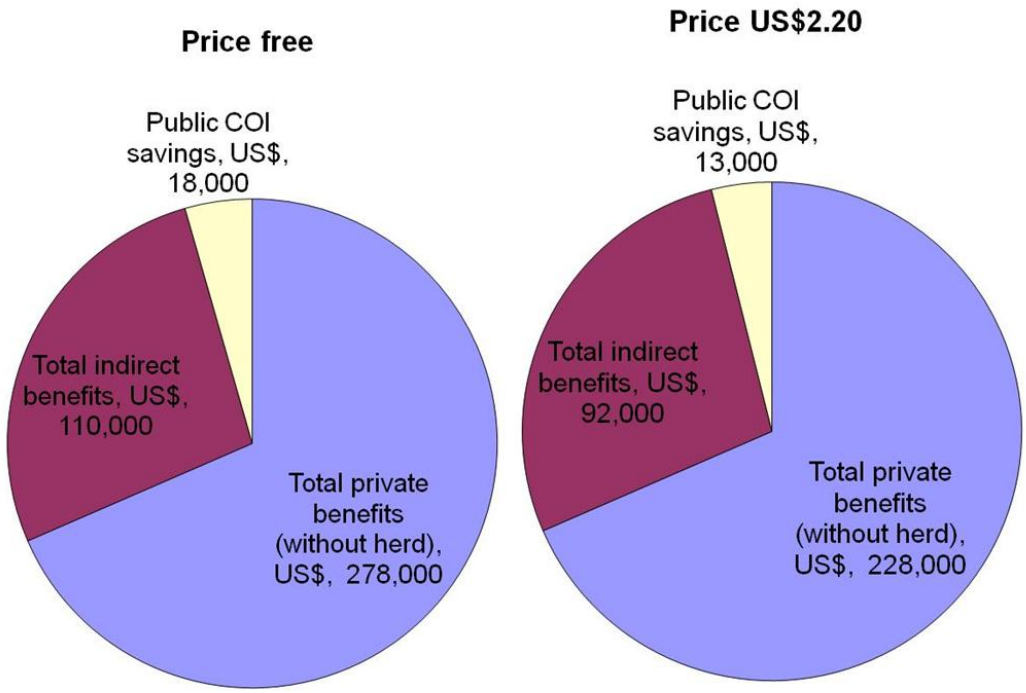


Figure 7.5. Percentage composition of benefit components

Net societal benefits and net revenue as functions of coverage are shown in Figure 7.6. These represent the objective function and revenue constraint for net societal benefit maximization if the same price were charged to all subgroups. Net societal benefits increase across the narrow range of prices from free to US$1.7. Net societal benefits are about US$170,000 for free vaccination and about US$210,000 if a user fee of US$1.70 is charged. If prices greater than US$1.70 are charged, net societal benefits decline from the maximum. The vertical dotted line shows the necessary external contribution to maximize net societal benefits,

which is about US$35,000. The net societal benefit curve is very flat across the price range from US$1 to US$3. Thus, one could change any price within this range and achieve near optimal net societal benefits. In contrast, the choice of price has a great effect on net revenue. If a price of US$1 is charged, an external contribution of about US$90,000 would be required. Alternatively, if a price of US$3 is charged, the program would generate a profit of about US$15,000. This demonstrates why the external contribution had a small impact on net societal benefits as reported in Table 7.4. It is sub-optimal to provide free vaccinations. Net societal benefits would decline considerably if there were a compulsory vaccination program to increase coverage rates to closer to 100%.

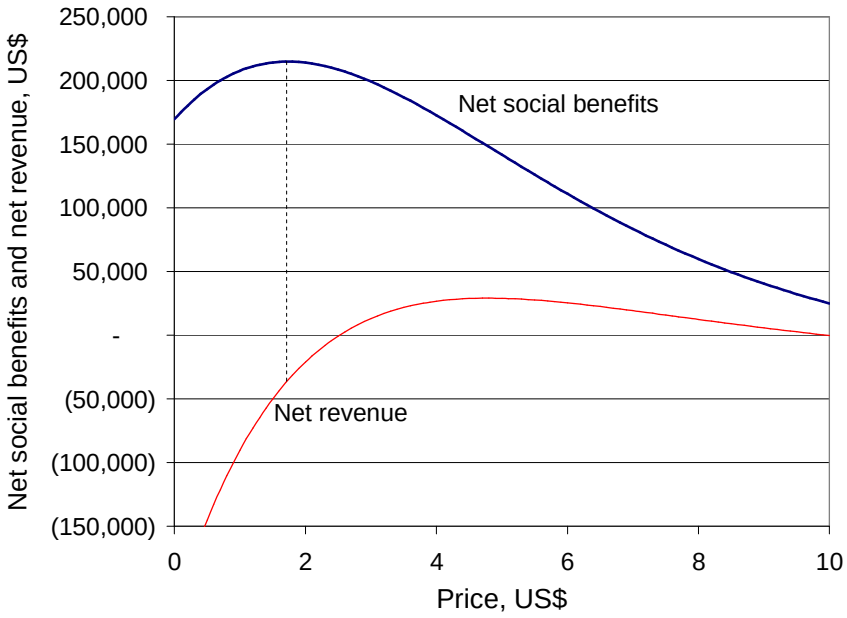


Figure 7.6. Net societal benefits, net revenue, and cases avoided as functions of price

The average cost per DALY, marginal cost per DALY, average cost per vaccination, and total DALYs saved functions are shown in Figure 7.7. A more thorough examination of the average and marginal costs per DALY is included in Appendix 4. Since the program has both fixed and variable costs, the average cost per vaccination delivered is not constant. As coverage increases, the average cost per vaccination decreases toward the variable cost of vaccination,

US$2. At low coverage rates, the average cost per vaccination may be very high, a maximum of US$16 at price US$10. Thus, it is important to consider fixed costs if coverage rates are expected to be low. At these low coverage rates, the fixed cost dominates variable costs in the average cost calculation.

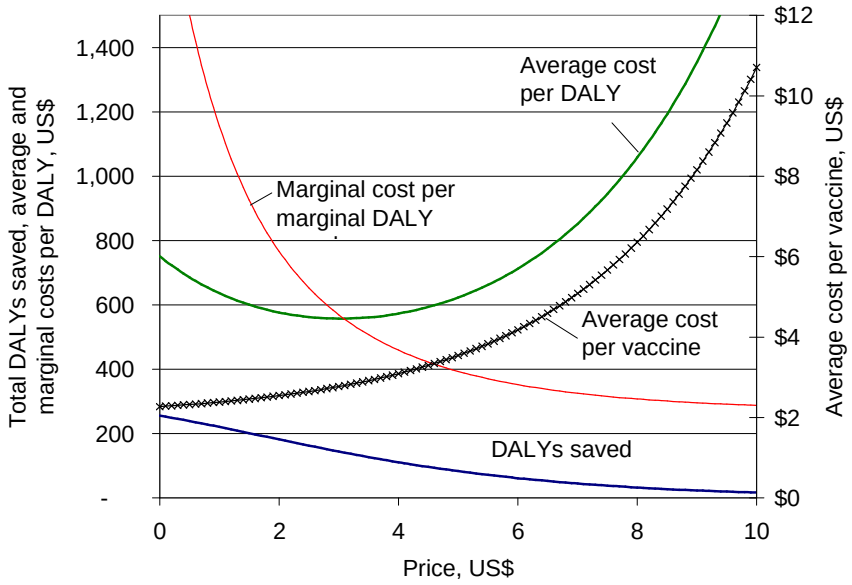


Figure 7.7. DALYs saved, average cost per vaccine and per DALY saved, and marginal cost per DALY saved

The marginal cost per DALY is calculated based on the change in total cost divided by the change in DALYs saved in moving from price A to price B. Because the calculation is marginal, the fixed cost drops out of the calculation (in contrast to the average cost calculation). The marginal cost per DALY saved is minimized at low coverage rates because the marginal change in herd protection effects is greatest at low coverage rates. As more people become vaccinated, the number of cases avoided per vaccination decreases because incidence rates have already been reduced considerably for both vaccinated and unvaccinated persons.

The shape of the average cost per DALY saved is influenced by both the average cost per vaccination and marginal cost per DALY curves. At very low prices and high coverage rates, the marginal cost per DALY is large, but the average cost per vaccination is minimized. Because the marginal cost per DALY is very high for free vaccination, the average cost per DALY will

decline as price is increased from free to US$3. After the marginal cost curve intersects the average cost curve at US$3, the average cost per DALY increases with price. At very high prices and low coverage rates, the average cost per DALY is very high, because fixed costs dominate marginal cost even thought the marginal cost per DALY is minimized. If the fixed cost were zero, the average cost per DALY would increase monotonically as coverage increases across the entire range of prices.

7.3 Sensitivity analysis

Due to the considerable uncertainty in parameter estimates and assumptions, I performed a sensitivity analyses using Monte Carlo simulation (MCS), treating most of the model parameters in Table 7.1 as random variables. I consider each objective function separately: 1) the maximization of net societal benefits and 2) the maximization of DALYS saved. Further, I assume that no external contribution will be available to help offset program costs. The basic features of the original model apply to the MCS without change, e.g. the child and adult populations by village type, the ability to apply discounted public treatment cost savings to the net revenue constraint, and the financial and DALY discount rates.

The remaining parameters are variable based on the parameter ranges included in Table 7.1. For each random variable, the probability density function (pdf) is assumed to be triangular, based on the best estimate and bracketed lower and upper bound values shown in Table 7.1. The sensitivity analysis produces an optimal solution for each of 500 MCS trials. The same 500 parameter draws are used to solve both models separately.

Cholera incidence is assumed to be higher in children than in adults for both village types. This was ensured in the MCS by using correlations that resulted in child incidence exceeding adult incidence for 100% of the trials. The ratio of child to adult cholera incidence was about 2.8 in the deterministic case, and in the MCS it ranged from 1 to 8 with a median of 2.8. Similarly, the median ratio of incidence for high incidence versus low incidence villages is 3.7,

which is similar to the ratio assumed in the deterministic models, 4. Correlations were also used for the parameters of the demand functions, α and β, to ensure that child coverage would exceed adult coverage for identical prices; the median ratio of α-values for children relative to adults in the MCS was about 1.7 (on a percentage basis), and the median ratio of β-values for adults relative to children was about 1.2, both of which closely match the ratios in the deterministic model. It was assumed that demand functions would be the same for high incidence and low incidence villages, as in the deterministic model. The same probability density function for the herd protection coefficients cases was used for both adults and children, but the model allowed for differences by age group. Herd protection effects for children and adults, γ_c and γ_a, are drawn independently in case either adults (or children) are more efficient at spreading cholera once they become ill.

For 10% of the simulations, it was not possible to achieve revenue neutrality. These scenarios include simulations with high average and marginal costs. In addition, the demand function parameters and herd protection coefficients tend to be smaller. I omit these scenarios for the rest of this discussion and focus on simulations in which revenue neutrality is possible. For the net societal benefit model, the mean optimal prices across simulations are US$2.90 for children in high incidence villages, US$3.00 for adults in high incidence villages, US$2.90 for children in low incidence villages, and US$2.90 for adults in low incidence villages. For any individual draw, it might be optimal to charge certain subgroups slightly more or slightly less than others. On average, net societal benefits are maximized when approximately equal prices are charged. This is because WTP benefits are considered to be independent of the uncertainty in incidence, case fatality rate, and other public health parameters within the MCS, (i.e. no correlations were assumed between demand function parameters and these public health parameters).

In contrast, for the DALY model, the mean optimal prices across simulations are US$1.50 for children in high incidence villages, US$1.90 for adults in low incidence villages,

US$3.10 for children in low incidence villages, and US$3.10 for children in low incidence villages. Thus, it is optimal to target program subsidies for the high incidence villages where the program cost per DALY saved is likely to be less. However, it is generally not optimal to provide free vaccinations to the high incidence villages. The optimal child price in high incidence villages is zero in just 5% of the simulations and the optimal adult price is zero in less than 1%.

Next, I examine the differences in outcome measures from the two models. In Figure 7.8, the cumulative distribution of net societal benefits from both the DALY and Net Benefit models are shown. Since net societal benefits are included in the objective function of the Net Benefit model, it is expected that estimates are larger for the Net Benefit model relative to the DALY model. However, differences are very small, less than 5%, across the entire distribution. The 5%-to-95% confidence interval for net societal benefits is about US$110,000 to US$380,000 for the 448 simulations in which the net revenue constraint can be satisfied.[30]

The cumulative density functions of DALYs saved from the Net Benefit and DALY models are shown in Figure 7.9. The DALYs saved are greater for the DALY model, but, again, differences are small. The maximum difference across all simulations is only about 20%. The median number of DALYs saved is about 250, and the 5% to 95% uncertainty range is about 110 to 580 DALYs.

Thus, the type of model, Net Benefit or DALY, appears to have more influence on setting prices than on program outcomes.[31] I believe that differences are limited by herd protection effects, which allow for significant incidence reductions in unvaccinated groups. Since incidence is reduced to some degree for both vaccinated and unvaccinated persons, cross-subsidies are less influential in changing program outcomes.

[30]Net societal benefits are greater than zero across the other 52 simulations for which the net revenue constraint cannot be satisfied. Thus, properly designed cholera vaccination programs should easily pass a benefit-cost test.

[31]It is also possible to solve a model in which all subgroups are charged the same price. Program outcomes from this model are very similar to the Net Benefit and DALY models. I omitted this model from Figures 8 and 9 so that the minimal difference between the Net Benefit and DALY models would be easier to see.

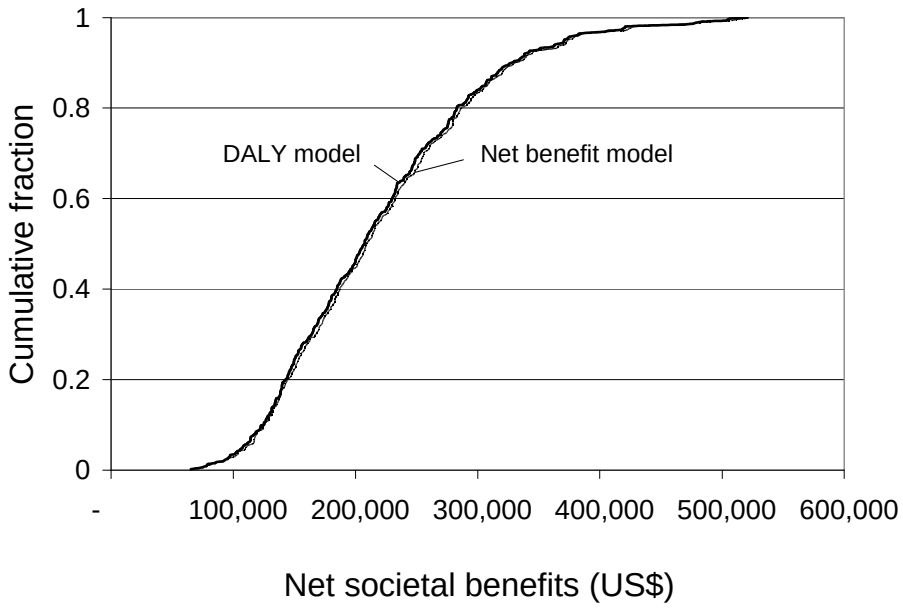


Figure 7.8. Net societal benefits from MCS

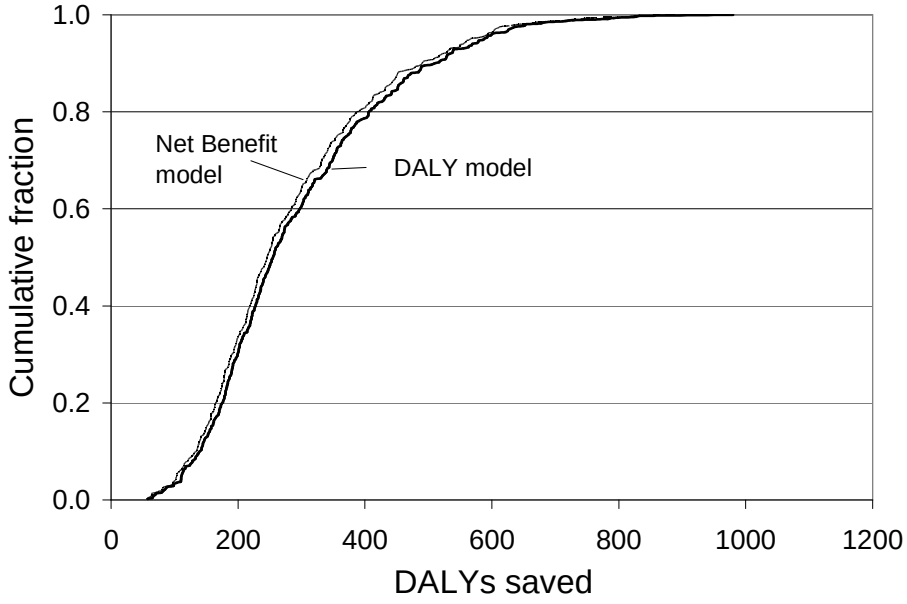


Figure 7.9. Number of DALYs saved from MCS

In Table 7.5, I present the results of an analysis of variance for the Net Benefit Model. It is clear that average and fixed costs are the most important determinants of optimal prices

(columns 1-4), accounting for between 75-85% of the total variation across the four prices. For simulations with high costs estimates, all prices must be set relatively high to achieve revenue neutrality. Other important parameters include: adult and child herd protection coefficients and adult and child demand coefficients. When one age group has a greater influence on herd protection than the other, it is typically optimal to subsidize that group to increase indirect protection benefits.

It is illustrative to consider the ratio of weighted average adult to child prices. Average adult and child prices can be calculated from a population-weighted average of prices charged in high incidence and average incidence villages. The fifth column of Table 7.5 shows an analysis of variance for this ratio. This clearly shows the importance of herd protection coefficients, which account for 65% of the variation. This is further demonstrated in Figure 7.10, which plots the ratio of adult to child price relative to the ratio of adult to child herd protection coefficients on a log scale. When the adult herd protection coefficient is larger in magnitude than the child coefficient, $\gamma_a > \gamma_c$, it is optimal to charge adults lower user fees, $p_a < p_c$, to take advantage of these effects (see bottom-right corner of Figure 7.10. In contrast, if $\gamma_a < \gamma_c$, it optimal to charge children lower prices (see upper-left corner of Figure 7.10). It is important to note that I chose tightly bounded uncertainty ranges for herd protection coefficients. The largest gamma ratio is just 2.3. If I had used a larger uncertainty range, it is likely that herd protection coefficients would play a larger role in analysis of variance calculations. This is a potentially important topic for future epidemiological research.

Table 7.5. Analysis of variance for Net Benefit model

	P_{ch}, Child price in high incidence villages, US$ (1)	P_{ah}, Adult price in high incidence villages, US$ (2)	P_{cl}, Child price in average incidence villages, US$ (3)	P_{al}, Adult price in average incidence villages, US$ (4)	Weighted average price difference between children and adults, US$ (5)	Net societal benefits, US$ (6)	Benefit-cost ratio (7)
Common parameters							
Vaccine efficacy, *Eff*,	1%	2%	0%	0%	1%	10%	19%
Variable cost, *C*, US$	62%	57%	64%	60%	0%	19%	35%
Fixed cost, *F*, US$	17%	17%	21%	18%	0%	6%	12%
Public COI per case- *PUBCOI*, US$	2%	1%	1%	1%	0%	1%	0%
Indirect protection correction factor for vaccinated and unvaccinated, πx	0%	0%	0%	0%	0%	2%	6%
Duration of vaccine protection, *VACCDUR* (years)	1%	2%	0%	0%	0%	0%	0%
Length of illness, *ILLDUR* (days)	0%	0%	0%	0%	0%	0%	0%
Case fatality rate (%)	0%	0%	0%	0%	0%	0%	0%
Adult expected remaining life years, LE_a	0%	0%	0%	0%	0%	0%	0%
DALY weight, *DALYweight*	0%	0%	0%	0%	0%	0%	0%
Child parameters							
Baseline annual incidence for children in high incidence villages, $INCU^0_{ch}$, cases per 1,000 persons	2%	2%	0%	0%	0%	0%	0%
Baseline annual incidence for children in average incidence villages, $INCU^0_{cl}$, cases per 1,000 persons	0%	0%	1%	0%	0%	0%	0%
Child demand intercept, α_{cx}	0%	0%	1%	0%	0%	7%	2%
Child price coefficient, β_{cx}	1%	2%	0%	5%	10%	24%	11%
Herd protection coefficient for child coverage, γ_{cx}	4%	5%	5%	4%	31%	1%	2%

	P_{ch}, Child price in high incidence villages, US$ (1)	P_{ah}, Adult price in high incidence villages, US$ (2)	P_{cl}, Child price in average incidence villages, US$ (3)	P_{al}, Adult price in average incidence villages, US$ (4)	Weighted average price difference between children and adults, US$ (5)	Net societal benefits, US$ (6)	Benefit-cost ratio (7)
Adult parameters							
Baseline annual incidence for adults in high incidence villages, $INCU^{0}_{ah}$, cases per 1,000 persons	1%	2%	0%	0%	0%	0%	0%
Baseline annual incidence for adults in average incidence villages, $INCU^{0}_{al}$, cases per 1,000 persons	0%	1%	0%	0%	0%	0%	0%
Adult demand intercept, α_{ax}	0%	3%	0%	0%	0%	10%	2%
Adult price coefficient, β_{ax}	4%	0%	4%	3%	22%	19%	9%
Herd protection coefficient for adult coverage, γ_{ax}	4%	4%	3%	7%	34%	0%	1%

Table 7.6. Analysis of variance for DALY model

	P_{ch}, Child price in high incidence villages, US$ (1)	P_{ah}, Adult price in high incidence villages, US$ (2)	P_{cl}, Child price in average incidence villages, US$ (3)	P_{al}, Adult price in average incidence villages, US$ (4)	Weighted average price difference between children and adults, US$ (5)	DALYs saved (6)	Average cost per DALY (7)
Common parameters							
Vaccine efficacy, *Eff*,	0%	2%	0%	0%	0%	0%	0%
Variable cost, *C*, US$	36%	29%	57%	48%	0%	9%	10%
Fixed cost, *F*, US$	21%	16%	19%	11%	1%	3%	4%
Public COI per case- *PUBCOI*, US$	1%	0%	1%	1%	0%	0%	0%

	P_{ch}, Child price in high incidence villages, US$ (1)	P_{ah}, Adult price in high incidence villages, US$ (2)	P_{cl}, Child price in average incidence villages, US$ (3)	P_{al}, Adult price in average incidence villages, US$ (4)	Weighted average price difference between children and adults, US$ (5)	DALYs saved (6)	Average cost per DALY (7)
Indirect protection correction factor for vaccinated and unvaccinated, πx	0%	0%	0%	0%	0%	0%	0%
Duration of vaccine protection, *VACCDUR* (years)	0%	1%	0%	1%	0%	9%	11%
Length of illness, *ILLDUR* (days)	0%	0%	0%	0%	0%	0%	0%
Case fatality rate (%)	0%	1%	0%	0%	0%	59%	58%
Adult expected remaining life years, LE_a	0%	0%	0%	0%	0%	1%	0%
DALY weight, *DALYweight*	0%	0%	0%	0%	0%	0%	0%
Child parameters							
Baseline annual incidence for children in high incidence villages, $INCU^0_{ch}$, cases per 1,000 persons	11%	3%	0%	0%	0%	2%	4%
Baseline annual incidence for children in average incidence villages, $INCU^0_{cl}$, cases per 1,000 persons	2%	1%	2%	0%	0%	8%	7%
Child demand intercept, α_{cx}	0%	0%	1%	0%	0%	1%	0%
Child price coefficient, β_{cx}	0%	13%	2%	10%	18%	1%	0%
Herd protection coefficient for child coverage, γ_{cx}	3%	11%	4%	2%	13%	2%	2%
Adult parameters							
Baseline annual incidence for adults in high incidence villages, $INCU^0_{ah}$, cases per 1,000 persons	0%	2%	0%	0%	0%	1%	0%

	P_{ch}, Child price in high incidence villages, US$ (1)	P_{ah}, Adult price in high incidence villages, US$ (2)	P_{cl}, Child price in average incidence villages, US$ (3)	P_{al}, Adult price in average incidence villages, US$ (4)	Weighted average price difference between children and adults, US$ (5)	DALYs saved (6)	Average cost per DALY (7)
Baseline annual incidence for adults in average incidence villages, $INCU^{0}_{al}$, cases per 1,000 persons	0%	0%	0%	0%	0%	0%	1%
Adult demand intercept, α_{ax}	0%	0%	0%	0%	0%	2%	1%
Adult price coefficient, β_{ax}	16%	5%	11%	16%	48%	2%	1%
Herd protection coefficient for adult coverage, γ_{ax}	10%	16%	2%	9%	20%	0%	1%

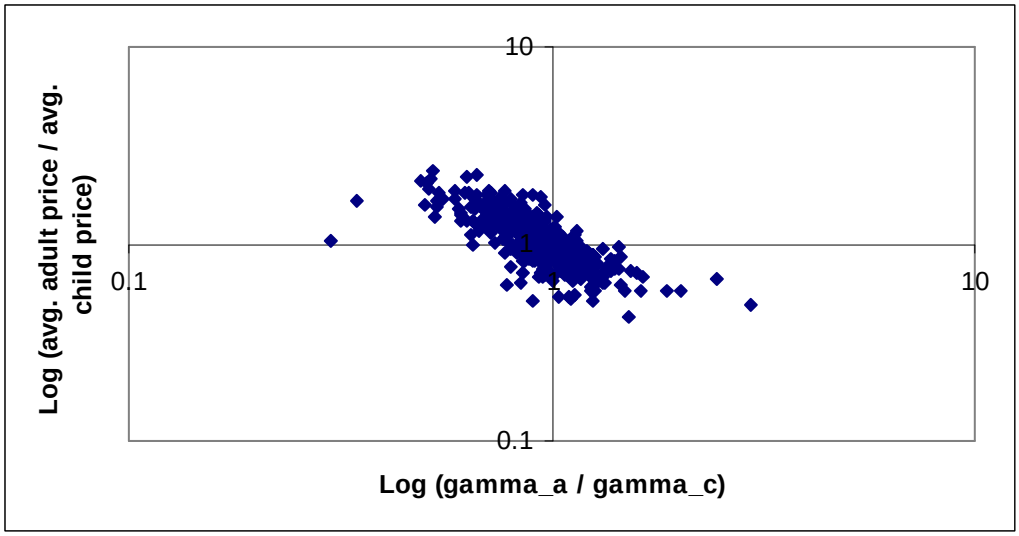


Figure 7.10. Adult to child price ratio versus adult to child herd protection coefficient ratio

The variation in societal net benefits (column 6 of Table 7.5) is primarily due to a combination of cost function and demand function parameters, such that societal net benefits would be large in scenarios for which adult and child WTP for vaccinations is greater than average and for which program costs are less than average. These parameters are also primarily responsible for the variation in benefit-cost ratio calculations (column 7).

It is also important to identify parameters that do not affect societal net benefit calculations. Incidence and public COI estimates have very little effect on program outcomes indicating that public COI savings are small relative to other economic benefits in almost all simulations. In addition, many of the parameter inputs to the DALY calculations (e.g., duration of illness, case fatality rate, DALY weight) have no impact on Net Benefit model outcomes. This is not surprising because these parameters are not included in the vaccine demand functions, which are primarily used to estimate benefits for this model.

Table 7.6 shows an analysis of variance for the DALY model. Uncertainties in program fixed and variable costs are again the most important contributor to variation in optimal prices (columns 1-4) for the DALY model. This is again because of the necessity to achieve revenue neutrality, which impacts prices for all subgroups. Other important contributors to variation in the price for children in high incidence villages (column 1) include

their incidence rate, $INCU^{0}_{ch}$, (11%) the adult price coefficient (16%) and the adult herd protection coefficient (10%). These parameters are all important in determining the effectiveness of adult-to-child cross subsidies. If adult coverage rates are expected to decline quickly as a function of price, it would be difficult to subsidize child vaccinations by charging adults more. This is especially true in light of herd protection effects, which may be strongly influenced by adult coverage rates.

Similar to the Net Benefit model, the variation in the ratio of population-weighted average adult to child price for the DALY model (column 5) is primarily determined via adult and child price coefficients (66% total) and herd protection coefficients (33% total). Again, this is due to the importance of herd protection in reducing community-wide disease rates (and thereby increasing the number of DALYs saved). Incidence rates have very little impact on this outcome, although this is probably because I used a correlation coefficient between adult and child incidence rates for the parameter draw. Thus, the ratio of adult to child incidence is not likely to vary much from one simulation to the next.

Next, I consider an analysis of variance for the number of DALYs saved (column 6). The single greatest source of uncertainty is the case fatality rate (almost 60%). The baseline incidence rates for children (10% total), the duration of protection (9%), and program costs (12% total) are also important. The importance of uncertainty in case fatality rates relative to uncertainty in incidence is slightly exaggerated, because I incorporate separate incidence values by subgroup, but only a single case fatality rate. The causes of variation in the average cost per DALY saved (column 7) are very similar to those for total DALYs.

In Table 7.7, I calculate 5% to 95% uncertainty intervals for a number of important vaccination metrics. The data are taken from Net Benefit model results, but these metrics would be very similar if I used the DALY model instead. The average number of vaccinations per case avoided (column 1) depends primarily on incidence rates, vaccination efficacy and duration, and herd protection effects. The median is 50 vaccinations per case avoided with a tightly bounded 5% to 95% range of 32 to 78 vaccinations per case avoided. The ratio of public treatment cost savings to total costs (column 2) is small all across parameter draws.

The median ratio of public treatment savings to total costs is about 11% and the 95th percentile value is 18%. Thus, one could neglect these to simplify the net revenue constraint. The 5% to 95% uncertainty range for the societal benefit-cost ratio (column 3) is between 2.2 and 3.6, with a median of 2.8. This uncertainty range is very tightly bound as the 95th percentile value is only about 1.6 times greater than 5th percentile value. Variation is primarily determined by cost and price coefficient parameters.

Table 7.7. MCS uncertainty ranges for important vaccination program metrics

Cumulative %	Vaccinations / cases avoided	COI savings / total cost (%)	Societal benefit-cost ratio	Net cost per DALY saved	Net cost per life saved
	(1)	(2)	(3)	(4)	(5)
5	32	0.06	2.2	185	4,664
10	35	0.07	2.3	213	5,521
15	38	0.07	2.4	233	5,952
20	40	0.08	2.4	256	6,628
25	43	0.08	2.5	279	7,203
30	44	0.09	2.6	293	7,673
35	45	0.09	2.6	320	8,192
40	47	0.09	2.7	346	8,944
45	48	0.10	2.7	370	9,448
50	50	0.11	2.8	388	9,930
55	52	0.11	2.8	420	10,567
60	54	0.12	2.9	450	11,617
65	56	0.12	2.9	482	12,362
70	58	0.13	3.0	514	13,109
75	60	0.14	3.1	554	13,964
80	63	0.15	3.2	593	14,807
85	65	0.16	3.3	651	16,574
90	70	0.17	3.4	738	18,894
95	78	0.19	3.6	850	21,405

There is considerably more variation in the cost utility metrics, net cost per DALY saved (column 4) and net cost per life saved (column 5), than in the benefit-cost ratio. The 5% to 95% uncertainty range for the net cost per DALY is 185 to 850; the median is 388. Thus, the 95th percentile value is about 4.6 times greater than 5th percentile value. Since the World Bank's 'very cost-effective' threshold for Bangladesh is about US$510, about 70% of the simulation results would qualify as 'very cost-effective'. The variation in this parameter is primarily due to the uncertainty assumed for the case fatality rate, which varied from 0.5% to

3% in the sensitivity analysis. This is why the MCS distribution appears to be more favorable than the deterministic models, which assumed a 1% case fatality rate.

The uncertainty range for the cost per life saved is shown in column 5 of Table 7.7. The median cost per life saved is about US$10,000 and the 5% to 95% range is US$4,600 to US$21,000. My best estimate of parental VSL for a youngest child is about US$15,000, with a range of US$10,000 to US$25,000. Since the cost per life saved is less than US$15,000 in about 80% of the simulations, revenue-neutral cholera vaccination programs would pass cost-benefit tests in a majority of simulations even if private COI savings and avoided pain and suffering were not valued. Thus, cholera vaccination programs in the Matlab area would pass benefit-cost tests regardless of whether WTP benefits or private COI + mortality risk reduction benefits are used. It may be easier to estimate benefits for private COI + mortality risk reductions in locations where private demand surveys are not conducted. A lot of the variation in the cost per life saved is again driven by the uncertainty for the case fatality rate.

8 Conclusions

I believe that this dissertation makes the following contributions to the existing literature on vaccination policy. First, I was able to collect and synthesize vaccination benefit data from multiple sources. The collection of data from multiple sources allows me to test for consistency, which increases validity of my results. Second, I developed new approaches to modeling vaccination policy, including new methods to account for economic herd protection benefits for both vaccinated and unvaccinated persons. My approach varies from that reported in Cook et al. (2009) because my economic benefit estimates for both vaccinated and unvaccinated groups are based on consumer surplus generated from predicted demand functions and adjusted for herd protection. In contrast, Cook et al.'s estimates of economic benefits for the unvaccinated are based on *ex ante* mortality risk reduction and private treatment cost savings. One potential deficiency in the Cook et al. approach is the use of a population-average VSL for the unvaccinated subgroup when it is likely that the average VSL for the unvaccinated group is less than that for the population as a whole as evidenced by the fact that they chose not to purchase vaccines. Cook et al.'s use of different valuation methods for the vaccinated and unvaccinated subgroups also leads to a discontinuity in the net benefit function.

In addition, I split the Matlab population into four subgroups with varying incidence rates and demand function parameters, while Cook et al. only consider a single population. Thus, my approach can examine whether cross-subsidies might be useful to increase the economic efficiency of cholera vaccination in consideration of herd protection. Finally, my study also examines the differences in program outcomes when non-monetary health utility units are used in the objective function in place of net economic benefits. In fact, I believe this is the first attempt to use cost utility metrics in an optimization analysis.

I estimated cholera vaccination WTP benefits and the value of statistical life from CV surveys. These allow me to compare average cholera vaccine WTP to *ex ante* cholera mortality and morbidity benefit estimates per person based on VSL, incidence and private COI data. The *ex ante* cholera vaccination benefits per person include the sum of expected morbidity and mortality savings over the duration of vaccine protection and should be approximately equal to the product of average WTP for vaccination after accounting for the fact that cholera vaccinations are not 100% effective and assuming prospective purchasers are risk neutral.

The average WTP per person is greatest for young children age 1 to 5 years (US$2.4) followed by older children age 5 to 17 years (US$1.2) and adults (US$1). I only collected VSL estimates for children. The average VSL across age groups is US$15,000 but appears to be greater for older children who face a lower baseline risk of death. My best estimates of the sums of *ex ante* mortality risk reduction and morbidity risk reduction benefits are US$1.7 for young children and US$0.24 for older children. The *ex ante* estimate for young children (US$1.70) is about 70% of the WTP estimate (US$2.40). For older children, the *ex ante* morbidity and mortality risk reduction benefits per person, US$0.24, are only about 20% of the WTP benefits per person (US$1.20). I believe that differences result because the *ex ante* morbidity plus mortality estimate ignores the cost of pain and suffering, which might compose a larger fraction of total vaccination benefits when mortality risks are small, as is the case for older children. It may also be the case that parents overestimated their older children's baseline risk of death from cholera, which is likely to be very small. It is also important to note that there is greater uncertainty in calculating *ex ante* morbidity plus mortality estimates than in calculating the WTP estimates. This is because there is uncertainty in both cholera mortality rates and VSL estimates. These uncertainties are compounded when the two variables are multiplied.

I examined a number of different pricing models for vaccination programs. These include simple models in which all four groups are charged the same price and optimized models in which different subgroups are charged different prices. The optimized models attempt to

maximize either net societal benefits or total DALYs saved. The net societal benefit curve is almost flat over the range of likely prices, US$1.00 to US$3.00, for a cholera vaccination program in Matlab (see Figure 7.6). Over this range of prices, net societal benefits vary between US$200,000 and US$220,000. Thus, there is very little difference in the absolute maximum net benefits, US$220,000, and the maximum net societal benefits possible from a revenue neutral program, US$210, 000. A public or donor contribution of US$32,000 could be used to boost net societal benefits by about US$5,000, a 2% change. Thus, donor contributions are unnecessary to increase net societal benefits; however, the number of DALYs can be increased to a small degree by external contributions.

The optimal prices that maximize net societal benefits tend to fall within tightly bound ranges around the marginal cost of vaccination. As a result, the prices for each of the four groups would typically fall within US$1 of one another when societal net benefits are maximized. This occurs because the demand functions are found to be independent of incidence differences across villages. Since demand functions drive the calculation of direct and indirect benefits, the difference in optimal prices result solely from small differences in herd protection effects and public COI savings. However, public COI savings tend to be small relative to direct and indirect benefits (see Figure 7.5). In the deterministic model, it is assumed that herd protection effects are same for vaccinating adults or children. Thus, the targeting of vaccinations is unnecessary for maximizing herd protection.

Program outcomes are very similar for models that maximize DALYs saved. Relative to net benefit maximization models, the optimal prices derived from models that maximize DALYs show more variability across subgroups. The optimal prices for groups with high incidence tend to be smaller (i.e. for children relative to adults and for high incidence villages relative to average incidence villages). As a result, predicted coverage rates at optimal prices are greater for groups in which the numbers of cases avoided per vaccination are greater. However, the population-average coverage rates remain about the same. Hence, herd protection effects accrue equally to

vaccinated and unvaccinated persons and are assumed to be independent of who is vaccinated. Thus, there are very small differences in the numbers of DALYs saved for the Net Benefit versus the DALY model, despite the differences in optimal prices. Monte Carlo Simulation results indicate that the differences in net societal benefits or DALYs saved for the Net Benefit or DALY models are less than 10% across a range of 500 independent parameter draws.

It is possible to increase the number of DALYs saved if external funding is available. However, the marginal cost per DALY saved would be high. The cost per DALY saved varies depending on the coverage rate of the program (see Figure 7.7 and refer to Appendix 4). At very low coverage rates, the average cost per vaccination is very high because fixed costs are spread across a small number of vaccinated individuals. As a result, the cost per DALY saved is also high. As coverage increases, the cost per DALY saved decreases as more people become vaccinated and fixed costs across a larger number of vaccination recipients. The cost per DALY is minimized when the average price charged is about US$3 and the average coverage rate is about 20%. As coverage rates increase beyond 20% the average cost per DALY saved decreases. This is because of the diminishing returns to scale of herd protection. If fixed costs were assumed to be zero, the average cost per DALY saved would increase monotonically with coverage, because of these declining returns to scale.

I performed sensitivity analysis on a number of model input parameters using Monte Carlo Simulation with 500 parameter draws. The uncertainty in optimal pricing is driven primarily by uncertainty in the fixed and variable costs of vaccination programs. If program costs are greater than expected, it would be necessary to charge all subgroups higher prices in order to maintain revenue neutrality. When higher prices are charged, coverage rates decline, herd protection effects are diminished, and fewer cholera cases are avoided. Thus, variation in societal net benefits and DALYs are also strongly affected by uncertainty in program costs. Uncertainty in net societal benefits is also driven by uncertainty in demand function parameters. If demand is greater than expected, net societal benefits increase because cholera protection is perceived to be

more valuable to the community. The uncertainty in DALYs saved is primarily driven by variability in case fatality rate and incidence rates, such that more DALYs are saved when incidence and case fatality rates are greater. It is believed that cholera case fatality rates may be lower in Matlab relative to other rural communities because Matlab's ICDDR,B hospital is available to provide high quality treatment. If case fatality rate were greater than 1%, it is likely that cholera vaccination in the Matlab area could be considered 'very cost-effective' based on World Bank Standards, but only at modest coverage rates (20-40%). At higher coverage rates, the cost per DALY saved would be higher due to diminishing returns to scale of herd protection.

In the MCS, I allowed the shape of the herd protection curve to be influenced by who is receiving vaccinations. Individuals in different subgroups may spread disease differently than members of other subgroups.[32] I am not aware of attempts to model differential herd protection effects of cholera vaccination based on coverage rates by different subgroups (e.g., school children, elderly, males, females). The Matlab trial is the only cholera vaccine trial that has been modeled for herd protection (Ali et al., 2005; Ali et al., 2008; Longini et al., 2007; Emch et al., 2009). This trial only included children older than 2 years and adult women. In addition, modeling of the coverage-protection relationship is only available for the population as a whole, not for different age groups. Ali et al. (2008) reported that cholera incidence for children less than 2 years is significantly correlated with the fraction of adult females vaccinated in their bari, but not statistically correlated with the coverage rate for older children. Thus, it would appear that vaccinating women is more effective than vaccinating children for boosting herd protection of infants.

The authors consider different reasons for the greater impact of vaccinating women. They rule out transmission of immunogenic compounds via mothers' breast milk, which had been examined during the trial (Clemens et al., 1990a). Instead, they suggest that physical (rather than

[32]For example, in the United States and Japan, researchers have found that school children spread influenza more than other age groups. As a result, greater herd protection effects are realized by targeting children relative to other age groups (Patel et al. 2005).

biological) transmission methods are more likely (possibly because of women's roles in the preparation of household food or infants' contacts with soiled saris) (Stanton and Clemens, 1986; St. Louis et al., 1990). It is not know if vaccinations of adult women were also more effective for reducing incidence in older children or adults. It would be difficult to draw inferences for other age groups, who do not spend all of their time in the care of their mother.

In the MCS, I allowed adult and child herd protection coefficients to vary independently, such that vaccination of one group may have a greater herd protection effect than the other. If child herd protection coefficients are larger than adult coefficients, the optimal child prices would be reduced relative to the base case models, but differences are small (see Figure 7.10). Differences in outcome measures are also relatively small. Similar conclusions are reached if the magnitudes of adult herd protection coefficients are greater than child coefficients. It should be noted that I used tightly bounded uncertainty ranges in the MCS. At maximum, the herd protection effect was 2.2 times greater for one group than the other. If I used larger uncertainty ranges, I may have seen a more pronounced effect. However, discussions with epidemiologists at the International Vaccine Institute indicated that such large differences would be unlikely.

I also examined differences in outcome measures after estimating monetary benefits for those with zero WTP for vaccines. This assumes that some fraction of the population would have chosen to receive free vaccinations if there were no time costs or if they were completely certain there would be no side effects. The inclusion of these benefit measures has a very small impact on optimal prices and program outcomes because the majority of cholera protection benefits would still accrue to those with non-zero WTP for cholera vaccinations.

A number of conclusions may be drawn from my analysis. For diseases like cholera, it may be unnecessary and excessively costly to maximize vaccine coverage rates. Due to herd protection, increases in coverage beyond 30% would lead to very small changes in the number of cases avoided. It may not be a worthwhile investment of resources to try to increase coverage rates beyond this rate.

A priori, it is difficult to determine whether vaccination benefits should be modeled based on WTP benefits or public health measures. For net societal benefit maximization, the value of protection is determined by how much people are willing to pay for vaccines, which is heterogeneous across the population and which depends on socioeconomic characteristics and individual perceptions about the likelihood and severity of contracting cholera. Thus, the objective function is greatly influenced by those with higher than average WTP, which may not be directly correlated with those who face the greatest risk of cholera morbidity or mortality. On the other hand, public health benefits are generally weighted by incidence and case fatality rates, which are assumed to be homogenous within subgroups and heterogeneous across subgroups. Thus, vaccinations may be easily targeted to vulnerable populations.

The existence of herd protection effects tends to smooth out the differences in outcomes between the Net Benefit and DALY models. For the most of the models, the unvaccinated incidence rates are reduced by 45% – 55%. Thus, additional differences in direct protection across groups are minor relative to the indirect protection experienced. As a result, differences in outcome measures are relatively small even if differences in prices are substantial. When estimating the difference in incidence rates for Matlab's highest incidence villages, I tried to use the maximum possible difference in incidence across villages. It is likely that the high-incidence-village to average-incidence-village ratio for Matlab is smaller than four, in which case there would be less incentive to subsidize high incidence villages. Thus, the value of cross-subsidies would be further reduced. In practice, it should be much easier to charge the same price to all subgroups. While this is likely to be true in many rural areas, more careful consideration may be required for urban areas in which slum communities may face drastically higher risks of cholera than their middle and upper income neighbors. In the urban case, cross-subsidies might be a more useful policy tool.

Appendix 1: Questionnaire: Willingness to pay for Cholera Vaccines in Matlab, Bangladesh

Cover Sheet

_____
Questionnaire Number

Number (same as item 1.5)
CID Number

RID Number ☐☐☐☐☐☐☐☐☐☐

Patient's Hospital ID Number (if applicable)

_____

Block number ☐

_____

Respondent Address _____

_____

Interviewer, how long did you have to wait, after arriving at the respondent's home, to conduct this interview? (Please fill in below in minutes, if you didn't have to wait, please record "zero")

_____ minute

For manager use only (write initials)

☐ Submitted with consent form

☐ Questionnaire ready for data entry

For data entry only:

Entry 1 Code ☐☐ **Entry 2 Code** ☐☐

1.0 If the survey is not completed, please indicate the reason why?

(1) _____ Respondent seriously ill, cannot reschedule

(2) _____ Respondent refused to be interviewed

(3) _____ Respondent refused to sign consent

(4) _____ Respondent decided to stop before finishing interview

(5) _____ Respondent absent

(6) _____ No children under 18 yrs. in the family

(7) _____ Respondent is not a parent of children less than 18 years of age

(-95) _____ _____ others, specify ☐☐

Part 1 Demographics

1.1 *Interviewer, when did you meet with the respondent? Mark the time you started and finished in the appropriate box. If the survey required a second interview, mark the start and finish time of that second interview also, and so on. 1.1*

	First visit	Second visit	Third visit	Fourth visit
1.1A Date (dd/mm/yy)	___/___/___			
1.1B Time start	— : — hours/minutes	— : —	— : —	— : —
1.1C Time stop	— : — hours/minutes	— : —	— : —	— : —
1.1D Total minutes	_____ minutes	_____	_____	_____

1.2 ☐☐☐ - ☐ - ☐☐☐ - ☐☐☐

Questionnaire Version Number Vacc price VSL eff VSL price NTT/TTT

1.3 _____

Questionnaire Number

1.4 Interviewer Code ☐☐

1.5 Respondent's ID Number
CID Number ☐☐☐☐☐☐☐☐☐

RID Number | | | | | | | | | | |

1.6 Block number | |

1.7 Respondent's Gender

(1) _____ Male
(2) _____ Female

1.8 **Enumerator: Do you have a signed consent form for this respondent?**

(1) _____ Yes (Skip to 1.9)
(2) _____ No (Continue)

Give the consent form to the respondent and allow him/her to read it. Make sure that he/she understands the information. If the respondent can't read then read out the consent form to the respondent and try to make him/her understand. If the respondent agrees to interview then take his/her signature/left thumbprint on the consent form and keep the signed consent form with you.

Fill in the table on your laminated card for all household members. Then copy the information into the table below.

	1.9 Current Age	1.10 Gender 1=Male, 2= Female	1.11 Relationship to respondent
Self			
Spouse			
Other 1			
Other 2			
Other 3			
Other 4			
Other 5			
Other 6			
Other 7			
Other 8			
Other 9			
Other 10			
Other 11			
Other 12			
Other 13			
Other 14			
Other 15			
Other 16			
Other 17			
Other 18			
Other 19			
Other 20			

(1.11) Relationship to respondent/patient	
1 = Respondent	7 = Spouse of the respondent
2 = Son/daughter of the respondent	8 = Spouse of the son/daughter of the respondent
3 = Grandchildren of the respondent	9 = Spouse of the grandchildren of the respondent
4 = Brother/sister of the respondent	10 = Brother in law/Sister in law of the respondent
5 = Mother/father of the respondent	11 = Mother/father in law of the respondent
6 = Extended Family	(-95) = Others

1.12 ***Enumerator: are there children under 18 years old listed in the table above?***

(1) _____ Yes
(2) _____ No *[Go to 1.0 and check (7)]*

1.13 **How many married couples are living in this household?**

_____ couple

1.14 **Have you heard anything about this study from your friend, neighbors, or family members?**

(1) _____ Yes

(2) _____ No (Skip to section 2)

1.15 What have you heard about this study? *(Enumerator: record their response below)*

2: Perceptions and Attitude Towards Cholera

The next questions I would like to ask you are about the disease cholera.

2.1 Have you ever heard of the disease cholera?

(1) _____ Yes
(2) _____ No (*Skip to statement after 2.2*)
(-98) _____ Don't know/not sure (*Skip to statement after 2.2*)

2.2 What are the symptoms of cholera? (Spontaneous response, more than one response permitted)

	(Yes)	(No)	
1.			Watery diarrhea many times
2.			Rice watery stool
3.			Sunken eyes
4.			Continuous diarrhea
5.			Vomiting
6.			Leg and hand cramps
7.			Dry mouth
8.			Crying without tears
9.			Increasing thirst
10.			Dehydration
11.			Weakness
12.			Fever
(-95)			_____ Others, specify
(-98)			Don't know/not sure

Please read the following description to all respondents:

Cholera is a disease often characterized by severe diarrhea, frequent episodes of watery diarrhea, vomiting, and weakness.

2.3 How does someone become infected by cholera? (Spontaneous response, more than one response permitted: check all that apply)

	Yes	No
a. drinking unboiled water		
b. eating unhygienic foods		
c. eating food from street vendors		
d. eating unclean, uncooked vegetables		
e. eating unripe fruit		
f. bad weather		
g. using unhygienic latrines		
h. not washing hands before eating		
i. flies touching food		
j. other(s) specify:		
k. don't know/not sure		

2.4 How common do you think cholera is in your neighborhood? (read all responses before taking answer; one response permitted)

(1) _____ Not very common
(2) _____ Common
(3) _____ Very common
(-98) _____ Don't know/not sure

How serious is cholera for the following groups? (For each group, read all responses: allow respondent to answer very serious/serious/not so serious/don't know/not sure)

		(1) Very serious	(2) Serious	(3) Not so serious	(-98) Don't know/not sure
2.5	Children (under 18)				
2.6	Adults				

2.7 How likely is it that you would get cholera some time in the next five years? (read all responses; one response permitted)

(1) _____ very unlikely
(2) _____ unlikely
(3) _____ somewhat likely
(4) _____ very likely
(-98) _____ don't know/not sure

2.8 How likely is it that the young children (under 18) in your household would get cholera some time in the next five years? (read all responses; one response permitted)

(1) _____ very unlikely
(2) _____ unlikely
(3) _____ somewhat likely
(4) _____ very likely
(-98) _____ don't know/not sure

2.9 Has anybody in your household (including yourself) ever had cholera?

(1) _____ Yes
(2) _____ No (*Skip to 2.11*)
(-98) _____ Don't know/not sure (*Skip to 2.11*)

2.10 Who has had cholera, and when did they have cholera? (Multiple response permitted)

List	Check	When?	
		Year	Don't know, not sure (check)
Self			
Spouse			
Other 1			
Other 2			
Other 3			
Other 4			
Other 5			
Other 6			
Other 7			
Other 8			
Other 9			
Other 10			
Other 11			
Other 12			
Other 13			

Other	14			
Other	15			

2.11 Has anyone in your household ever died of cholera?

(1) _____Yes (continue)
(2) _____No (Skip to Question 2.13)
(-98) _____ Don't know/not sure (*Skip to 2.13*)

2.12 For each person in your household who died of cholera, please tell me how old they were when they died. (Spontaneous response; record total number of individuals who died of cholera in each group)

	Number of people	
(1)		Infant less than one
(2)		Child (1 to 5 years)
(3)		Child (6 to 10 years)
(4)		Child (11 to 18 years)
(5)		Other adult (19 to 54 years)
(6)		Other adult (Over 54)
(-98)		Don't know/not sure

2.13 Have you known personally anyone (other than a household member) who has been sick due to cholera?

(1) _____Yes
(2) _____ No (Skip to Question 2.15)
(-98) _____ Don't know/not sure (Skip to 2.15)

2.14 Have you known personally anyone (other than a household member) who has died due to cholera?

(1) _____Yes
(2) _____ No
(-98) _____ Don't know/not sure

2.15 Imagine you are sick. It's not an emergency, but you need to see a doctor. If you went to public hospital, how long would you usually have to wait after arriving there before a doctor/nurse would be able to see you? (i.e., how long is the queue likely to be?) [Enumerator: record the respondent's answers in minutes, if you never have to wait, record '0']

_____ No. of minutes
(-93) _____ I have never visited central hospital
(-94) _____ The queue varies in length, it is difficult to say
(-95) _____ _____ others, specify
(-98) _____ Don't know/not sure

2.16 Imagine you are sick. It's not an emergency, but you need to see a doctor. If you went to private medical facility (private physician, hospital or clinic) how long would you usually have to wait after arriving there before a doctor/nurse would be able to see you? (i.e., how long is the queue likely to be?) [Enumerator: record the respondent's answers in minutes, if you never have to wait, record '0']

_____ No. of minutes
(-93) _____ I have never visited a private physician/hospital/clinic
(-94) _____ The queue varies in length, it is difficult to say
(-95) _____ _____ others, specify
(-98) _____ Don't know/not sure

3: Vaccines and 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 always consuming only safe, clean food and water and washing your hands thoroughly after defecation and before taking food.

Cholera is caused by a type germ. 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 plenty of oral saline and when severe, take intravenous saline/ cholera saline. 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.

3.1 Do you have any questions or anything you are not clear about?

(1) _____ Yes
(2) _____ No

If yes, record the respondent's questions:

	☐☐

[Enumerator: If you know the answer to the respondent's questions, please answer them truthfully and briefly. If you are not sure you know the answer, please tell the respondent that you are not sure.]

I would like to ask you the following questions about vaccines.

3.2 Have you ever heard about vaccines?
(1) _____ Yes
(2) _____ No (Skip to statement after 3.3)

3.3 In your opinion, what is the purpose of a vaccine? (Spontaneous response, multiple response permitted)

	(Yes)	(No)	
(1)			Prevent disease for children
(2)			Prevent disease for pregnant women
(3)			Prevent disease for all people
(4)			Cure disease
(-95)			_____ other, specify
(-98)			Don't know/not sure

Read the following **statement** to all respondents
Vaccine is for "prevention", not for treatment. You have to take a vaccine before you get sick.

3.4 Have you been vaccinated before?

(1) _____ Yes
(2) _____ No
(-98) _____ Don't know/not sure

Read the following statement to all respondents
Several years ago, an old cholera vaccine and an old combined (cholera and typhoid) vaccine called TABC was available to people in Matlab.

3.5 Has anyone in this household including yourself had either the old cholera vaccine or the old combined TABC vaccine?

(1) _____ Yes
(2) _____ No (Skip to question 3.9)
(-98) _____ Don't know/not sure (Skip to question 3.9)

3.6 Which members of the household had the old cholera or the old TABC vaccine? [*Enumerator: Please record the time of vaccination, price paid and whether or not the respondent thinks the vaccine is still working. Please record (-98) if they do not remember the date for the vaccination or the price paid.*]

List	Check	TABC 1= Cholera 2= TABC 3= Both TABC or Cholera (1=Cholera, 2= TABC vaccine, 3=Both)	When? (Year)	Price paid ?	Do you believe the vaccine is still working for this		
					Yes	No	Don't know/ Not sure
Self							
Spouse							
Other 1							
Other 2							
Other 3							
Other 4							
Other 5							
Other 6							
Other 7							
Other 8							
Other 9							

3.7 Were you satisfied with the old vaccine?

(1) _____ Yes (Skip to question 3.9)
(2) _____ No
(-98) _____ Don't know/not sure (Skip to question 3.9)

3.8 If no, why not? (Spontaneous response, record only the most important) [*Enumerator: If the respondent gave more than one reason, please ask which is the most important reason*]

(1) _____ Did not prevent Cholera
(2) _____ Was not satisfied with the characteristics of vaccine (i.e. smell or color or taste)
(3) _____ Was not satisfied with the method of administering the vaccine
(4) _____ Minor side effects (i.e. diarrhea, rash, leaves scars on skin, fever, headache, loss of appetite, vomiting)
(5) _____ Caused other major health problems
(6) _____ Because the vaccine was locally produced
(7) _____ Injection was very painful
(-95) _____ _____ other, specify ☐☐
(-98) _____ Don't know/not sure

3.9 In your household, who would be primarily involved in making the decision whether or not to purchase cholera vaccines for your household members? (Spontaneous response, multiple responses permitted)

	(Yes)	(No)	
(1)			myself (respondent)
(2)			spouse of respondent
(3)			parents of respondent
(4)			parents in-law(s) of respondent
(5)			children of respondent
(-95)			_____ other, specify ☐☐
(-98)			Don't know/not sure

Cholera CV Scenario

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].

Vaccine effectiveness

Now I want to explain exactly what I mean when I say the vaccine would be [50%] effective.

Suppose that each of these little blue or red figures (*Enumerator: show the picture*) represents a person. (Enumerator: point out the circle). The 100 figures inside this circle represent 100 persons who have taken the vaccine, while the figures outside the circle represents those who have not taken the vaccine. The cholera vaccine is not 100% effective; that is the vaccine is only (50%) effective. Therefore, of the 100 people taking the vaccine in the circle, there will be (50%) of the people who have taken the vaccine that are protected (i.e., the vaccine works for them) for a period of 3 years. The blue figures inside this circle represent these people.

The rest of the people (the red ones inside the circle) who have been vaccinated [50] will not be protected against cholera even though they have taken the vaccine, because the vaccines did not work for them. They will still be at risk of getting cholera just like they were before they got the vaccine or just like the people outside the circle who haven't received vaccines. However, even if they get cholera, their symptoms may not be quite as severe compared to someone who has not received the vaccine.

The people who receive cholera vaccine will not be able to know if the vaccine works for them. Of course, we don't know who would actually get cholera. A red person outside the circle who has not taken a vaccine still has a relatively small risk of being infected.

Now I am going to ask you some questions to make sure that the information I told you is clear.

First round

3.10 Please point to all the people who have taken the vaccine [*Interviewer: put a mark into a relevant place*]

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give the correct answer
(-98) _____ respondent did not know/not sure

3.11 Please point to all the people who have taken the vaccine and it works for them. [I*nterviewer: put a mark into a relevant place*]

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give the correct answer
(-98) _____ respondent did not know/not sure

3.12 How many years would the cholera vaccine work for them?

_____ If respondent gave incorrect answer, please correct it
(-98) _____ respondent did not know/not sure

3.13 How many people have taken the vaccine but can still get cholera? [*Interviewer: put a mark into a relevant place*]

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give the correct answer
(-98) _____ respondent did not know/not sure

3.14 If an unvaccinated person gets infected by cholera, can the vaccine be used to cure them?

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give the correct answer
(-98) _____ respondent did not know/not sure

⇒ *If respondent gave incorrect answer, please correct it.*

3.15 Interviewer: did the respondent give the correct answer to all three effectiveness questions (3.10, 3.11 and 3.13)?

(1) _____ Yes (Skip to 3.19)
(2) _____ No

Enumerator: If No to 3.15 tell the respondent:

"I feel that I need to explain about the effectiveness of the vaccine a little bit more." (explain the effectiveness of the vaccine again) "Now I would like to go over the questions again, to make sure that the information I told you is clear."

Display card to be explained again. **(Re-ask 3 following questions)**

Second round

3.16 Please point to all the people who have taken the vaccine [*Interviewer: put a mark into a relevant place*]

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give the correct answer
(-98) _____ respondent did not know/not sure

3.17 Please point to all the people who have taken the vaccine and it works for them. [*Interviewer: put a mark into a relevant place*]

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give the correct answer
(-98) _____ respondent did not know/not sure

3.18 How many people have taken the vaccines but can still get cholera? [*Interviewer: put a mark into a relevant place*]

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give the correct answer
(-98) _____ respondent did not know/not sure

Note: Whether the respondents gave the correct answer or not, please skip to the next page.

3.19 Please indicate what you believe to be the most important benefit of the vaccine. ((Enumerator: read all answers))

(1) _____ Prevent pain and suffering of cholera
(2) _____ Avoid payments for treating cholera after getting sick
(3) _____ Prevent risk of death from cholera
(4) _____ Avoid lost wages or time at work because of cholera
(-98)____ Don't know/No answer

4. Willingness to pay for Cholera Vaccine

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.

[No Time to Think Only]

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 dehydration 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.

[Enumerator: Please hand the laminated reminder card to the respondent, to remind the respondent of the important information for their decision. Also show them the relevant effectiveness card. If a respondent is illiterate, show them only the relevant effectiveness card]

4.1a Do you have any question or anything you are not clear about?

(1) _____ Yes
(2) _____ No

Record the respondent's questions/comments:

First I'm going to ask you about your willingness to purchase the vaccine for yourself. Then I am going to ask you about whether you would purchase the vaccine for other member of your household.

[Time to Think 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.

This card summerizes this information (*Enumerator: hand respondent laminated card*)

Please consider the following: yours and your family's income and economic status, and your risk of getting cholera. Apart from the vaccine, remember that we still have other ways to treat cholera such as oral dehydration 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.

When is a convenient time for me to return tomorrow?

Date: _____

Time: _____

(*Enumerator: record the time this interview was completed in Section 1.*)

[**TIME TO THINK ONLY**]

Second Interview

(Enumerator: record the time this interview started in Section 1.)

Let's begin where we left off yesterday. Again, 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.

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 new vaccine in preventing cholera is 50% effective for three years. Again, the new cholera vaccine cannot be used by children under 1 year and pregnant women.

First I'm going to ask you about your willingness to purchase the vaccine for yourself. Then I am going to ask you about whether you would purchase the vaccine for other members of your household.

4.1b Do you have any question or anything you are not clear about?
(1) _____Yes
(2) _____No

Record the respondent's questions/comments:

□□

4.2 Suppose that this cholera vaccine costs (Tk.10, Tk.25, Tk.50, Tk.75, Tk. 300, Tk. 600) for the two doses needed for one person. Would you buy this vaccine for yourself? (*Spontaneous response; one response permitted*)
(1)_____ Yes (*Skip to question 4.3*)
(2)_____ No (*Skip to question 4.5*)
(-98)_____ Don't know/not sure (*Skip to question 4.5*)

4.3 What is the main reason that you would buy the vaccine? (*Do not read choices; record only the most important reason*)

(1) _____ Vaccine is useful for me because it is good for prevention and safety (*Skip to question 4.4)*
(2) _____ Price is reasonable, can afford easily (*Skip to question 4.4*)
(3) _____ I think I have a chance of getting cholera (*Skip to question 4.4*)
(4) _____ Cholera is a dangerous disease (*Skip to question 4.4*)
(-95) _____ _____□□ Other, specify (*skip to 4.4)*
(-98) _____ Don't know/not sure (*Skip to question 4.4*)

4.4 Are you certain of your answer that you would purchase the vaccine for yourself if the price of the vaccine were (Tk.10, Tk.25, Tk.50, Tk.75, Tk.300) for the two doses needed for one person? (read all responses: one response permitted).

(1)_____ Very certain of my answer(skip to 4.9b and mark "Yes")
(2)_____ Somewhat certain (skip to 4.9b and mark "Yes")
(3)_____ Not certain; unsure (skip to 4.9b and mark "Yes")

4.5 What is the main reason that you will not pay / you are not sure that you will pay for the vaccine for your self (*Do not read choices, record only the most important reason)?*

(1)_____ No money
(2)_____ Too expensive
(3)_____ I am too old
(4)_____ I would buy this vaccine only for someone else (ie children, other family members etc.)
(5)_____ I would buy this vaccine only if many people around me get cholera
(6)_____ I would buy this vaccine only if it is very convenient
(7)_____ I would take the vaccine only if other people around me took the vaccine.
(8)_____ Do not think that I'd have a chance to get cholera
(9)_____ Afraid that the vaccine might not be safe
(10)_____ Afraid that the syringe/container might be dirty
(11)_____ Do not think that the vaccine can prevent cholera
(12)_____ Concerned that the vaccine will cause the cholera.
(13)_____ Have previously had a cholera vaccine, and therefore do not need this vaccine.
(-95)_____ _____☐☐ Other (please specify)
(-98)_____ Don't know/not sure

4.6 How certain are you of your answer that you would not pay/you are not sure that you will pay for the vaccine for your self? (*read all responses, one response permitted*)

(1)_____ Very certain of my
(2)_____ Somewhat certain
(3)_____ Not certain; unsure

4.7 If you could get vaccine for free, would you want to be vaccinated?

(1) _____ Yes (*Skip to question 4.9a)*
(2) _____ No *(continue)*
(-98)____ Don't know/not sure *(continue)*

4.8 Why would you not want to receive a vaccine if you could get it for free? *(Do not read choices, record only the most important reason)*

(1)_____ Vaccine has little use or not useful *(skip to 4.9b and mark "No")*
(2)_____ I don't think I have a chance to get cholera (skip to 4.9b and mark "No")
(3)_____ Afraid that the vaccine might not be safe (skip to 4.9b and mark "No")
(4)_____ Afraid that the syringe/container might be dirty (skip to 4.9b and mark "No")
(5)_____ Do not think that vaccine can really prevent cholera (skip to 4.9b and mark "No")
(6)_____ Concerned that the vaccine will cause the disease. *(skip to 4.9b and mark "No")*
(7)_____ Have previously had a cholera vaccine, and therefore do not need this vaccine. (skip to 4.9b and mark "No")
(-95)_____ _____ ☐☐ other specify *(skip to 4.9b and mark "No")*
(-98)_____ Don't know/not sure (skip to 4.9b and mark "No")

4.9a Would you pay anything for this vaccine?

(1)_____ Yes (mark YES for 4.9b)
(2)_____ No (mark NO for 4.9b)
(-98)_____ Don't know/not sure (mark NO for 4.9b)

4.9b. Enumerator: You will refer to this question later to determine whether to do "stoplight" exercise

(1)_____ Yes
(2)_____ No

4.10 [*Enumerator: How many people are listening to the interview?]*

Adults: _____
Children: _____
Total: _____

[Interviewer: explain to respondent]

The following questions are about your willingness to pay for the cholera vaccine for your family members who are living with you.

4.11 Suppose that this cholera vaccine costs (Tk.10, Tk.25, Tk.50, Tk.75, Tk. 300, Tk. 600) for the two doses needed for one person (same price for adults and children), how many people in your household (not including yourself) would you be willing to purchase vaccines for? Remember, the cholera vaccine cannot be used by children under 1 year or pregnant women.

_____ Number of household members (ONLY FOR HOUSEHOLD MEMBERS, NOT INCLUDING YOURSELF)

[Enumerator: If respondent would pay for 0 vaccines, skip to 4.16]

4.12 Who would you buy this vaccine for? (*Record whether or not the family member whom you want to get the vaccine lives in your house*.)

List	Check	Live in this house?	
		Yes	No
Spouse			
Other 1			
Other 2			
Other 3			
Other 4			
Other 5			
Other 6			
Other 7			
Other 8			
Other 9			
Other 10			
Other 11			
Other 12			
Other 13			
Other 14			
Other 15			
TOTAL			

[NOTE to the enumerator: If the respondent would not buy the vaccine for anyone, including themselves, skip to 4.16.]

[Enumerator: multiply the total number of household members respondent said they would purchase for, plus one if they said they would buy a vaccine for themselves (check 4.2) at the specified price, by the price of the vaccine to obtain the total amount]. If the total number of people listed in the table above differs from the number of people in the answer to 4.11, **use the number of people in the table above.**

[Enumerator: Please skip this question if the total amount of the vaccine is "zero"]

4.13 You've said that you would buy vaccines for a total of _____ household members including yourself at this price. This would amount to a total cost to you of _____.

4.14 How confident are you that you would be able to afford this amount of money (*calculated above*)? (*Read all responses, one response permitted)*

(1)_____ Very confident (skip to 4.16)
(2)_____ Confident (skip to 4.16)
(3)_____ Not confident

4.15 How many vaccines are you confident you could afford to buy?
_____ , # vaccines
(-98) _____ don't know/not sure

4.16 *Enumerator: Skip to Section 5 if the answer to 4.9b is No.*

Please think about the decision to buy a vaccine for yourself. There are bad prices, when you are completely sure that you would not purchase a vaccine for yourself . There are good prices when you are completely sure that you would definitely purchase the vaccine for yourself **.** And then there are some prices at which you are not sure whether you would purchase or not purchase the vaccine.

Now I would like to read you a list of prices. First, I will start with a very high price and I will read you lower and lower prices. I would like you to tell me when we get to a price where you are unsure if you will buy it for yourself. That is, you might purchase the vaccine for yourself at that price but you might not. Then I will tell you a very low price and then read higher and higher prices. Again, tell me to stop when we get to a price when you are not completely sure you would pay that price for the vaccine. Remember, we want to know here about the price you'd be willing to pay for the vaccine for yourself—not for other members of your family.

Do you have any questions about anything I've told you?

4.17 [*Enumerator: copy the respondent's marks onto the scale below.]*

Price	You are completely sure that you would purchase	Uncertain	You are completely sure that you would NOT purchase
Tk. 5000			
Tk. 1000			
Tk. 500			
Tk. 400			
Tk. 300			
Tk. 200			
Tk. 100			
Tk. 75			
Tk. 50			
Tk. 25			
Tk.15			
Tk. 10			
Tk. 5			
Tk. 1			
Tk. 0			

4.18. How difficult was this exercise for you? (Enumerator: Read the responses)

(1)_____ Very easy
(2)_____ Somewhat easy
(3)_____ Somewhat difficult
(4)_____ Very difficult

5 Value of Statistical Life

The cholera vaccine will protect your child from cholera only. Your child may also become sick with pneumonia, cancer, typhoid, or other diseases. The cholera vaccine will not protect your child against these other illnesses.

Let us consider your child's risk of death from a number of different illnesses and other causes. This next picture shows many ways that a child might die. *(Enumerator: show risk-ladder picture and say the name of each cause of death).* Some causes of death are more common than others. The most common causes of death for children, such as respiratory disease, are shown at the top of the scale. The least common causes of death, such as getting struck by lightning, are shown at the bottom of the scale. The rest of the causes of death fall in between the risks from respiratory disease and from lightning strikes.

5.1 Please point to the cause of death on this list that you think is most common for children in your community. *(Enumerator: please mark answer)*

(1)_____ All respiratory disease
(2)_____ Drowning
(3)_____ All diarrhea
(4)_____ Cancer
(5)_____ Infections
(6)_____ Lack of nutrition
(7)_____ Homicide
(8)_____ Gastro-intestinal disease
(9)_____ Lightning strike
(-98)____ No response

5.2 Please point to the cause of death on this list that you think is least common for children in your community. *(Enumerator please mark answer)*

(1)_____ All respiratory disease
(2)_____ Drowning
(3)_____ All diarrhea
(4)_____ Cancer
(5)_____ Infections
(6)_____ Lack of nutrition
(7)_____ Homicide
(8)_____ Gastro-intestinal disease
(9)_____ Lightning strike
(-98)____ No response

5.3 Please consider how cholera affects children in your community. Also, consider how the risk of death from cholera compares to the other risks of death shown in the picture. Some causes of death on the scale may be more likely than cholera. Other causes of death may be less likely than cholera. Please point to the cause of death on this list that you believe is about the same as the risk of death from cholera for children in your community. *(Enumerator please mark answer)*

(1)_____ All respiratory disease
(2)_____ Drowning
(3)_____ All diarrhea

(4)_____ Cancer
(5)_____ Infections
(6)_____ Lack of nutrition
(7)_____ Homicide
(8)_____ Gastro-intestinal disease
(9)_____ Lightning strike
(-98)____ No response

Next, I would like to talk about the concept of probability. Later I will talk about how this relates to the risk of death. Then we will discuss how a hypothetical nutritional supplement might be used to decrease the risk of death and how you would value this decrease. To begin, let's start with a coin toss. If you flip a coin, half of the time it will land on “chand”, and half of the time it will land on “lota”.

I will be using graphs like this one *(Enumerator: show coin picture)* to show you the likelihood of certain outcomes. This graph has1000 squares and is colored to represent the chances of flipping a coin and it landing on “chand”. Half of the squares are red- corresponding to the coin landing on “chand”. The other half are white- corresponding to “lota”. This means that if you flipped the coin 1000 times, it would land on “chand” about 500 times and it would land on “lota” about 500 times.

Now, let us examine the chances of throwing a “five” with a die. Since the die has six sides, the chance that it lands on one of the sides (such as the “five”) is one out of six. In this diagram *(Enumerator: show dice picture)*, the red squares show the number of times that the die would land on “five”, and the white squares show the number of times it would land on something else, such as “one”, “two”, “three”, “four”, or “six”. If you rolled this die 1000 times, it would land on “five” about 170 times on average. The more red squares that you see, the more likely it is that an event will occur. Since, we see more red squares in the coin flip diagram, we know that it is more likely to get "chand " in a coin flip than it is to get five in a die throw.

5.4 *(Enumerator show both cards side by side)* Which is more likely in one throw—getting “chand” in one coin flip or getting a “five” in one die throw?

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give correct answer
(-98)_____ respondent did not know/not sure

(Enumerator: If respondent gets question wrong, say "Remember that the more red squares that you see, the more likely an event will occur. Since the coin picture has more red squares, it is more likely an event will occur. Since the coin picture has more red squares, it is more likely to get chand in a single coin flip than five in a single die throw.")

Section 5.2

Now let us consider the risk of death for your child. For this example, we will consider the village of Dighaldi. Pretend that Dighaldi has about 1000 households. Assume that each household has one child. Some children in Dighaldi will probably die during the next five years. A few children may die from disease, such as pneumonia, cholera, or cancer. Other children may die from drowning accidents, homicides, or lightning strikes. If each of these 1000 squares represents one child in Dighaldi, the 5 red squares *(Enumerator: point to squares)* represent the number of children that we would expect to die from disease only in the next 5 years. The 995 white squares represent the number of children that we expect will not die from disease in the next 5 years.

Again, the causes of death from disease, the red squares, include cancer, heart disease, respiratory disease, infections, diarrhea, and gastro-intestinal disease. The number of children that die due to accidents not related to disease are not shown in this picture.(Enumerator : point to square picture). Additional children may die from drowning, homicide, and lightning strikes.

5.5 We have just covered an imaginary example for a village like Dighaldi. How many children (under 18 years) do you think live in your village?

(1) _____ number of children
(-98)_____ respondent did not know/not sure

5.6 Consider all the children in your village, how many would you expect to die from disease in the next 5 years?

(1) _____ number of children
(-98)_____ respondent did not know/not sure

Of course, we cannot know in advance which children will die in the next 5 years. Please assume that your child's risk of death is the same as that for any other child in your village. The chance that your child might die is about the same as the chance that your neighbor's child might die regardless of previous illnesses. Let's take another look at this picture. *(Enumerator: show risk-of-death chart)* If none of the squares were colored, you would know with certainty that your child would **not** die from disease in the next 5 years. However, all children have a small risk of getting sick and dying. Since only a few squares have color, we know that the chance that your child might get sick and die in the next 5 years is much lower than the chance that you would get "chand" in a single coin flip or roll a "five" with a single die throw. (Enumerator: compare death risk picture to coin and die picture.)

5.7 Which is more likely, your child getting sick and dying in the next 5 years or throwing a die one time and getting a "five"?

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give correct answer
(-98)_____ respondent did not know/not sure

(Enumerator: if answer is correct, proceed to section 5.3. If the answer is incorrect or person does not know, please re-read Section 5.2. After second reading, ask question 5.8)

5.8 Which is more likely, your child getting sick and dying in the next 5 years or throwing a die one time and getting a "five"?

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give correct answer
(-98)_____ respondent did not know/not sure

Section 5.3

(1 in 1,000 protection)
Imagine that doctors and scientists are working on a nutritional supplement that would help to reduce your child's risk of death from all diseases. Although this supplement would not prevent your child from contracting diseases, it would help to boost your child's immune system. After taking the supplement, your child will be more likely to survive if he/she becomes sick with any disease. The nutritional supplement would have no taste and no side effects. It could easily be mixed into meals or drinks. The nutritional supplement would generally not have any effect other than reducing your child's risk of death from disease.

*This picture shows the decrease in risk of death from disease for children who take the supplement. If 1000 children took this supplement, only four children, instead of five children would die from disease. We see that 1 child would *not* die, because the supplement helped to protect him/her. *(Enumerator: point to the difference in the red squares in the charts with and without supplement)* The supplement would not provide any protection for children from accident-related deaths, such as drowning. We see that there are fewer red squares, so we know that it is less likely for children to die from disease if they take the supplement. (Enumerator: please point to the differences in pictures before and after supplement). Please assume that taking this supplement would give your child some protection from death from disease, but not full protection.

(same as above for 3 in 1,000 protection)
Imagine that doctors and scientists are working on a nutritional supplement that would help to reduce your child's risk of death from all diseases. Although this supplement would not prevent your child from contracting diseases, it would help to boost your child's immune system. After taking the supplement, your child will be more likely to survive if he/she becomes sick with any disease. The nutritional supplement would have no taste and no side effects. It could easily be mixed into meals or drinks. The nutritional supplement would generally not have any effect other than reducing your child's risk of death from disease.

*This picture shows the decrease in risk of death from disease for children who take the supplement. If 1000 children took this supplement, only two children, instead of five children would die from disease. We see that 3 children would *not* die, because the supplement helped to protect him/her. *(Enumerator: point to the difference in the red squares in the charts with and without supplement)* The supplement would not provide any protection for children from accident-related deaths, such as drowning. We see that there are fewer red squares, so we know that it is less likely for children to die from disease if they take the supplement. (Enumerator: please point to the differences in pictures before and after supplement). Please assume that taking this supplement would give your child some protection from death from disease, but not full protection.

5.9 If your child takes the supplement, is he/she less likely to accidentally drown?

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give correct answer
(-98)_____ respondent did not know/not sure

5.10 If your child takes the supplement, is he/she less likely to die from respiratory disease?

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give correct answer
(-98)_____ respondent did not know/not sure

5.11 If 1000 children take the supplement, how many fewer children would die from health-related causes because they were protected by the supplement?

_____ Number of children
(-98)_____ respondent did not know/not sure

5.12 *Enumerator:Did the respondent answer questions 5.9,5.10 and 5.11 correctly?*
(1) _____ respondent did give the correct answers (skip to question 5.16)
(2) _____ respondent did not give correct answer *please re-read the second paragraph (*) of Section 5.3. After second reading, proceed to question 5.13)*

5.13 If your child takes the supplement, is he/she less likely to accidentally drown?
(1) _____ respondent did give the correct answer
(2) _____ respondent did not give correct answer
(-98)_____ respondent did not know/not sure

5.14 If your child takes the supplement, is he/she less likely to die from respiratory disease?

(1) _____ respondent did give the correct answer
(2) _____ respondent did not give correct answer
(-98)_____ respondent did not know/not sure

5.15 If 1000 children take the supplement, how many fewer children would die from health-related causes because they were protected by the supplement?

_____ Number of children
(-98)_____ respondent did not know/not sure

5.16 Do you have any questions or anything you are not clear about?
(1) _____ Yes
(2) _____ No
If Yes, record the respondent's questions:

Enumerator: If you know the answer to the respondent's questions, please answer them truthfully and briefly. If you are not sure you know the answer, please tell the respondent that you are not sure.]

Section 5.4

Suppose that the government will not supply the new supplement for free. Those who want the supplement for their children would have to pay a fixed price for it. Everyone would pay the same price. Please imagine that the cholera vaccine mentioned previously is no longer available. In other words, if you said you would buy the cholera vaccine, please do not consider this as limiting your budget.

Now I'd like to know whether you would buy the nutritional supplement if it was available at a specified price. Some people say they cannot afford the price of the supplement or that they do not think that the benefit of the supplement is worth the price. Other people say that they would buy the supplement because the decrease in risk of death for their children is really worth it to them. 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.

5.17 Suppose that this nutritional supplement costs (Tk.10, Tk.20, Tk.50, Tk.100) for a one month supply for one child. You would have to buy a new supply each month to maintain protection for your child. Would you buy this supplement for your youngest child? (*Spontaneous response; one response permitted*)

(1) _____ Yes (Skip to question 5.18)
(2) _____ No (Skip to question 5.19)
(-98) _____ Don't know/not sure (Skip to question 5.19)

5.18 Now, suppose that this nutritional supplement costs (Tk.20, Tk.40, Tk.100, Tk. 200) for a one month supply for one child. You would have to buy a new supply each month to maintain protection for your child. Would you buy this supplement for your youngest child? (*Spontaneous response; one response permitted*)

(1) _____ Yes (Skip to question 5.20)
(2) _____ No (Skip to question 5.21)
(-98) _____ Don't know/not sure (Skip to question 5.21)

5.19 Now, suppose that this nutritional supplement costs (Tk.5, Tk.10, Tk.25, Tk.50) for a one month supply for one child. You would have to buy a new supply each month to maintain protection for your child. Would you buy this supplement for your youngest child? (*Spontaneous response; one response permitted*)

(1) _____ Yes (Skip to question 5.20)
(2) _____ No (Skip to question 5.21)
(-98) _____ Don't know/not sure (Skip to question 5.21)

5.20 What is the main reason that you would buy the supplement? (Do not read choices; record only the most important reason)

(1) _____ Supplement is useful for me because it is good for prevention and safety (Skip to next section)
(2) _____ Price is reasonable, can afford easily (Skip to next section)
(3) _____ I think my child has risk of disease-related death (Skip to next section)
(-95) _____ _____Others, specify (Skip to next section)
(-98) _____ Don't know/not sure (Skip to next section)

5.21 What is the main reason that you would buy the supplement? (Do not read choices; record only the most important reason)

(1) _____ No money
(2) _____ Too expensive
(3) _____ I would buy this supplement for my child only if other people around me took the supplement
(4) _____ Do not think that my child will die in the next 5 years anyway
(5) _____ Afraid that the supplement might not be safe
(6) _____ Do not think that the supplement can prevent death
(-95) _____ _____others, specify □□
(-98) _____ Don't know/not sure

5.22 Would you take the supplement if it were offered for free?

(1) _____ Yes
(2) _____ No
(-98) _____ Don't know/not sure

6: Socioeconomic questions

Enumerator: Please ask these questions in below table for the respondent, spouse, and adult and child members of the household that earn income. If the respondent says "don't know/not sure" record (-98). If the respondent refuses to answer/does not answer, record (-99)

List	6.1 What class of school did you complete or what degrees have you received?	6.2 Occupation	6.3 Earnings per month (Tk. Per month)
Self			
Spouse			
Other 1	********		
Other 2	********		
Other 3	********		
Other 4	********		
Other 5	********		
Other 6	********		
Other 7	********		
Other 8	********		
Other 9	********		
Other 10	********		
Other 11	********		
Other 12	********		
Other 13	********		
Other 14	********		
Other 15	********		

6.1 Education level	6.2 Occupation List	
1= Have never attended school 2= 1 to 5 years of school 3= 6 to 9 years of school 4= 10 to 12 years of school 5= Vocational studies/college diploma 6= University/college 7= Post-graduate studies 8= Professional course 9= Madrasha education 10=Informal education 11=Others (Specify) _____	1= Student 2= Retired 3= Housewife 4= Unemployed 5= Professional (Specify) _____ 6= Unskilled office worker 7= Owner of business 8= Unskilled manual worker (Specify) _____ 9= Skilled manual worker (Specify) _____	10= Street seller 11= Farmer 12= Chowkider/Village Defense Party 13= Small business 14= Fisherman 15= Service worker (eg. driver, servant, cook, hotel or restaurant worker) 16= Other (Specify) _____

6.4 How much does your household earn per month?

_____ Tk./month
(-98)____ Don't know/not sure
(-99)____ No response

6.5 Can you read a newspaper? *(If no, record 3, if yes, probe to find out if they can read a newspaper easily, or with difficulty.)*

(1)_____ Yes, Easily
(2)_____ Yes, with difficulty
(3)_____ No, cannot read a newspaper.

6.6 What is your religion?

(1) _____ Muslim
(2) _____ Hindu
(3) _____ Christian
(4) _____ Buddhist
(-95) _____ _____ Other (Specify)

House Characteristics

6.7 Who owns this house?
(1) _____ Own (Go to 6.8)
(2) _____ Rent (Go to 6.9)
(3) _____ Provided by employers (Go to 6.10)
(-95)_____ Others specify (*Go to 6.10*) _____

6.8 What would someone expect to pay each month to rent a house like yours?

Tk._____ (Go to 6.10)
(-98)_____ Don't know/not sure (Go to 6.10)
(-99)_____ No response (Go to 6.10)

6.9 What is your monthly rent?

_____ Tk./month
(-98)____ Don't know/not sure
(-99)____ No response

6.10 How many rooms does your house have (including the kitchen)?

_____ Number of Rooms
(-98)____ Don't know/not sure

6.11 What is the main fuel used for cooking in the house? (*Enumerator: Read response*)

(1)_____ Electricity
(2)_____ Gas/LPG
(3)_____ Firewood
(4)_____ Kerosene
(5)_____ Charcoal
(6)_____ Cow dung
(7)_____ Leaves
(-95)_____ Others specify _____
(-98)_____ Don't know/not sure

Household Assets

6.12 Could you tell me whether or not someone in your household owns a(n) (category name)?

(yes)	(no)	
		Cot
		Cabinet (Cupboard)
		Table/dinning table
		Wardrobe/showcase
		Dressing table
		Radio
		Ceiling fan (mark (1) for 6.13)
		Black and White TV (mark (1) for 6.13)
		Color TV (mark (1) for 6.13)
		Refrigerator, (mark (1) for 6.13)
		Motor-cycle
		Cycle
		Engine boat/country-boat

Electricity

6.13 Does this household have electricity?

(1) _____ Yes
(2) _____ No (Skip to Water section)

6.14 Did your household pay the entire electricity bill, or share the bill with anyone outside your household?

(1)_____ Household paid entire bill
(2)_____ Shared bill with someone else

6.15 How much was your household's own electricity bill last month? Or, if you share the bill, how much was your share?

_____ Household's own share of electricity bill (Rs.)
(-93) _____ We pay no monthly charge for electricity
(-94) _____ Electricity is included in the rent
(-98) _____ Don't know/not sure
(-99) _____ No response

Water

6.16 What is the main source of drinking water in the house? [*Enumerator**: Spontaneous response**; one response permitted*]

(1)_____ Own shallow well
(2)_____ Own hand pump
(3)_____ Shared hand pump
(4)_____ Surface water
(5)_____ Rain water
(6) _____ Communal tap
(7)_____ Communal well
(-95) ___ _____ Other (please specify)

6.17 Is water generally boiled before drinking? (*Enumerator: read responses*)

(1) _____ Always
(2) _____ Sometimes
(3) _____ Never
(-95) ____ Other (please specify) _____
(-98)_____ Don't know/not sure

6.18 Do you do anything else to the water to make it safer to drink? (*Do not read list. Check all answers that respondent mentions.*

(1) _____ Add bleach/chlorine
(2) _____ Sieve it through cloth
(3) _____ Water filter (ceramic, sand, composite)
(4) _____ No other treatment
(-95) _____ Other, *please specify* _____
(-98) _____ Don't know

6.19 How do you store your water?

(1)_____ Overhead tank
(2)_____ Barrels
(3)_____ Small Buckets and containers
(4)_____ Metal/clay containers
(5)_____ Do not store
(6)_____ No need for Storage
(-95)_____ Others (Specify)_____
(-98) _____ Don't know/not sure

6.20 What kind of toilet do the household members usually use? (*Enumerator: spontaneous responses*)

(1)_____ Go into the bush, river, lake or canal?
(2) _____ Public flush toilet
(3)_____ Sanitarylatrine
(4) _____ Open pit toilet/latrine
(5)_____ Hanging latrine
(-95) _____ Other (please specify) _____

6.21 Is the flush toilet/latrine shared or private? (Check only one answer)

(1)_____ Private
(2)_____ Shared

Telephone

6.22 Does your household have a telephone or mobile phone?

(1) _____ Yes
(2) _____ No (Skip to "Health Behavior" section)

6.23. How much was your household's last own monthly telephone + mobile bill? Or, if you share the bill, how much was your share? (*Ask only if respondent has land line)*

_____ Tk.
(-98) _____ Don't know/not sure

Health Behavior

6.24 How often does your family eat food sold by street vendors? (*Enumerator: read responses)*

(1)____ Never /Rarely
(2)____ 1-2 Times per week
(3)____ 3-5 Times per week
(4)____ 6 or more times per week
(-98)___ Don't know/not sure

6.25 In the last month, how much did your household spend on health care? (Treatment costs, including pharmacy, purchase of medicine, hospital fees)

_____ Tk.
(-98) _____ Don't know/not sure

Economic Status and Access to Credit

6.26 How would you classify the economic status of your household relative to others in this neighborhood? (*Enumerator: read responses*)

(1)_____ Much better than most people
(2)_____ Better than most people
(3)_____ About average
(4)_____ Below average
(5)_____ Much worse than average
(-98)___ Don't know/not sure

6.27 Over the next five years, how do you think your household's economic situation will change? (*Enumerator: read responses*)

(1)_____ Certainly improve greatly
(2)_____ Probably improve somewhat
(3)_____ No change
(4)_____ Probably decline somewhat
(5)_____ Certainly get much worse
(-98)____ Don't Know / Not sure

6.28 Does anyone in your house have a bank account?

(1) _____ Yes
(2) _____ No
(-98)____ Don't Know / Not sure

6.29 How easy would it be to borrow Tk.1000? (*Enumerator: read responses)*
(1)_____ Very easy
(2)_____ Somewhat easy
(3)_____ Somewhat difficult
(4)_____ Very difficult
(5)_____ Impossible (Skip to Next section)
(-98)____ Don't Know/Not sure (Skip to Next section)

6.30 If you want to borrowTk.1000 and cannot borrow it from a family member, where would you want to go to borrow it? (*Enumerator: spontaneous response; only one answer*)
(1)_____ Relative/neighbor Neighbor/Friend
(2)_____ Bank
(3)_____ Market money lender
(4)_____ Pawn shop
(-95) _____ Other (please specify) _____☐☐
(-98)_____ Don't Know / Not sure

6.31 If you borrowed Tk. 1000 from the place you mentioned in 7.48, how many additional Taka would you have to pay back after one month?

Tk._____ (additional)
(-98) _____ Don't know/not sure

[TIME TO THINK ONLY]

Section 7

7.1 How long did you spend discussing or thinking about the decision to buy these vaccines?

_____ minutes

7.2 Did you discuss with anyone in your household about the choice to buy vaccines?

(1)_____ Yes
(2)_____ No (*Skip to question 7.5*)

7.3 Who did you discuss your decisions with in your household?

List	Check
Spouse	
Other 1	
Other 2	
Other 3	
Other 4	
Other 5	
Other 6	
Other 7	
Other 8	
Other 9	
Other 10	
Other 11	
Other 12	
Other 13	
Other 14	
Other 15	

7.4 How long did you spend in discussions with them?

_____ minutes

7.5 Did you discuss with anyone else outside your household?

(1)_____ Yes
(2)_____ No (*Skip to question 7.7)*

7.6 Who did you discuss with outside your household? (*Record the relationship of the person(s) to the respondent, open-ended question)*

_____

7.7 How difficult did you find it to make your decision? (Read all responses)

(1)_____ Very difficult
(2)_____ Difficult
(3)_____ Easy
(4)_____ Very easy

Section 8: "End" End of questionnaire

This is the end of the interview. Thank you very much for your participation. We'd like to stress that it is necessary for you to protect yourself from contracting cholera and typhoid. The objective of this survey is to learn about your willingness to pay for cholera and typhoid vaccines either for yourself or your household members. We need to ask different households their willingness to purchase at different prices. Thus, don't worry if you hear that other people in your community have been asked about purchasing the vaccines at different prices.

Interviewer's opinion

8.1 Time Finish (*record in 1.1C*) _____

8.2 How reliable do you think is the information you got from the respondent?

(1) _____ Very reliable
(2) _____ Reliable
(3) _____ Fairly reliable
(4) _____ Not reliable
(5) _____ Very unreliable

8.3 Do you think the respondent understood about the vaccine efficacy scenario?

(1) _____ Did not understand
(2) _____ Understood
(-98) _____ Don't know/not sure

8.4 Did the interview finish?

(1) _____ Not complete (*Make sure you check the option (6) in 1.0.)*
(2) _____ Yes, complete (*Skip to 8.6)*

8.5 Were you able to make another appointment to finish the interview?

(1)_____ Yes
(2)_____ No

8.6 *Enumerator: Please note the type of flooring material*

(1)_____ Mud
(2)_____ Cement
(3)_____ Mosaic[floor tiles]
(4)_____ Brick
(-95)____ Others, Specify_____

8.7 *Enumerator: Please note the type of material used in the Wall*

(1)_____ Thatch/ bamboos
(2)_____ Mud
(3)_____ Corrugated tin
(4)_____ Plastic/polythene
(5)_____ Brick
(6)_____ Wood
(-95)____ Others, Specify_____

8.8 *Enumerator: Please note the type of material used in the Roof*

(1)_____ Thatch/bamboo/wood etc.
(2)_____ Plastic/polythene
(3)_____ Corrugated tin
(4)_____ Concrete
(-95)____ Others, Specify_____☐☐

8.9 What type of house does the respondent live in?

(1)_____ Own homestead
(2)_____ Government quarters
(3)_____ Single-family home in good condition
(4)_____ Flat/home shared by multiple families
(5)_____ Single-family home in poor condition
(-95)_____ Others, specify _____☐☐

8.10 Other suggestions/ comments

_____

_____

_____☐☐

Appendix 2. Private Demand for Cholera Vaccines in Rural Matlab, Bangladesh

Abstract

Objectives: To estimate household willingness to pay (WTP) for cholera vaccines in a rural area of Bangladesh, which had participated in a 1985 oral cholera vaccine trial.

Methods: An in-home contingent valuation study was undertaken in Matlab, Bangladesh in summer 2005. All respondents (N = 591) received a description of a cholera vaccine that was 50% effective for three years and had negligible side effects. Respondents were asked how many vaccines they would purchase for their household at randomly pre-assigned prices. Negative binomial regression models were used to estimate the number of vaccines purchased by each household and to calculate average WTP.

Results: On average, respondents were willing to pay about US$9.50 to purchase vaccines for all members of their household (i.e. US$1.70 per vaccine). Average WTP per person is US$2.40 for young children (1 to 4 years), US$1.20 for school-age children, and US$1.05 for adults. Median WTP estimates are significantly smaller: US$1.00 for young children, US$0.05 for schoolchildren, and less than US$0 for adults.

Conclusions: There is significant demand for cholera vaccines in Matlab at low prices. Recent herd protection research suggests that unvaccinated persons would also experience reduced incidence via indirect effects at low coverage rates.

Private Demand for Cholera Vaccines in Rural Matlab, Bangladesh (publiahed in Health Policy)

1. Introduction

In many less developed countries, cholera remains a serious public health problem. Most cases are concentrated in the "cholera belts" of coastal and delta areas in the tropics, of which Bangladesh is a classic example [1]. Incidence of cholera can be reduced through access to clean drinking water and proper disposal of sewage. However, infrastructure additions and improvements are expensive and progress has been slow, especially in rural areas. In Bangladesh oral rehydration solution (ORS) has successfully reduced the case fatality rate of cholera to less than 1% [2, 3]. While the widespread use of ORS has limited the risk of death in areas with quality health care, it does not reduce the risk of contracting cholera upon exposure.

New-generation oral cholera vaccines were tested in Matlab, our research area, during 1985 and found to have protective efficacies of approximately 50% over three years [4, 5]. Additionally, Ali et al. [6-7] reanalyzed the data from the Matlab trial and found reduced disease incidence among unvaccinated individuals in localities with high coverage (i.e. herd protection effects).

Despite evidence of vaccine effectiveness, policy makers in Bangladesh reported that they did not place a high priority on providing cholera vaccines, even in areas with high endemic incidence rates [8]. The reasons for the lack of interest include 1) the success of ORS in reducing cholera mortality, 2) a desire to spend limited resources on other interventions, 3) the limited duration and effectiveness of cholera vaccines, 4) the higher cost of cholera vaccines relative to

others included in World Health Organization's Expanded Program on Immunization (EPI), and 5) the inability to administer the cholera vaccine as part of the existing EPI schedule.

Given the lack of public sector support for a cholera vaccination program in Bangladesh, a key issue in developing a successful vaccination program is whether it can be financially sustainable. Our research attempts to quantify private willingness to pay for cholera vaccines in a highly endemic area, where free, high quality treatment facilities already exist. This study attempts to determine how much families are willing to pay for vaccines and how household decision makers would allocate vaccines among family members. Because residents of the Matlab area have previous experience with oral cholera vaccines, this area should offer useful evidence of the private value of the cholera vaccine.

Our research group surveyed a sample of 591 households in the Matlab area, where cholera is prevalent. In our in-home interview with the representative of each household, we presented a description of a hypothetical cholera vaccine that was 50% effective for three years and had negligible side effects; then, we asked if that individual would be willing and able to purchase the vaccine at a single specified price (preassigned from an array of six) for personal immunization and for immunization of other household members. This technique, known as the contingent valuation method, permits measurement of demand for goods that are not widely available or do not have markets; it has been used frequently to measure the demand for vaccines in developing countries [9-13], as well as for environmental goods and services [14-16].

1.1 Background

Centered at the town of Matlab, the Matlab Health Research Centre study area lies some 55 km southwest of Dhaka and has a population of approximately 224,000 [17]. The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) operates a hospital in Matlab town whose services include free treatment to anyone with diarrhea. ICDDR,B also provides basic health services to approximately 111,000 people in Matlab town and 67 outlying villages.

Once a month, ICDDR,B's Health and Demographic Surveillance System (HDSS) gathers information from each person in the ICDDR,B service area as well as from an additional 113,000 people in 75 other nearby villages who receive basic health care services from government facilities.[33] ICDDR,B has collected this information for more than 35 years, and the sample frame for the present study was generated from that database.

From 1963 through 1996, ICDDR,B conducted a number of health intervention studies in the area, many of which included the free provision of products aimed at improving the health of participants. In addition to the 1985 cholera vaccine trial, residents of the government service area were included in 30 to 35 studies while residents of the ICDDR,B service area participated in 55 to 65 studies. These studies may have conditioned people in the area to believe that public health programs should be provided free of charge.

According to data from ICDDR,B's hospital surveillance records, the annual incidence of cholera ranges from 1 to 5 cases per 1,000 persons. Because not all cases arrive at the hospital and some are misdiagnosed, the actual cholera incidence rate is unquestionably higher; epidemiological studies have estimated that the annual incidence rate could be 4 to 20 cases per 1,000 persons in the Matlab area [18]. The most recent records, from 2003, show that 62 people among the HDSS population died from all diseases related to diarrhea, including cholera, corresponding to a mortality rate of 2.8 deaths per 10,000 persons [17]. Cholera transmission occurs year-round and peaks during April–May and September–October (i.e. just before and after the summer monsoon [19]).

Using the Matlab area as an example, Sack [18] compares the cost effectiveness of cholera treatment versus vaccination by performing break-even analyses of the cost per cholera death avoided using different incidence rates and vaccination costs. Sack estimated the treatment cost per death avoided at about US$350 (based on a 20% case fatality rate without treatment versus 0.5% with treatment). He reports that vaccines might be more cost effective per death

[33]The ICDDR,B hospital will provide free treatment for anyone that travels to the hospital, including people that reside outside of the MHRC.

avoided than the provision of free treatment if per capita vaccine cost is less than US$1 and if annual incidence exceeds 1 in 1,000. However, this analysis ignores the disutility and financial costs of illness prevented through vaccination. Also, it may not be necessary to choose between vaccination and treatment. Instead, we might assess the marginal benefits of adding vaccination efforts to existing treatment programs.

Although cholera vaccines are not currently available, people in the Matlab area have had experience with the new-generation oral vaccine and a combined typhoid, paratyphoid A and B, and cholera (TABC) vaccine that was administered during the 1950s and 1960s. ICDDR'B's 1985 field trial administered two distinct oral cholera vaccines and a placebo. The vaccination program targeted children and mothers. More than 62,000 people took three doses, approximately 27,000 took one or two doses, and about 31,000 were absent or refused to participate [5].

Ali et al. [6] used a GPS database in combination with vaccine trial records to examine herd immunity benefits for the first year after the 1985 Matlab trial. They found a significant inverse monotonic relationship between local coverage rates and disease incidence in unvaccinated persons. The raw data showed that at coverage rates greater than 50%, disease incidence was about the same for vaccinated and unvaccinated persons and roughly 80% less than the incidence for placebo recipients in areas with low vaccination rates (i.e. less than 28% coverage). These results also suggest that researchers may have underestimated vaccine effectiveness in previous evaluations of the Matlab trial. In a separate study, Ali et al. [7] found significant herd protection effects for children less than 2 years of age who were not eligible for the Matlab trial. The local coverage rate for women greater than 15 years of age was a statistically significant correlate for incidence among children less than 2 years. However, the coverage rate for children age 2-15 years was not statistically significant.

People in the Matlab area also have access to vaccines from EPI, which are distributed by ICDDR,B's community health workers once per month [20]. The private market for vaccines in the area is minimal, with only a few pharmacies in Matlab town providing tetanus vaccines (US$0.30–$1.34, Tk 20–Tk 90) and rabies vaccines (US$5.95–$6.40, Tk 400–Tk 430). This is

based on a conversion rate of US$1 = 67.2 Bangladeshi Taka (1 August 2005). Unless otherwise noted, we present price information and results in 2005 US dollars using this exchange rate. These numbers are, however, unadjusted for purchasing power parity. Nationwide, Levin et al. [20] report that the private sector only accounts for about 2% of vaccines delivered in Bangladesh.

2. Materials and Methods

2.1 Sampling procedure

The survey respondents were chosen via a two-stage cluster sample without replacement based on a household sample frame from ICDDR,B's HDSS database. The first stage selected a total of 3,000 households, each with at least one child less than 18 years of age. Two-thirds of these households were located in the government service area, and one-third in the ICDDR,B service area. We oversampled the government service area because we believed that it might be slightly more representative of rural Bangladesh than the ICDDR,B service area. This split also allowed us to test for differences in demand between service areas. The sample was then subdivided into 120 clusters of 22 to 28 households located within small geographic areas ranging about 1–4 km^2 depending on population density. This clustering reduced travel time between interviews.

In the second stage we randomly selected two sets of 15 clusters of households and assigned one cluster from each set to each enumerator. We required enumerators to interview the mother or father of children in the household and to allot half their interviews to fathers.[34] Only two households refused to grant interviews. However, it proved difficult to interview male parents, because many reside and work outside the Matlab area. Nonetheless, we wanted to obtain a fairly even gender split between male and female parents. As a result, we chose not to interview 160 households where female parents or grandparents were available for interview, but males were not. This approach may present some bias toward households for which males remain in the Matlab area, but allows us to test for differences in preferences for mothers and fathers.

[34]We interviewed two respondents who were grandparents, because the parents had died.

2.2 Survey instrument

The survey instrument was approved by the Institutional Review Boards at the University of North Carolina at Chapel Hill and at ICDDR,B. The instrument had six sections of questions and is included as an appendix. The first section recorded demographic information about the respondent and members of the household. The second section had questions regarding the respondent's perceptions of and experiences with cholera. The third section discussed how cholera was contracted, spread, prevented, and treated; it also included questions about the respondent's previous experience with the oral cholera and TABC vaccines. This section also introduced the cholera vaccine contingent valuation scenario, including descriptions of the vaccine's effectiveness and duration. Next, the respondents' understanding of the concept of vaccine effectiveness was tested. The fourth section contained the valuation questions that were used to estimate demand and willingness to pay (WTP) and is described in Research Design, below. The fifth section included questions to determine the value of a reduction in the risk of death for the respondent's youngest child [22]. The sixth section included socioeconomic questions about education, income, housing characteristics, assets, disease-averting behaviors, economic status, and access to credit.

Two sets of 60 pretest interviews helped us to adapt our survey to local conditions and to set an appropriate range of prices for the hypothetical cholera vaccine. We employed 20 local enumerators to conduct the interviews. These enumerators had experience working on other ICDDR,B public health studies, but had not administered contingent valuation surveys. They received two weeks of training according to the guidelines recommended in Whittington's review of CV practices in developing countries [16].

2.3 Research design

First, we explained that vaccine effectiveness was based on the joint probability of (1) being exposed to illness and (2) being protected by the vaccine. The explanation used a picture

with 50 blue and 50 red figures representing persons who would or would not be protected from disease after vaccination. After educating about effectiveness, each respondent was presented with a single price from an array of six randomly assigned prices (US$0.15, $0.37, $0.74, $1.12, $4.46, $8.93)[35] and asked if he or she would be willing to pay that price for a vaccine for personal immunization. Then, respondents were asked how many vaccines they would purchase for family members and which family members would receive those vaccines. Prior to the purchasing decision, respondents were instructed to consider their budget constraints and that there were no right or wrong answers.

The interviews were staged such that respondents were divided into two groups. NTTT (no time to think) respondents received the entire questionnaire in one sitting. TTT (time to think) respondents answered the first half of the survey, then were given overnight to consider the prospective "purchase" of the hypothetical vaccines and to discuss the decision with other family members; an interviewer returned the next day to finish the survey.

2.4 Modeling Strategy

Our household analysis is based on a model of decision making developed by Cropper et al. [11]. It is assumed that the decision maker maximizes the household utility function, which is a function of each family member's consumption and health, subject to a household budget constraint. Demand depends on nonwage income, the prices of vaccines and other preventive and mitigating health products, and a vector of individual and household characteristics.[36]

Count models are useful for examining household demand because they employ integer estimates for the number of vaccines purchased by each family. We used the negative binomial model, which is a variation of the Poisson regression model. The dependent variable (number of

[35]Equivalent prices in Bangladeshi taka are Tk 10, 25, 50, 75, 300, 600.

[36]Note that we also analyzed data for individual demand, but do not report results here in order to decrease the length of the article.

vaccines demanded) is a random draw from a negative binomail distribution with a mean λ_i, where *i* denotes the household. If V_i* is the solution to the maximization problem and n_i is household size, the model can be written as

$$\Pr[V_i^* = n_i] = (e^{\lambda_i} \lambda_i^n) / n_i! \text{ where } n = 1 \text{ to } n_i, \quad (1)$$

where $\lambda_i = e^{Xi\beta + \varepsilon i}$ and X_i is a vector of characteristics describing household *i* and the vaccine price offered to that family. The term ε_i is an error with a gamma distribution. The number of occurrences are distributed with mean λ_i and variance $\lambda_i + \alpha^{-1}\lambda_i^2$ where α is the common parameter of the gamma distribution.[37] The coefficient estimates can be used to construct a demand curve for each respondent. The area underneath the demand curve is the Marshallian consumer surplus, which we define as household willingness to pay. The fraction covered can be estimated by dividing the estimated number of vaccines purchased by the population size.

[37]A truncated Poisson model was also estimated for this data. This model avoids demand predictions that exceed the number of household members for each respondent. Because WTP estimates are similar for truncated Poisson and standard negative binomial models, we concluded that the negative binomial model should be employed because it allows for overdispersion.

3. Results

Generally, respondents understood the cholera vaccine scenario and provided reasoned answers to our valuation questions. Only 9 of the 591 respondents rejected our hypothetical description of vaccines or vaccine effectiveness either because they believed that the vaccine would not be effective or would have negative side effects. These respondents were dropped from further analysis.[38]

3.1 Sample sociodemographic characteristics

The sociodemographic characteristics of the sample households are summarized in Table 1. About 37% of respondents are from the ICDDR,B service area, and their average age is about 40 years. Average household size is 5.8 persons, including 0.1 infants less than one year old, 0.7 young children (1–5 years), 1.7 school-age children (6–17 years), 3.0 adults (18–65 years), and 0.2 elderly adults (66 years and up). The average amount of education was about 3.6 years, with 35% of the sample reporting that they never attended school. The average monthly household income was about US$75, which corresponds to an average monthly per capita income of US$13. About 39% of respondents received electricity directly from a grid. A few other respondents had installed solar panels or used large batteries because connections were not yet available in their village. **(Insert Table 1)**

3.2 Water and sanitation behaviors

Respondents' water and sanitation behaviors are reported in Table 2. The primary source (85%) of drinking water for most respondents was hand pumps; most (60%) shared pumps with their neighbors. Hand pumps have reduced diarrheal disease but have proved problematic because of extensive, naturally occurring arsenic contamination in the local groundwater aquifers. Nearly

[38]Overall, 90% of respondents reported that they were would be "primarily involved" in the cholera vaccine purchase decision. By gender, 85% of female respondents and 95% of male respondents would be involved. Thus, our sample should be representative of household decision makers.

all households (92%) surveyed did not boil their drinking water, though some did treat water with bleach (5%), via sedimentation with alum (4%) or with filters made of cloth, ceramics, sand, or composite material (7%).[39] The respondents primarily used improved pit, unimproved pit, and hanging latrines[40] for waste removal, the latter two of which may promote increased prevalence of pathogens in the environment. **(Insert Table 2)**

3.3 Previous experience with oral cholera or TABC vaccines

In our survey 182 of 591 respondents had reported receiving the oral cholera vaccine during the 1985 trial. From respondents' accounts of their household members' experience with vaccines, it appears that about 10% of respondents and their household members had received vaccines. (This is likely an underestimate, because respondents may not have been aware of vaccines received by others.) Most respondents, 90%, reported that they were satisfied with the vaccines received by themselves and their family members. They thought that most of the vaccinated persons in their households (72%, including themselves and other members) were still protected by the vaccine.

3.4 Attitudes about cholera and vaccines

The variables thought to influence demand for cholera vaccines are summarized in Table 2. About 37% of respondents reported that at least one member of their household had suffered from cholera in the past; 6% reported a death in the family. Another 27% of respondents knew of someone other than a household who had suffered from cholera. The proportion of households that had experienced a cholera death was more than twice as high in the government service area,

[39]An unrelated arsenic health intervention promoted the use of filters and sedimentation to reduce arsenic exposure.

[40]The improved pit latrines had cement floors and solid walls, providing better privacy than unimproved pit latrines. Unimproved pit latrines generally consisted of a hole in the ground surrounded by walls made of poor materials.

possibly because ICDDR,B's provision of health care and previous research studies have reduced cholera-related deaths. More respondents believed that cholera is serious or very serious for children (84%) than for adults (64%). Also, more respondents believed that their children would be likely to contract cholera in the next five years (40%) than believed that they themselves (20%) were at risk. Thus, it appears that respondents consider cholera to be dangerous, especially for children; however, most do not believe their risk of contracting the disease is very high.

Most respondents understood our description of vaccine effectiveness. About 75% correctly answered four questions designed to test understanding. With those who did not answer correctly, we repeated the vaccine effectiveness description, then repeated the test questions. After this second round, the overall success rate rose to about 93%: only some 7% of all respondents were unable to answer the test questions correctly.

A majority (68%) believed that the most important benefit of a cholera vaccine is to prevent pain and suffering. Others (24%) cited avoiding the risk of death from cholera as most important. Very few (8%) cited avoided treatment costs or lost wages as the primary benefit of a cholera vaccine. These answers suggest that economic analyses that rely primarily on cost of illness estimates would underestimate vaccine benefits.

3.5 Household demand

Table 3 shows the raw stated data for the average fraction of household members vaccinated at each price. The average fraction of household members vaccinated decreases as the price increases and for respondents given time to think. We found that many respondents (74%) either decided to purchase vaccines for all family members or for none of their family members. Relatively fewer respondents (26%) chose to purchase vaccines for some, but not all of their family members. **(Insert Table 3)**

Negative binomial regression results for the household demand model are summarized in Table 4. Model 2 includes all possible covariates, while Model 1 only considers variables that are

unrelated to cholera and vaccine experience. Average marginal effects, which reflect the change in population average demand for a unit change in a single variable, are summarized in Table 5. Price is highly significant and there is an average marginal decrease in stated demand of 0.58 vaccines per family for a price increase from US$0.50 to US$1. Generally, respondents residing in the ICDDR,B service area and TTT respondents state that they would purchase fewer vaccines for their families; average marginal decreases are about 1.3 vaccines if given TTT and 0.7 for the ICDDR,B service area. Male respondents and respondents from wealthier families purchase significantly more vaccines; average marginal demand increases by 0.05 vaccines per US$1 increase in monthly per capita income. Average marginal demand decreases by 0.04 vaccines as respondent age increases by one year. As expected, respondents with larger families are shown to purchase more vaccines. This is true for all age groups, although the coefficients for the number of school-age children are smaller than those for young children or adults. **(Insert Tables 4-5)**

Interestingly, we find that the number of vaccines purchased increases significantly for respondents who believe that cholera is a serious disease for adults or who believe that adults are likely to contract cholera. However, the coefficients for these beliefs for children are smaller and less significant. The average marginal increase in demand if respondents believed that cholera is likely for adults is 1.2 compared to only 0.25 for the same belief for children. This may occur if parents are more risk averse about their children's health than their own (i.e. they will purchase vaccines for children even if they do not think the disease is serious). Respondents that previously received a cholera vaccine generally purchase more vaccines for their families, unless they were not satisfied with the first vaccine. We also find that respondents that treat their drinking water generally purchase significantly more vaccines (average marginal effect is one vaccine), indicating common preferences for risk averting behaviors.

Each model's estimated average WTP for vaccinating all household members including the respondent is shown at the bottom of Table 4. The estimates of WTP are stable among both model specifications and vary from US$9.00 for TTT respondents in the ICDDR,B service area to

US$14.30 for NTTT respondents in the government service area. Considering the average household has 5.7 members, the average household WTP per person varies from US$1.60 to US$2.50 depending on location and method of survey administration.

We can also use separate negative binomial models to estimate vaccine demand for discrete age groups. The dependent variable is redefined to represent the demand for each age group and separate models are estimated. The estimated average WTP per person for young children age 1–5 years (US$2.40) is higher than for school-age children age 5–17 years (US$1.20) and adults (US$1.05). Figure 1 shows that the predicted fraction of young children vaccinated is higher than that for the other age groups at any price. These findings suggest that respondents place precedence on vaccinating young children relative to older children and adults.

It is also useful to compare mean WTP estimates to median WTP estimates. The median WTP by age group corresponds to the price in Figure 1 at which 50% of an age group population is vaccinated. The median WTP is about US$1.00 for young children, US$0.05 for school-age children, and US$0 for adults. The fairly large differences between mean and median WTP estimates indicate that there is great heterogeneity in WTP for cholera vaccines among households. In other words, there is a large portion of the population that is only willing to pay small amounts of money if any for cholera vaccines, while there is also a small fraction of the population with high WTP. Specifically, although the estimated average adult WTP is US$1.05, we predict that only about 25% of the adult population would choose to buy vaccines at a price of US$1.

4. Discussion

The study reported here provides the first estimates of private demand for cholera vaccines in Matlab, an impoverished rural area of Bangladesh where cholera is endemic

Because many respondents or their family members participated in the 1985 cholera vaccine trial, they should be familiar with benefits of the vaccine. They should also be aware that the vaccine was not 100% effective. In addition, these respondents have had experience in participating in other health surveys and should be less prone to yay-saying. Thus, this sample is uniquely suited for valuing the vaccine. Factors associated with vaccine demand include age, income, gender, and opinions about the severity and likelihood of contracting cholera. Consistent with prior research in other developing countries, we found that hypothetical demand estimates were dependent on whether respondents received time to think about and discuss the purchasing decision. The provision of time to think reduced average household WTP by about 30%, resulting in a best estimate of average household WTP of about US$9–$10. We prefer the TTT estimates because we believe the extra time and discussion is more consistent with actual purchasing decisions.

According to our model estimates, there is considerable heterogeneity in demand. The fraction of young children (age 1–5) vaccinated would be higher than that of school-age children or adults. In addition, the mean WTP per person is much higher than the median for all age groups. This indicates that some households are willing to purchase vaccines at very high prices, while many have little demand even at very low prices.

The ICDDR,B diarrhea hospital located at the center of our study site is nationally renowned for excellence in providing free treatment for cholera and other diarrheal disease. This may result in lower demand for cholera vaccines relative to other areas in rural Bangladesh. In fact, we found that, on average, people in the ICDDR,B service area expressed less demand for cholera vaccines than those in the government service area. But

our interviewees in the government service area resided within only a moderate distance (within 2.5 hours by traditional methods of transportation) of the ICDDR,B hospital, and many had participated in prior ICDDR,B studies (though they probably participated in fewer studies than those residing inside the ICDDR,B service area). As a result, our estimates from the government service area are also likely affected by ICDDR,B's imprint. Other communities in Bangladesh that experience high incidences in the absence of ICDDR,B services may have higher willingness to pay.

While beyond the scope of this paper, our cholera vaccine demand models can be used in combination with recent herd protection findings to aid policy development. At present, cholera vaccine herd protection models are not very well defined. Ali et al. [6-7] provide only five data points to show the coverage-incidence relationships for population clusters that are either 0.5 km [6] or 2 km [7] in radius. In addition, the 1985 campaign targeted women and children only; we do not know how adult male coverage rates would impact results. We are not aware of more comprehensive cholera herd protection modeling efforts, which might examine how vaccination rates within subgroups (e.g. age groups, gender, sanitation method) affect herd protection.

Patel et al. [23] found that targeting influenza vaccines for school-children relative to other age groups would result in proportionately greater herd protection for the community. In contrast, Ali et al. [7] found that cholera vaccine coverage rates for women over 15 years were more important than coverage rates among children for effecting herd protection in children less than 2 years (who were excluded from the Matlab campaign). As epidemiological models for cholera vaccine herd protection become available, the demand relationships (e.g. demand by age and gender) presented in this paper could help set vaccine pricing if government and non-profit groups choose not to fully subsidize campaigns. Demand, incidence and herd protection data could be used to examine tradeoffs between the

number of cases avoided, public investment, and the vaccine price charged. In addition, we could also examine the potential for cross-subsidies to enhance herd protection effects. Our findings suggest that households would place precedence on vaccinating young children; however, the community might be better served to prioritize women over 15 years based on herd protection evidence.

With these reservations, we can see that a cholera vaccination program in the Matlab area could possibly charge a small fee for cholera vaccines and still achieve some herd protection. Ali et al. [6] observed herd protection effects at coverage rates as low as 30% of the target population and very large effects at coverage rates greater than 50%. We predict that a cholera vaccination program could achieve a 30% coverage rate with a US$1.50 user fee and a 50% coverage rate with a US$0.50 user fee. (Note that these coverage predictions are for the whole population rather than the target population as presented in [6-7].) If poorer households are co-located with wealthier ones, there is potential for these poorer households to experience a reduction in cholera incidence when wealthier households purchase vaccines. However, if the wealthy households that purchase vaccines are geographically distant from poor, high incidence neighborhoods, herd protection effects will be less significant. Thus, we have to evaluate the spatial patterns of demand to fully understand the potential for herd protection.

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Tables

Table 1. Variable definitions and descriptive statistics (Respondent and household characteristics)

Variable name	Description	Mean (SD) (*N* = 591)
Respondent characteristics		
Male	Gender =1 if male, = 0 if female	0.49 (0.50)
Age	Age (yrs), continuous	40 (9.7)
Practice Hinduism	Religion = 1 if Hindu, 0 = else	0.06 (0.25)
Education 1–5 years	= 1 if respondent completed 1–5 years of school	0.36 (0.48)
Education 5–10 years, vocational	= 1 if respondent completed 5–10 years of school, vocational school, or madrassa	0.18 (0.38)
Education more than 10 years	= 1 if respondent completed university, postgraduate or professional course	0.12 (0.32)
Unable to read	= 1 if respondent is not able to read a newspaper	0.53 (0.50)
Household characteristics		
Infants	number of infants (<1 year), continuous	0.12 (0.34)
Young children	number of children age 1–5, continuous	0.7 (0.72)
School-aged children	number of children 6–17, continuous	1.7 (1.11)
Adults	number of adults age 18–65, continuous	3.0 (1.45)
Elderly adults	number of elderly adults age >65, continuous	0.20 (0.43)
Monthly income per capita	Household income divided by number of household members (US$ per month), continuous	13.7 (11.5) [a]
Log income per capita	Natural log of household income divided by number of household members, continuous	6.8 (0.7)

[a] The average household monthly income was US$75 (Tk. 5000).

Table 2. Variable definition and descriptive statistics (Perceptions of disease, vaccine history and characteristics of research design)

Variable name	Description	Mean (SD)
Risk behavior, perceptions of disease, vaccination history		
Treat drinking water	= 1 if household treats water for drinking;	0.15 (0.36)
Someone in household has had cholera	= 1 if someone in household has had cholera	0.37 (0.48)
Know person who has had cholera (outside hh)	= 1 if knows someone outside hh who has had cholera, but not some in hh	0.27 (0.50)
Cholera is very serious for adults	= 1 if respondent believes cholera is (very) serious for adults	0.64 (0.48)
Cholera is serious for children	= 1 if cholera (very) serious for children	0.84 (0.50)
Cholera likely for respondent	= 1 if respondent believes he or she is likely or very likely to contract cholera in next 5 years	0.20 (0.40)
Cholera likely for respondent's child	= 1 if respondent believes his or her child will likely contract cholera in next 5 years	0.40 (0.49)
Believes cholera is common in community	= 1 if respondent believes cholera is common in his or her community	0.20 (0.40)
Respondent believes vaccine is still working	= 1 if respondent had oral cholera vaccine and believes that it is still effective	0.24 (0.43)
Respondent had cholera vaccine satisfied, not working	= 1 if respondent had oral cholera vaccine was satisfied, but does not think vaccine still works	0.06 (0.25)
Respondent unsatisfied with vaccine	= 1 if respondent was not satisfied with previous vaccine for self or family member	0.03 (0.16)
Characteristics of research design		
Time to think	= 1 if given time to think overnight, =0 else	0.47 (0.50)
ICDDR,B	Health service area; = 1 if ICDDR,B, = 0 if government	0.37 (0.48)
Price	Referendum price (Bangladeshi Tk), continuous	157 (198)

Table 3. Household demand for vaccines (raw data)

Price US$ (Tk)	$0.15 (10)	$0.37 (25)	$0.74 (50)	$1.10 (75)	$4.50 (300)	$9.0 (600)
Household demand[a]						
NTTT Sample size	54	54	57	52	54	39[b]
Avg. no.of vaccines per family	4.4	4.4	3.2	2.8	0.8	0.2
TTT Sample size	51	48	47	46	46	38[b]
Avg. no. of vaccines per family	4.1	3.1	1.8	1.6	0.3	0.5
NTTT						
% family members vaccinated	76%	75%	60%	53%	16%	4%
TTT						
% family members vaccinated	63%	53%	31%	27%	4%	10%

[a] Number of vaccines purchased divided by number of persons in household
[b] Sample size was smaller for the highest price, because it was only used to choke off demand.

Table 4. Household negative binomial regression results and WTP estimates

	Household Model	
Model	**1**	**2**
Price (Tk)	–0.005***	–0.005***
	(–6.5)	(–13)
Time to think	–0.38***	–0.44***
	(–3.85)	(–4.3)
Male	0.27***	0.27**
	(2.64)	(2.4)
Resident from ICDDR,B service area	–0.18*	–0.25**
	(–1.78)	(–2.1)
Age	–0.008	–0.009
	(–1.40)	(–1.4)
Education 1–5 yrs.	0.18	0.16
	(1.48)	(1.3)
Education 6–10 yrs.	0.28*	0.22
	(1.92)	(1.5)
Education >10 yrs.	0.12	0.14
	(0.83)	(0.81)
Log income per capita	0.37***	0.39***
	(4.43)	(4.5)
No. of hh members		
No. of infants < age 1	0.041	–0.020
	(0.29)	(–0.14)
No. of children age 1–5	0.19***	0.21***
	(2.59)	(2.8)
No. of children age 6–17	0.13***	0.13***
	(2.75)	(2.7)
No. of adults age >18	0.17***	0.17***
	(5.32)	(5.2)
Practice Hinduism	0.30	0.034
	(0.17)	(0.17)
Serious or very serious for children		–0.26**
		(–1.9)
Serious or very serious for adults		0.32***
		(3.0)
Cholera likely for respondent		0.30**

		(2.2)
Cholera likely for children		0.079 (0.72)
Someone in hh has had cholera		0.023 (0.20)
Know someone other than hh member that has had cholera		–0.13 (–1.0)
Resp had prior vaccine; was satisfied and thinks vaccine still works		0.050 (0.42)
Resp had prior vaccine; was satisfied but thinks vaccine no longer works		0.33* (1.7)
Resp. had prior vaccine; not satisfied		–0.38 (–0.97)
Treats water		0.23* (1.8)
Constant	–1.8*** (–2.9)	–1.9*** (–2.8)
R^2	0.093	0.11
Estimated average WTP, NTTT Govt. Service Area (US$)	14.30	14.30
Estimated average WTP, NTTT ICDDR,B service area (US$)	12.30	12.30
Estimated Average WTP, TTT govt. service area (US$)	10.00	10.00
Estimated Average WTP, TTT ICDDR,B service area (US$)	9.00	9.00

* indicates significance at the 10% level
** at the 5% level
*** at the 1% level
T–statistic in parentheses

Table 5. Average marginal effects for household negative binomial regression

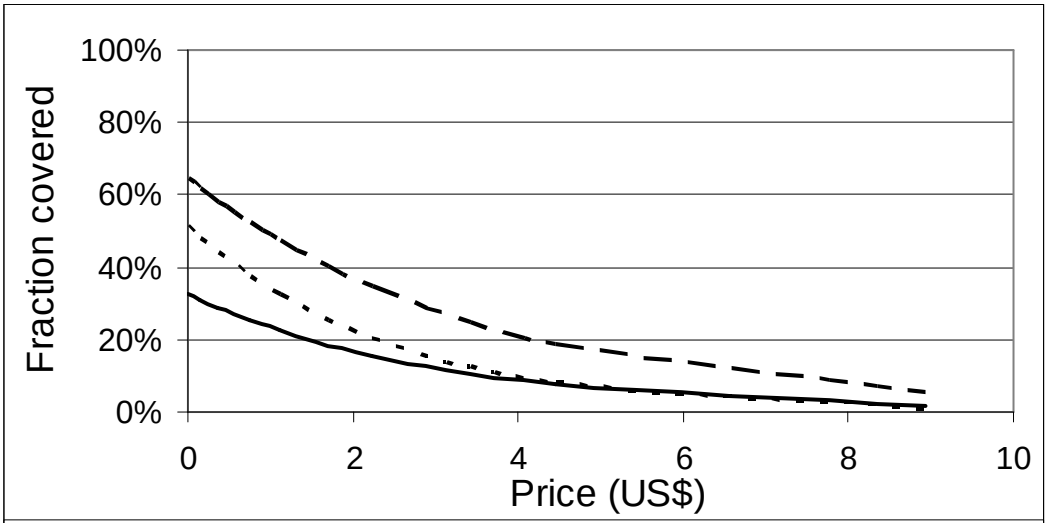
	Household Model	
Variable (change in variable)	**Price = US$0.50**	**Price = US$1.00**
Price (US$; 1 unit US$0.50)	–0.58 (0.000)	–0.45 (0.000)
Time to think	–1.3 (0.000)	–1.1 (0.000)
Male	0.84 (.005)	0.71 (0.005)
Resident from ICDDR,B service area	–0.73 (0.068)	–0.62 (0.068)
Age (yrs)	–0.037 (0.048)	–0.031 (0.050)
Education (category- 0, 1—5, 6—10, >10)[1]	0.29 (0.098)	0.25 (0.10)
Monthly income per capita (US$1 per cap)	0.045 (0.000)	0.032 (0.000)
No. of infants < age 1	–0.12 (0.79)	–0.10 (0.79)
No. of children age 1–5	0.58 (0.018)	0.49 (0.19)
No. of children age 6–17	0.39 (0.012)	0.33 (0.11)
No. of adults age >18	0.55 (0.000)	0.47 (0.000)
Practice Hinduism	–0.07 (0.91)	–0.06 (0.91)
Cholera likely for respondent	1.2 (0.023)	1.0 (0.025)
Cholera likely for children	0.16 (0.66)	0.13 (0.66)
Someone in household has had cholera	0.25 (0.49)	0.22 (0.49)
Unsatisfied with previous vaccine	–1.2 (0.15)	–1.0 (0.15)
Treats water	0.99 (0.09)	0.84 (0.092)

(p-value in parentheses)

[a] As opposed to the educational dummy variables used in the negative binomial regression, an education categorical variable is necessary for average marginal effect analysis. The same educational levels used are used to differentiate the category variable, which increases from lower to higher education (i.e. 1= no formal education, 2= 1—5 years, 3= 6—10 years, 4= greater than 10 years).

Figures

Figure 1. Predicted coverage rates as a function of price by age group



Legend

Appendix 3. An Estimate of the Economic Value that Parents in Rural Bangladesh Place on *Ex-ante* Mortality Risk Reductions for their Children

November, 2008

Running title: Value of Children's Mortality Risk Reductions in Bangladesh

Abstract

An Estimate of the Economic Value that Parents in Rural Bangladesh Place on *Ex-ante* Mortality Risk Reductions for their Children

Empirical estimates of parents' willingness to pay (WTP) to reduce mortality risk for their children were derived from a contingent valuation survey of 591 parents in rural Bangladesh. The interviewer introduced a hypothetical nutritional supplement that would reduce the risk of death from disease and asked if respondents would purchase it for their youngest child. Average WTP for large reductions (20% to 60%) in risk of death from disease was about 1-2% of average household income, resulting in estimates of the value of statistical life between US$10,000 and US$25,000 for children between one and seventeen years.

Keywords: children, VSL, WTP, CV

Parents constantly make decisions that reveal their attitudes toward health and mortality risks for themselves and their children, including how to protect children from accidents in the road or near water bodies or whether to purchase preventative health products. These decisions involve trading off mortality and morbidity risks with monetary expenditure (e.g., for a safety helmet or a vaccine) and/or allocation of parents' time (e.g., transportation choice, amount of direct child supervision). By observing these tradeoffs, economists can estimate the economic values that parents place on risk reductions for their children.

Such estimates are useful for analyzing the benefits of many types of health and environmental programs that aim to reduce mortality risks. We postulate that health improvements offer four principal economic benefits: (1) avoided direct medical treatment costs, such as medicine and doctor fees, (2) avoided indirect costs, such as lost productivity (e.g., wages, school, housework) of patients and their caretakers, (3) avoided disutility of the pain and suffering of illness, and (4) reduced risk of death. Many studies have estimated the direct and indirect costs of illness per case (1 and 2) via surveys with patients (Cookson et al. 1997; Bahl et al. 2004; Cropper et al. 2004; Fischer et al. 2005). These cost of illness estimates provide lower bounds of the monetary benefits from disease reduction. But this approach ignores the values attached to reduced pain and suffering or mortality risk (3 and 4), which are especially difficult to quantify. Ideally, mortality risk benefits could be standardized across interventions for economic analysis of public policy options.

Data from a contingent valuation (CV) survey were used to estimate parents' willingness to pay (WTP) for mortality risk reductions for their children. Specifically, we compared an estimate of the value of a generic mortality risk reduction (derived from responses to an offer of a hypothetical nutritional supplement that would reduce risk of death from all diseases) to the implicit value of mortality risk reduction via a hypothetical cholera vaccine.

Our respondents, parents from 591 households in the Matlab area of rural Bangladesh, were individually interviewed during the summer of 2005. They were provided with information

about the relative risks of death that children in the community face, illustrated with pictures showing the most likely causes of death for the children and their average risk of death. Interviewers then asked whether respondents would purchase a hypothetical nutritional supplement that would reduce the risk of death for the youngest child in the household if it were available at a specified price. Their replies provided estimates of WTP for mortality risk reduction for the households' youngest children; these data were also used to calculate an average value of statistical life (VSL) for children. A second CV scenario for a new-generation cholera vaccine (50% effective for 3 years) was also presented to respondents in the same interview. Although the vaccine valuation questions did not directly elicit mortality risk information from the respondents, we used the average WTP for a cholera vaccine in addition to expected cholera mortality risk to calculate implicit VSL estimates for comparison with the nutritional supplement scenario.

Our results show that parents are willing to spend a portion of their income to reduce mortality risk for their youngest child. Average WTP for the hypothetical supplement was about US$1 to US$2 per month, 1% to 3% of average monthly household income (US$75). Our best VSL estimate is a range from US$10,000 to US$25,000, and is based on large risk reductions (20% or 60% of all disease-related risk of death). Because these estimates involve large changes in risk, it is less likely that they are overstated relative to estimates derived from smaller changes.

The VSL estimates for the hypothetical nutritional supplement were similar to the implicit VSL estimates based on cholera vaccine demand. Our results are also similar to a recent VSL study for commuters in Delhi, India (Bhattacharya, Alberini, and Cropper 2007), but smaller than those calculated via hedonic wage studies performed in India (Simon et al. 1999; Shanmugam 2000, 2001). Overall, our estimates generally fall in line with other values in the literature after adjusting for income.

1. Background

The three methods commonly employed for estimating VSL include (1) hedonic wage or compensated wage studies, (2) stated-preference techniques, and (3) averting-expenditure studies. The literature includes examples of VSL estimates from each type of methodology that may be compared to our results. The hedonic wage literature is the most widely implemented and includes studies in some less developed countries. The averting-expenditure studies include some estimates of parents' valuations of risk reduction for their children, but there are few if any studies available from less developed countries. Estimates from stated preference studies are available for some less developed countries, but generally focus on adults and may introduce bias if respondents misunderstood risk magnitudes or because people did not actually pay for the hypothetical risk intervention.

The average WTP per person divided by the magnitude of risk reduction per person is the normalized value of a statistical life (VSL) or statistical life year (VSLY). Table 1 presents results from illustrative hedonic wage, stated preference, and averting expenditure studies, with special emphasis on meta analyses, studies conducted in developing countries and of parents' valuations for reducing their children's mortality risks. If available, we report the magnitude and type of risk reduction considered, average or median annual household income, as well as the ratio of VSL to annual household income. The VSL to income ratio is useful for identifying trends amongst high and low income countries and for identifying outlier estimates.

Generally, the highest VSL estimates (both in value and ratio) have been obtained from hedonic wage studies. Thus far, few hedonic wage VSL studies have focused on the developing world, although there are estimates for India and Taiwan. The Indian VSL estimates range from US$150,000 in 1991 USD (Simon et al. 1999) to US$3 million in 1990 USD (Shanmugam 2001). The VSL to income ratios for the Indian studies, especially those by Shanmugam, are much higher than most others in Table 1. Both Viscusi and Aldy (2003) and Mrozek and Taylor (2002) report VSL income elasticity estimates in the range of 0.45 to 0.6 based on a review of

international studies. The estimates from Simon et al. and Liu et al. are consistent with other work after adjusting for income (this is not true of Shanmugam's studies[41]).

(Table 1 here)

Relative to the hedonic wage studies, the stated preference VSL estimates tend to exhibit more variation between and within studies, often depending on the magnitude of risk reduction presented in the hypothetical scenario. The North American and European scenarios from Alberini et al. (2004) and Alberini, Hunt, and Markandya (2006) presented "general purpose" scenarios in which the hypothetical product reduced risk of death from all causes. In contrast to the "general purpose" studies, with the exception of Mahmud (2005), the studies from less developed countries were based on hypothetical products/interventions that would reduce risk from one or more specific causes of death. While the use of specific interventions (e.g., air pollution, SARS, etc.) would provide a more realistic valuation scenario (i.e. it is unlikely that any intervention would reduce risk from all causes simultaneously), the risk for any single cause is usually just a small fraction of the risk from all causes. It is difficult to communicate smaller magnitudes in risk, especially for populations with limited education. In addition, the use of specific causes of death might have influenced results if those causes were dreaded, like cancer, or somewhat avoidable, like traffic accidents (Subramanian and Cropper 2000). Thus, there is a tradeoff between providing a more realistic scenario versus an easier to understand change in mortality risk when choosing between general and specific intervention scenarios.

The study by Mahmud (2005) is the only known stated preference study for mortality risk reductions in Bangladesh. The hypothetical intervention (a series of vaccinations) reduced respondents' baseline risks of death from all causes by either 25% or 50%, which is a much larger change in risk than for any other studies. In addition, the scenario required an up-front payment

[41]Shanmugam (2001) extended the work in Shanmugam (2000) by adjusting for individuals' abilities to select their jobs based on the assumption that some may have unobserved attributes that allow them to work more efficiently in risky occupations. Using a different econometric procedure, his VSL estimate increased about three-fold to US$3.0 million. This approaches the US estimates and demonstrates the sensitivity of results to underlying model assumptions.

for five years of protection, while other studies typically used annual payment mechanisms. The large changes in risk and up-front payment requirements probably contributed to the very small VSL estimates, US$1,300 to 2,500 in US$2003. Mahmud's VSL-to-annual-income ratios are easily the smallest observed among those reported in Table 1.

Bhattacharya, Alberini, and Cropper (2007) estimated VSL for commuters in Delhi, India to reduce their risk of death from road traffic accidents. As might be expected, they found that people who traveled from home on a daily basis had the highest WTP for improved safety. They estimated average VSL at about PPP$150,000 (US$30,000). The ratio of VSL to average household income (US$3,000) in Delhi is low relative to other studies, but within the general range. Other estimates from Thailand (Vassanadumrongdee and Matsuoka 2005) and Taiwan (Hammit and Liu 2004; Liu et al. 2005) generated much higher VSL estimates relative to annual income. However, the VSL estimate based on reduction of risk in SARS requires special consideration, because the surveys were performed during an epidemic.

Overall, the ratios of VSL to annual household income tend to be lower for the stated preference studies relative to other methods, with the exception of the SARS study. The ratios also appear to be sensitive to the magnitude of risk reduction; the use of smaller hypothetical risk reductions typically result in larger VSL estimates within a given study. The only known stated preference study that examined parents' willingness to pay to reduce their children's risks of death is from the United States (Dickie and Gerking 2003; Dickie and Gerking 2006).[42] However, this work examines latent mortality risk. Thus, estimates are not comparable to other results in Table 1.

[42]Dickie and Gerking estimated parents' WTP for protective sunscreen that would reduce morbidity and mortality risks of skin cancer for themselves and their children. They found that parents were willing to pay about twice as much to protect their children than to protect themselves. They could not develop a VSL estimate comparable to those above, because of the latent nature of mortality risk from skin cancer, especially for children. The results from this study are similar to two studies that examine parents' WTP to avoid an episode of illness for their children. Liu et al. (2000) and Dickie and Messman (2004) both found that parents were willing to pay more for one of their children to avoid an episode of illness than for themselves.

Most estimates of parents' WTP to reduce their children's mortality risk come form the averting behavior literature. These studies attempted to estimate parents' willingness to purchase of products that reduce their children's risk of death. Blomquist (2004) summarized averting behavior VSL estimates for the US market. The VSL-to-annual-income ratios for these studies were generally lower than the hedonic wage estimates summarized in Viscusi and Aldy (2003). However, the ratios from studies that accounted for the disutility of time spent using safety equipment or that made adjustments for perceived versus actual risk (e.g., (Blomquist, Miller, and Levy 1996; Mount et al. 2001)) approach hedonic wage estimates. Although definitive conclusions cannot be drawn from these few studies, it appears that VSL estimates for children are similar in magnitude to those for adults. Unfortunately, we are not aware of any studies performed in less developed countries.

2. Study Site and Research Methods

2.1 Study area and mortality statistics

Centered on the town of Matlab, the study area lies some 55 km southwest of Dhaka and has a population of approximately 224,000 ((ICDDRB) 2005). The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) operates a hospital in Matlab town whose services include free treatment to anyone with diarrhea. ICDDR,B also provides basic health services to approximately 111,000 people in Matlab town and 67 outlying villages. Once a month, ICDDR,B's Health and Demographic Surveillance System (HDSS) gathers information from each person in the ICDDR,B service area as well as from an additional 113,000 people in 75 other nearby villages who receive basic health care services from government facilities. ICDDR,B has collected this information for more than 35 years. Over the years, a number of

health intervention studies have been conducted in both the ICDDR,B and government service areas.[43]

The HDSS data includes annual mortality rates for a number of causes by age group, as summarized in Table 2 (ICDDRB 2002, 2003, 2004). The most common causes of death differ by age group. For children less than 1 year of age, respiratory disease is the most likely cause of death; next most common are diarrhea and nutritional deficiency. For children age 1 to 4, drowning is the most likely cause of death; next are diarrhea and respiratory disease. Mortality rates drop significantly for children age 5 to 9 years relative to younger children. Mortality rates for children age 10 to 19 drop again by half relative to children age 5 to 9 and are six times less than among children age 1 to 4 years. In comparison to the United States, mortality rates in the Matlab area are about 6.5 times greater for children less than one year of age, about 14 times greater for children age 1 to 4 years and about 5 times greater for children age 5 to 14 years ((NCHS) 2005). The mortality rates for older children and young adults are similar for the two countries.

(Table 2 here)

2.2 Field work and data collection

2.2.1 Sampling procedure

Survey respondents were chosen randomly from the HDSS surveillance database via a two-stage cluster sample without replacement. The first stage selected a total of 3,000 households, each with at least one child less than 18 years of age. Two-thirds of these households were located in the government service area, and one-third in the ICDDR,B service area. The sample list was subdivided into clusters of 22 to 28 households located in small areas ranging about 1 km^2 to 4 km^2 depending on population density. In the second stage we randomly selected

[43]From 1963 through 1996, ICDDR,B conducted 30 to 35 studies in the government service area and 55 to 65 studies in its own ICDDR,B service area. Many of these studies included the free provision of products aimed at improving the health of participants.

clusters of households and assigned one each to enumerators. Enumerators were instructed to allot half their interviews to males and to restrict interviews to the primary caretaker of the children in the household, typically one of the parents.[44] The second stage sampling was implemented twice to coincide with staging of the interviews. In total, 591 households granted interviews and only two households refused. Another 160 households were dropped because the selected male parents lived and worked outside the village and were not available.

2.3 Survey instrument: overview

The survey instrument included two sets of questions designed to accomplish two separate research objectives. One set of questions investigated the value of a new-generation cholera vaccine, as reported in Islam et al. (2008). The other set assessed the respondent's willingness to pay (WTP) for a hypothetical nutritional supplement that would reduce the mortality risk of the household's youngest child. Throughout the survey, the respondent was asked questions to test comprehension of what was being said and to maintain interest in the interview.[45]

The survey instrument had seven sections of questions. The first section recorded demographic information about the respondent and members of the household. The second, third and fourth sections dealt with perceptions of cholera and with the vaccine valuation scenario as discussed in more detail by Islam et al. (2008). After receiving information about cholera and vaccines (50% effective for 3 years), respondents were asked if they would purchase vaccines for themselves and for their family members at a single price (preassigned to each respondent from an array of six). The interview then proceeded to the hypothetical nutritional supplement CV

[44]Two respondents were the grandparents of children.

[45]We used two iterations of 60 pretest interviews to help us to adapt our survey to local conditions in the Matlab area and to set an appropriate range of prices. We employed 20 local enumerators to conduct the interviews. They received two weeks of training according to the guidelines recommended in Whittington's recent methodological review of CV practices in developing countries (2002).

scenario, our focus here (detailed below).[46] The sixth section included socioeconomic questions about education, income, housing, assets, and disease-averting behaviors. The seventh section recorded the enumerator's assessment of the quality of the interview.

2.4 The survey instrument: mortality risk instruction and nutritional supplement scenario

The fifth section of the questionnaire informed respondents about children's risk of death, presented a hypothetical nutritional supplement that would reduce the risk, and elicited respondents' willingness to pay for such a supplement in terms of its efficacy (two levels) and price (from five possible sets of paired amounts). Although the primary causes and numerical risks of death are different for children younger than 5 years compared to older children (Table 2), we used the same CV nutritional supplement scenario for all ages of children because of the length and complexity of the survey instrument, the distances traveled by interviewers to respondents' households, and other limitations of working in rural areas. For respondents with more than one child less than 18 years, the questions always referred to the youngest child. Younger children were the focus because they are often targeted for vaccination and public health campaigns.

The entire CV nutritional supplement scenario is available from the authors. The first objective of this section was for respondents to consider all possible risks of death for children and the relative likelihood of each. Following Corso et al. (2001), we presented a scale that showed pictures of a number of different causes of death such that the most common causes appeared at the top of the scale and the least common at the bottom (Figure A-1 of the survey). Next, using techniques similar to Mahmud (2005), the enumerator instructed the respondent about probability using coin flips and die rolls as examples.

[46]In the survey interviews, the set of cholera vaccine questions was always presented prior to the nutritional supplement scenario. Thus it is possible that the vaccine valuation scenario affected respondents' answers to the mortality risk reduction scenario.

Next, the enumerator introduced the notion of average risk of death for children in the Matlab area. The respondent was asked to imagine a large village in the Matlab area that had 1,000 children, then was told that about 5 children out of 1,000 would be expected to die from disease in the next 5 years (Figure A-2 of the survey). (This estimate was lower than the actual risk for children less than 5 years old and higher than the risk for older children.) The enumerator further explained that the risks of death from drowning and other accidents were not included in this representation. To calculate perceived risk of death from disease, the enumerator asked the respondent to estimate how many children lived in his or her own village and how many of those children the respondent thought might die from disease in the next 5 years. The enumerator proceeded to relate the risk of death for children in the village to the risk of death for the respondent's own child and told the respondent to assume that all children in the village had the same risk. To demonstrate that the likelihood of the child's dying from disease was much smaller than the chances of rolling a die or flipping a coin, the enumerator placed a grid showing 5 red squares in 1,000 (Figure A-3 in the survey) next to similar 1,000 square grids introduced for coin flips and die rolls.

Next the enumerator introduced the hypothetical nutritional supplement that would reduce the child's risk of death. Each respondent received a randomly assigned scenario such that the supplement reduced the child's risk of death from disease from 5 in 1,000 to either (a) 2 in 1,000 or (b) 4 in 1,000 over 5 years.[47] These figures represent (a) a 60% reduction and (b) a 20% reduction in the child's risk of death. Respondents were shown another figure (Figure A-4 in the survey) to visualize how the supplement would decrease the already small baseline risk for their child. We chose to use large risk reductions in our scenarios to improve respondent comprehension and because large changes in risk generate conservative VSL estimates. Most

[47]Although we realized the challenge of explaining the notion of mathematical reduction in risk to our respondents, we hoped that our visual presentations would clearly show that the baseline risk of death was quite small and that the hypothetical nutritional supplement would reduce that small risk of death significantly.

other VSL studies use smaller risk reductions relative to baseline.[48] The magnitude of risk reduction was post-corrected to an age-specific risk reduction prior to analysis. This was accomplished by multiplying the percentage change in risk by the baseline risk specific to a particular age group. Before proceeding to the valuation questions, respondents received a short "cheap talk" script to remind them of budget constraints and to dissuade them from trying to please enumerators. These reminders have decreased yea-saying in other studies (Cummings and Taylor 1999).

We chose a monthly payment mechanism because of Matlab's low average income and because many respondents were farmers and did not have large amounts of cash on hand. Thus, the enumerator explained that the parent would need to continue buying the supplement every month to maintain protection for the child. Respondents were not required to commit to a stream of payments. They could choose to stop purchasing the supplement at any time. Each respondent was asked if they would purchase the hypothetical supplement at a monthly price that was randomly assigned from an array of five: US$0.15, $0.30, $0.75, $1.50, and $7.50. Next, the respondent was asked if they would purchase at a specified follow-up price, which was either higher or lower, depending upon whether the respondent agreed to the initial price.[49]

Before the interviews began, respondents were divided into two groups for the cholera vaccine scenario. NTTT (no time to think) respondents received the entire questionnaire in one sitting. TTT (time to think) respondents answered the first half of the survey, then were given overnight to consider and discuss the prospective "purchase" of the hypothetical vaccine; an interviewer returned the next day to finish the survey. Because the VSL section was always presented after the vaccine scenario, it always occurred in a single session—either in the single-day NTTT interview, or in the return-visit portion of the TTT interview. Several recent studies

[48]Mahmud (2005) also used a very large mortality risk reduction for Bangladeshi adults.
[49]Equivalent prices in Bangladeshi taka (Tk) are Tk 10, 25, 50, 75, 300, 600, where 1 US dollar = Tk 67.2 in August 2005. These prices were not adjusted for purchasing power parity.

have shown that TTT yields lower average WTP results (Whittington et al. 1992; Lauria et al. 1999; Cook et al. 2006). Although TTT considerations were not directly applied to the nutritional supplement purchase decision, TTT would have allowed respondents to carefully consider their budget constraints prior to hearing the supplement scenario.

2.5 Modeling strategy

Theoretical approaches for modeling parents' willingness to pay to reduce mortality risk for children turn on whether parents value mortality risk reductions for children due to altruistic intentions, or paternalistic intentions. As Jones-Lee (1991; 1992) explains, a purely altruistic concern would optimally result in a direct wealth transfer from giver(s) to receiver(s), who could then freely choose to purchase an optimal level of risk reduction without further involvement of the giver. A purely paternalistic approach assumes that the giver only values mortality risk reduction for the receiver, being indifferent to the preferences of the receiver. Of course parents' regards for children are somewhere between pure altruism and pure paternalism. Parents are concerned about a variety of aspects of their children's well-being besides their mortality risk. However, parents' interests in reducing their children's mortality risk is likely to be greater than that of the children themselves, owing to children's lack of experience with causes and risks of death (Jones-Lee 1991; 1992; Cropper and Sussman 1988).[50]

For our analysis, we simplified Jones-Lee's unitary decision maker approach (1992) to modeling familial WTP for a public good that reduced mortality risk for all family members simultaneously (as well as for the public at large). In our model the household decision maker decides whether to purchase a private good that would reduce the mortality risk only for one member of the family. Unlike Jones-Lee's model, our hypothetical nutritional supplement was a

[50]An additional complication is introduced when comparing a mother's and a father's separate valuations for a mortality risk reduction for one of their children. Some authors (e.g., Mount et al. 2001) have developed game theoretic constructs to explore how parents make joint decisions. Others (e.g., Cropper et al. 2004; Dickie and Gerking 2003) use a simpler unitary household model where a single decision-maker optimally allocates resources among family members.

private good that would only affect the survival probability of the family member that used it, (i.e. the youngest child). We assume that the decision maker maximizes the household utility function, which includes the family's consumption of a numeraire good *w*, the probability of death for each of *n* family members prior to the next period (π_i), and a vector of socioeconomic characteristics of each family, *X*. The representative utility function is represented as

$$U = u(w, \pi_1, \pi_2, \ldots, \pi_n, X). \quad (1)$$

We assume that the utility function is increasing in *w* and decreasing for each π_i, and that the marginal willingness to trade off a decrease in current consumption, *w*, for a decrease in π_i, can be obtained by simple differentiation. The marginal rate of substitution between the numeraire good and a one-month risk reduction for one member can be considered as the VSL.

$$VSL_i = (\partial U / \partial \pi_i) / (\partial U / \partial w) = \partial w / \partial \pi_i . \quad (2)$$

This calculation assumes that VSL is constant regardless of the magnitude of mortality risk reduction. Given the large mortality risk reductions (20% or 60% of total health-related mortality risk) specified in our VSL scenario, our results may be limited by this assumption.

Our econometric model is based on a stochastic utility function $v(h,y;X) + \varepsilon_h$, with $h = 1$ if the respondent wanted to purchase the supplement and $h = 0$ if not. The other components are household income *y* and a vector of socioeconomic variables *X* expected to influence preferences. The stochastic term ε_h is assumed to be independent and identically distributed. Similar to other studies (Alberini 1995; Alberini, Boyle, and Welsh 2003), we found that answers to the follow-up price question in our survey were influenced by presentation of the initial price, and suffered from starting point bias issues.[51] As a result, we only used the first price to model the decision to purchase. The probability that an offer was accepted at price A_i is

[51]A bivariate normal model was used to jointly model the responses to the first and second prices. The coefficients estimates for the two questions were statistically different at the 1% level. We also estimated interval models based on normal, lognormal, and Weibull distributions. The Weibull distribution best fit the data and provided average WTP estimates that were very similar to those from the probit models. (Median WTP estimates from the interval model were smaller.)

$$\Pr(\text{yes}) = \Pr\left[\text{v}(1, y_i - A_i; X_i) - \text{v}(0, y_i; X_i) > e_0 - e_1 \right] = \text{F}(-\Delta v) = \text{F}(A_i, \theta). \quad (3)$$

We used the probit model (Haab and McConnell 2002) to evaluate equation 4 such that ε_i was assumed to be independent and identically distributed following a normal distribution with mean zero and variance σ^2 ($\varepsilon_i \sim N(0, \sigma^2)$). The parameter estimates from the probit regression can be used to calculate expected WTP according to

$$\text{E}(WTP | X_i, \beta) = (\hat{\beta}_r / \sigma) / (\hat{\beta}_p / \sigma), \quad (4)$$

where $\hat{\beta}_r$ is the coefficient estimate for the magnitude of risk reduction and $\hat{\beta}_p$ is the coefficient for price.

As discussed in Islam et al. (2008), household demand for cholera vaccines was modeled with negative binomial count models. Separate models and WTP estimates were developed for children age 1 to 4 years, children age 5 to 18 years, and adults.

3. Results

Generally, respondents seemed to understand the nutritional supplement CV scenario and provided reasoned answers. Only 13 of the 591 respondents rejected our description of the nutritional supplement as a vehicle for reducing mortality risk. These respondents already received nutrition supplements from the government or thought that their children were well fed. A few did not believe that the supplement could reduce mortality risk in children. These respondents were dropped from further analysis. We also excluded households in which the youngest child was less than one year old. We were unsure how parents would interpret the scenario for children that were breastfed. The baseline risk of death also decreases considerably during the child's first year; thus the average risk presented to parents would have been much different than the actual risk faced by their infants. In addition, the cholera vaccine is not

considered safe for children less than one year, and the comparison to the cholera vaccine WTP would be compromised. After excluding households with children less one year old, the final sample size was 532 households.

3.1 Sample sociodemographic characteristics

The sociodemographic characteristics of the sample households are summarized in Table 3. Slightly over one-third of respondents (37%) were from the ICDDR,B service area, and about half were male. Average household size was about 5.8 persons, including on average 0.1 infants less than one year old, 0.7 young children (1 to 5 years), and 1.7 school-age children (6 to17 years). Average respondent age was about 40 years and the youngest child was 7 years old; about 45% of the children were less than 5 years of age. The gender split for the youngest child was almost even, with slightly more males than females. On average, respondents had about 3.6 years of education; about 35% of the sample reported that they had never attended school. Average monthly household income was about US$75 and median income was US$60.[52] The average risk reduction presented to respondents was about 4.1×10^{-4} per year.

(Table 3 here)

3.2 Respondents' understanding of nutritional supplement CV scenario

Respondents generally seemed to understand that some causes of death were more likely than others. When asked to identify the most common cause of death for children in their village, about 98% pointed to one of the four highest causes listed in the HDSS surveillance report (respiratory disease, drowning, diarrheal disease, or malnutrition). A majority of respondents (72%) correctly chose lightning strikes as the least common cause presented in the figure. When

[52]The following variables are significantly correlated at the 5% level. Older children are correlated with older respondents and lower education levels. Older respondents are correlated with lower education, lower income, being male, and larger households. Income is highly correlated with education. Male respondents have lower income. Households with more school-age children have lower income per capita. Respondents with more education and younger children are more likely to treat their water.

respondents were asked to place risk of death from cholera within the scale of other causes, more than half (51%) believed that risk of death from cholera was most similar in magnitude to risk of death from one of the two most frequent causes (respiratory disease or drowning). However, the actual risk of death from cholera is much smaller than that; we assumed that 15% of all diarrheal deaths are due to cholera.[53] This apparent overestimation of the risk of death from cholera may have resulted in overstated WTP for cholera vaccines.

Our respondents provided estimates of the number of children that lived in their village (mean 2,300, SD 22,000) and then estimated how many might die from disease in the next 5 years (mean 62, SD 500). Many respondents (22%) were unable to answer one or both of the questions, despite encouragement to venture a "best guess". The median estimated risk of death based on these answers was 10 in 1,000, which is about 25% higher than the actual risk of death from disease for children age 1 to 4 years and about 400% higher than the risk of death from disease for older children (See Table 2).[54] We discovered than another 40% of the respondents reported that there were 500 or less children in their village. These small estimates of the child population would limit the resolution in respondents' estimates because the expected number of children that would die was always an integer.

Most respondents correctly answered questions designed to test comprehension of our explanations of probability and risk of death. For a series of three questions regarding whether the supplement was effective for reducing the risk of death from respiratory disease (yes) and from drowning (no) and the risk reduction effected by the supplement (either 1 or 3 in 1,000 over 5 years depending on the scenario); 65% answered all three correctly on the first try, and a total of

[53]This is based on the percentage of diarrhea patients with cholera-positive stool samples treated at the Matlab hospital. The actual relative risk of death from cholera varies by village, but should fall near the middle of the scale.

[54]Note that all answers were made in whole numbers and that some respondents reported a small number of children in the village. Thus, these estimates are somewhat imprecise.

87% had succeeded after a second try. These findings suggest that respondents were well instructed.[55]

3.3 Willingness to pay for a nutritional supplement

3.3.1 Raw data

The raw data for the proportion of respondents who were willing to "purchase" the hypothetical supplement for the household's youngest child at the initial preassigned price are shown in Table 4. The variation in baseline risk of death from disease varied from 0.4 deaths per 1,000 children older than 10 years to 2.1 deaths per children between 1 and 3 years of age. The effective risk reduction is the baseline risk for that age group multiplied by the percentage risk reduction that was randomly assigned. Generally, the willingness to purchase is greater for lower prices and for larger effective risk reductions. With eight different effective risk reduction values, the sample size for each risk reduction-price cell is very small. As a result, there would appear to be some kinks in the demand curve; however, these disappear when results are averaged over larger sample sizes.

(Table 4 here)

It is easier to visualize trends by combining these data into large risk reduction and small risk reduction subgroups. Figure 1 shows the expected fraction of the population that would purchase the hypothetical supplement as a function of price for these two subgroups. The first subgroup consists of respondents for which the risk reduction was greater than 4×10^{-4} and the second group consists of respondents with an effective risk reduction smaller than that. This figure shows that there distribution of WTP for the large risk reduction may have a large tail, and that a small fraction of the population has a very WTP for mortality risk reduction. The tail

[55]Communication of low probability risk is problematic in most settings, even in industrialized countries. Alberini et al. (2004a) report that 16% of respondents from the United States and 7% from Canada stated they poorly understood the probability description. Alberini et al. (2004b) report that 11% to 22% of respondents incorrectly answered a question designed to test understanding.

appears to be much smaller for the lower effective risk reduction. Although stated demand is greater for the group that received the larger risk reduction, the difference in demand is smaller than would be expected if WTP were linearly correlated with risk reduction magnitude.
(Figure 1 here)

Nonparametric Turnbull lower-bound estimators (Haab and McConnell 2002), can be calculated based on the raw demand reported in Table 4. The average WTP per month varied between US$0.6 and US$3, and generally decreased as the effective risk reduction decreased. It should be noted that these estimates are very sensitive to uptake at the highest price. Given the small sample sizes associated with each cell, a single affirmative response to the highest price will have a large impact on the Turnbull estimator. These Turnbull estimates can also be used to calculate VSL for each subgroup by dividing the average monthly WTP by the annual risk reduction (after adjusting units appropriately). Though WTP estimates are generally greater for larger risk reductions, VSL estimates are greater for the smaller risk reduction scenarios. This suggests that WTP was not linearly related to size of risk reduction. Although these estimates serve as a starting point for analysis, their accuracy is limited by the small sample sizes used per cell.

Next, we examine the most common reasons that respondents gave for not purchasing the supplement at either the initial or the follow-up price. These reasons included (1) no money available to make the purchase (61%) and (2) price is too expensive (30%). The most common reasons that respondents gave for purchasing the supplement included (1) supplement is good for prevention of death (91%) and (2) believe that child has a risk of death (4%). These results suggest that respondents generally understood the scenario and gave thoughtful answers.

3.3.2 Multivariate analysis

Coefficient estimates and cluster corrected standard errors from three multivariate probit models are shown in Table 5. Table 6 shows the marginal changes in the probability of purchase

for a 1-unit change in each variable after averaging over the sample. Because child age is directly correlated with respondent age (i.e. older respondents have older children), respondent age was strongly correlated with the estimated risk reduction and omitted from Model 1 to avoid endogeneity problems. The first model omits the potentially endogenous variable for water treatment. The second and third models include variables for water treatment and respondent age, and allow for comparison between continuous and dummy variables for income and respondent age.

Consistent with the raw data results, the analysis revealed that price was strongly correlated with the decision to purchase the supplement. As shown in Table 6, the probability of purchase decreased by about 5% for a US$0.50 increase in price. The effective risk reduction was also significantly correlated with the decision to purchase the supplement. The marginal probability of purchase would increase by about 2% if the risk reduction were to be increased by 1/10,000 per year. When respondent age is added to the model, the coefficient for effective risk reduction becomes smaller but remains significant. The coefficient for respondent age was of marginal significance in Models 2 and 3. This suggests that older parents would be less likely to purchase the supplement; however, this finding may be an artifact of the collinearity between respondent age and effective risk reduction. The predicted marginal decrease in probability is about 0.5% per additional year of respondent age or about 10% if all respondents were older than 55 years.

(Tables 5 and 6 here)

The coefficients for male respondents were consistently positive and the average marginal effect (4-7%) was quite large; however, these findings were not significant at the 10% level. There was no difference in demand among respondents living inside versus outside the ICDDR,B service area. All models showed that respondents with more education and higher income were significantly more likely to purchase the supplement. Average marginal probability

of purchase increased by about 10% for a one-category increase in education compared to 5% increase for a one-income-quartile increase.[56]

Respondents who were given time to think (TTT) overnight about the hypothetical cholera vaccine had significantly lower stated WTP for the hypothetical nutritional supplement, possibly because they had more time to consider budgetary constraints prior to approaching the supplement section of the interview. Giving respondents TTT produced a 16% average marginal decrease in the probability of agreeing to purchase the hypothetical supplement. The coefficient estimate for male children was positive for all three models, but of borderline significance. The average marginal increase in probability of purchase would be about 7% if the entire sample had male children.

Respondents' estimates of baseline risk of death for children in their villages were not included in the multivariate analysis because so many respondents were unable to provide estimates. In addition, we learned that respondent estimates of mortality risk were compromised by the way the question was presented as discussed in Section 3.2. As a result, we decided to focus exclusively on the actual risk reductions faced by children.

Average willingness to pay for a nutritional supplement was estimated from the parameter estimates for the first probit model. The population average WTP for the supplement was about US$1.50 per month for all three models. This estimate is within the range of Turnbull estimates presented in Table 4. The probit estimate is an average across all age groups and effective risk reduction scenarios. Thus, the probit estimate is not directly comparable to any of the Turnbull estimates presented in Table, but should fall within the range of estimates.

Approximate VSL estimates can be calculated by dividing the coefficient for risk reduction by the price coefficient. Although the average WTP per month was constant across

[56]For marginal effects, we had to estimate a model that combined dummy categorical variables into a single ordered categorical variable for income quartiles and education categories.

models, VSL estimates varied from US$16,000 to US$22,000 because the coefficient for risk reduction varied across the model specifications depending on whether respondent age was included and how respondent age was specified.

These VSL estimates represent the average tradeoff between mortality risk reduction and price in the demand equation. As demonstrated in Table 4, it is likely that WTP for a nutritional supplement would not be a linearly function of the magnitude of risk reduction. Rather, VSL estimates depend on the magnitude of risk reduction presented. We believe this is generally the case for this population. Thus, parents appear to be more willing to purchase the supplement for younger children that face greater baseline risks of death. However, they are still willing to purchase the product for older children with much smaller risks of death as long as the price is reasonable.

3.4 Comparison to implicit VSL from the cholera vaccine willingness to pay

We were also able to compare our nutritional supplement VSL results with implicit VSL estimates developed from the cholera vaccine scenario. As reported in Islam et al. (2008), analysis of negative binomial household demand models revealed that male respondents, high-income respondents, and respondents residing in the government service area had the highest demand for cholera vaccines. Results also showed that giving respondents time to think about the purchasing decision reduced demand considerably. Average WTP per vaccine was highest for young children (US$2.40 to $3.80), followed by school-age children (US$1.20 to $2.30), then adults (US$1.05 to $1.60).

Because the ICDDR,B diarrhea hospital provides free treatment for cholera patients, the patients' *ex ante* private costs of illness (COI) for cholera are very low. From a coinciding study of cholera disease burden we estimated that annual incidences of cholera were about 1.3 cases per 1,000 children less than 5 years old and about 0.7 cases per 1,000 children age 5 to 17 years. Private COI per case was about US$7 for children less than 17 years old. These correspond to

annual *ex ante* private cholera COI estimates of US$0.010 for children less than 5 years old and US$0.004 for children age 5 to 17 years. Thus, *ex ante* private COI estimates are much smaller than estimated average WTP per vaccine. We postulate that stated WTP for cholera vaccines is primarily due to the avoided risk of death and avoided risk of pain and suffering.[57] Given our assumption that cholera caused 15% of the deaths from diarrhea reported in Table 2, the estimated mortality risk reduction from a 50% effective 3-year cholera vaccine would be about 1.0×10^{-4} for children age 1 to 4 years and 8.4×10^{-6} for older children. The resulting implicit VSL estimates were about US$28,000 to $37,000 for younger children and US$170,000 to $230,000 for older children.

The implicit VSL for younger children is quite similar to the estimate for the nutritional supplement. This might seem surprising, as the number of deaths due to cholera comprise a relatively small fraction of the total number of child deaths in the Matlab area. However, the valuation scenario for the cholera vaccine required an up-front payment of the entire cost of the vaccine, which was then effective for 3 years. As a result, the total mortality risk reduction from a one-month supply of the nutritional supplement is similar to the protection provided by the cholera vaccine over a 3 year period (i.e. the risk of death from cholera was about 1/36 of the total risk of death from disease for young children). The implicit cholera VSL estimate for older children was much larger than that for the nutritional supplement. When considering the vaccine purchase decision for older children, parents might have overestimated the risk of death. Parents may also have been concerned about mitigating the potential pain and suffering that their older children might endure as a result of becoming ill. Similar to the nutritional supplement results, we find that parents are less willing to purchase vaccines for older children (i.e. WTP is lower); however, parents would still purchase the vaccine at a reasonable price for their older children.

[57] One of the questions in the survey asked respondents to identify the most important benefit of cholera vaccine. Most respondents believed that the most important benefit of a cholera vaccine was to prevent either pain and suffering or risk of death (24%). Very few (8%) cited avoided treatment costs or lost wages as the primary benefit.

After adjusting for the difference in mortality risk, the VSL estimate for older children would appear to be larger, but the estimate should be considered independently from the magnitude of risk reduction.

4. Conclusions

The results of this study are unique in three aspects: (1) they provide an estimate of VSL from a very low-income rural area in a developing country; (2) they provide one of the first estimates of parental WTP for reducing risk of death for a child (the youngest in the household), and (3) they provide a comparison of the value of a mortality risk reduction from a generic risk-reduction product (a hypothetical nutritional supplement) with the value of mortality risk reduction from a specific intervention (a hypothetical cholera vaccine). Our results show that parents are willing to spend about US$1 to US$2 per month, which was 1% to 3% of average monthly income (US$75). These results correspond to VSL estimates of about US$10,000 to US$25,000 for children age one to seventeen years. We would generally expect WTP to be greater for younger children, but VSL estimates to be larger for older children because the difference in WTP is not large enough to offset the much smaller baseline mortality risk faced by older children. This finding appears to be consistent across the nutritional supplement and cholera vaccine scenarios and is also consistent with the findings of other studies that calculate VSL based on variable risk levels (see Table 1).

We do not claim that respondents had full comprehension of the mathematical risk of death discussed in our scenario. Given the widespread lack of education among our respondents, we did not think it was possible to provide in-depth instruction in probability theory in the context of a short, in-person interview. Rather, we wanted our nutritional supplement scenario to (1) encourage respondents to consider the different causes of death for children that are common in their immediate neighborhoods, (2) convey that children's baseline risk of death was small

relative to other random events (such as coin flips or die rolls) and (3) present a hypothetical nutritional supplement that would reduce the already small risk significantly.

The baseline risk of death for children varied by the age of the youngest child, but logistical concerns prevented our interviewers from presenting respondents with baseline mortality risks specific to the child of interest. Thus, all respondents received the same description with a baseline risk that was averaged across age groups. The magnitude of effective risk reduction was then post-corrected for the model estimation. This approach was not ideal and we concede that we could have achieved better results if the baseline risk presented to respondents varied with the age of the youngest child.

Despite this limitation, we believe that our VSL estimates are useful for three reasons. First, our estimates were based a large decrease in baseline risk. This makes it less likely that they are overstated than if we had used small percentage reductions. Unless parents grossly overestimated their children's risk of death, our results should be fairly accurate as long as parents understood the visual depiction of the percentage risk reduction.

Second, our study population was unique in a number of aspects. We believe that because our study involved adults accustomed to participating in local public health surveys (ICDDR,B's systematic efforts over several decades), respondents would be less likely to engage in yea-saying to please our interviewers. This impression was reinforced by highly significant income, education, and price effects on demand, which imply that respondents considered their budget constraints carefully. In addition, we had very good data on the numerical risk of death for children in the community and the primary causes of death.

Third, the VSL estimates for the hypothetical nutritional supplement were similar to implicit VSL estimates for a WTP study of cholera vaccines involving the same population in a separate component of the survey. We can also calculate the ratio of our VSL estimates to respondent income for comparison with the studies presented in Table 1. Our ratio varies from 10 to 30. This range is smaller than those calculated via hedonic wage studies performed in India

(Simon et al. 1999; Shanmugam 2000, 2001), but similar to findings from a stated preference study performed in India (Bhattacharya et al. 2007). Overall, the ratios fall in the lower range of studies presented in Table 1.

In conclusion, as scientists aim to increase the number of vaccines and other health interventions available for children in developing countries, public health providers with limited budgets will be forced to make difficult decisions regarding the needs of their population. The results present in this paper should help them assess the tradeoffs between the cost and mortality risk reductions of different interventions. It also demonstrates that parents are willing to devote a portion of their limited incomes to interventions that improve their children's health. Thus, the implementation of private user fees may help to increase the ability of public health systems to provide new interventions and to broaden the intervention choice sets of households.

Table 1. Summary of relevant literature for VSL hedonic wage and stated preference studies

Researcher	Location, date, and data source	Average risk (10^{-5})	Average annual wage (US$)	VSL estimate (US$)	VSL to annual wage ratio ($/$)
Hedonic Wage Studies					
Viscusi and Aldy 2003	US subsample, 2000[a]	0.1 – 2	30,000	7 million	230
	Summary of studies[a]				
Liu et al. 1997	Taiwan, 1982-1986	2.25 - 3.82	4,100 - 5,100	135,000 - 600,000	33 - 130
	Taiwan Labor Force Survey				
Simon et al. 1999	India, 1985-1991	1.5	1,150	150,000 - 360,000	130 - 310
	Occupational Wage Survey and Annual Survey of Industry				
Shanmugam 2000	Madras, India, 1987-1990	1.0	600	0.75 - 1 million	1,250 - 1,700
	Survey of blue-collar workers				
Shanmugam 2001	Madras, India ,1987-1990	1.0	600	3 million	5,000
	Survey of blue-collar workers				
Averting Behavior Studies					
Blomquist 2004	US subsample, 2000	Not reported	30,000[c]	1.7 - 7 million	60 - 240
	Summary of studies[b]				
Mount et al. 2001	US hedonic study of 1997 vehicle	7 - 50[d]	34,000	3.4 - 6.4 million	100 - 190
	fatality rates and costs (adults)				
Mount et al. 2001	US hedonic study of 1997 vehicle	7 - 50[d]	34,000	2.6 - 7.7 million	75 - 230
	fatality rates and costs (children)				
Blomquist et al. 1996	Adult car seat belt use	5	22,000	1.7 - 2.8 million	75 - 130
	with time and disutility costs, 1983				
Blomquist et al. 1996	Child seat use (under 5 years of age)	10	22,000	2.3 - 3.7 million	100 - 160

Researcher	Location, date, and data source	Average risk (10^{-5})	Average annual wage (US$)	VSL estimate (US$)	VSL to annual wage ratio ($/$)
	with time and disutility costs, 1983				
Carlin and Sandy 1991	US, 1985 IN survey of child car seat use; crash safety data in WA	10	23,000 [c]	430,000 - 550,000	19 - 24
Jenkins et al. 2001	US, 1997, aggregate bicycle helmet price, use, and protection (adult)	0.55	37,000 [c] (lower bound)	2.0 - 4.0 million	54 - 108
Jenkins et al. 2001	US, 1997, aggregate bicycle helmet price, use, and protection (children)	0.4-0.6	37,000 [c] (lower bound)	1.1 - 2.7 million	30 - 70
Stated Preference Studies					
Alberini et al. 2004a	Canada, 1999 and US, 2000	1	47,000 - 53,000	0.9 - 1.5 million	19 - 28
	General	5	47,000 - 53,000	3.7 - 4.8 million	79 - 90
Alberini et al. 2004b	UK, Italy, France, 2002	1	41,000	2.5 million	60
	General	5	41,000	1.1 million	28
Vassanadumrongdee and Matsuoka 2005	Bangkok, 2003	0.3	9,000	1.4 - 1.5 million	150 - 170
	Traffic accidents and air pollution	0.6	9,000	0.9 million	100
Bhattacharya, Alberini, and Cropper 2007	Delhi, 2005 Traffic accidents	4 – 30	3,000	30,000	10
Hammitt and Liu 2004	Taiwan, 2001 Lung and liver cancer/ non-cancer	0.2 - 0.8 [e]	14,000	0.5 - 2.2 million [e]	36 - 160
Liu et al. 2005	Taiwan and Taipei, 2003	0.18	13,000 - 21,000	4.7 - 11 million	220 - 850
	SARS	0.6	13,000 - 21,000	2.8 - 6 million	130 - 460

Researcher	Location, date, and data source	Average risk (10^{-5})	Average annual wage (US$)	VSL estimate (US$)	VSL to annual wage ratio ($/$)
	Bangladesh, 2003	7.5 - 45[f]	1,200	2,300	2
Mahmud 2009					
	General	15 - 90[f]	1,200	1,300	1

[a] Viscusi and Aldy compile a number of studies. The risk reduction, average wage and VSL are ranges shown after conversion to 2000 US$.
[b] Blomquist compiles a number of studies. The risk reduction, average wage and VSL are ranges shown after conversion to 2000 US$
[c] Average household income is not reported in the study. The income reported in the table is taken from (U.S. Bureau of the Census 2004).
[d] Risk of death is calculated based on the sum of risks from 1-car, 2-car, and multi-car crashes. The differences in risk are based on the average risk for different categories of vehicles.
[e] Estimated VSL is calculated by average VSL for 2 in 100,000 and 8 in 100,000 risk reductions. Separate estimates for each magnitude of risk reduction are not available. Only median VSL values are reported
[f] The risk reduction used was either 25% or 50% of the baseline risk by age group. Hence, different age groups received different magnitude reductions. Estimates based on subjective risk were also made, but I only include estimates for objective risk

Table 2. Average annual number of deaths for children in Matlab area by cause (based on data from HDSS annual reports (ICDDR,B, 2002; ICDDR,B 2003; ICDDR,B, 2004)

Age range	<1	1-4	5-9	10-14	15-19	Total
(Population)	(5,764)	(21,024)	(24,985)	(27,024)	(23,944)	(102,741)
Disease related						
Respiratory	70	8.7	2.0	1.0	1.3	83
Diarrhea	17	9.3	2.0	1.0	0	29
Cancer	0.0	2.0	1.3	2.0	0.7	6.0
Infectious	7.0	2.7	1.0	1.3	1.3	13
Nutritional	12	4.3	1.3	1.0	0.3	19
Gastro-intestinal	2.3	0.3	1.0	0.7	1.0	5.3
Cardio-vascular	0.3	0	0	0.3	0.7	1.3
Neonatal	130	0	0	0	0	130
Avg. no. deaths due to disease	245	34	14	11	9	314
Rate of death (per 1,000 children per year)[a]	43	1.6	0.57	0.41	0.39	3.1
Accidents, Injuries	0	0	0	0	0	0
Drowning	3.3	49	8.0	1.3	0.7	63
Homicide/Suicide	1.0	1.0	0.3	1.0	3.0	6.0
Other accident	2.3	1.3	2.0	2.3	1.3	9.3
Avg. no. deaths due to accident/injury[a]	17	58	16	8	9	108
Rate of death[a] *(per 1,000 children per year)*	2.9	2.8	0.6	0.31	0.38	1.1
Other/Unknown	19.7	13.3	11.0	7.4	8.0	59
Avg. no. of deaths (all causes)[a]	260	92	30	19	18	420
Rate of death (all causes)[a] (per 1,000 children per year)	45	4.4	1.2	0.72	0.77	4.1

[a] Deaths attributed to other/unknown were split evenly between disease and accident/injury.

Table 3. Variable definition and descriptive statistics

Variable name	Description	Mean (SD) (N = 532)
Respondent characteristics		
Male	= 1 if male, = 0 if female	0.49 (0.50)
Age	Age (yrs), continuous	41 (9.8)
Hindu	Religion = 1 if Hindu, 0 = else	0.06 (0.25)
Education 1-5 years	= 1 if respondent completed 1-5 years of school	0.36 (0.48)
Education 5-10 years, vocational	= 1 if respondent completed 5-10 years of school, vocational school, or madrassa	0.18 (0.38)
Education more than 10 years	= 1 if respondent completed university, postgraduate or professional course	0.12 (0.32)
Unable to read	= 1 if respondent is not able to read a newspaper	0.53 (0.50)
Household characteristics		
Infants	number of infants age <1 year, continuous	0.12 (0.34)
Young children	number of children age 1-5, continuous	0.7 (0.72)
School-age children	number of children 6-17, continuous	1.7 (1.1)
Adults	number of adults age 18-65, continuous	3.0 (1.5)
Elderly adults	number of elderly adults age >65, continuous	0.20 (0.43)
Log income per capita	Natural log of household income divided by number of household members, continuous	6.6 (0.7)
Age of youngest child	Age (yrs), continuous	7.0 (4.6)
Gender of youngest child	=1 if male, = 0 if female	0.52 (0.50)
Risk behavior, perceptions of disease, vaccination history		
Treat drinking water	= 1 if household treats water for drinking;	0.15 (0.36)
Estimated risk reduction (1/1,000 per year)	= baseline risk (as a function of age) multiplied by the risk reduction presented to the respondent	0.41 (0.36)
Characteristics of research design		
Time to think	= 1 if given time to think overnight, =0 else	0.47 (0.50)
ICDDR,B	Health service area; = 1 if ICDDR,B, = 0 if government	0.37 (0.48)
Initial supplement price	referendum price (Bangladeshi Tk), continuous	104 (150)
Follow-up price	referendum price (Bangladeshi Tk), continuous	80 (160)

Table 4. Raw demand data as a function of price and risk reduction and associated Turnbull VSL estimates

Age group	Baseline risk	Percentage risk reduction	Effective risk reduction (1/1,000 yr)	Coverage Price = US$0.15	Coverage Price = US$0.30	Coverage Price = US$0.74	Coverage Price = US$1.49	Coverage Price = US$7.44	Turnbull Avg. WTP per month	VSL
Age 1-2.9	2.1	20%	0.42	0.9 (n=9)	0.7 (n=17)	0.8 (n=16)	0.4 (n=21)	0.2 (n=6)	US$2.0	US$58,000
	2.1	60%	1.26	0.9 (n=10)	0.6 (n=22)	0.7 (n=13)	0.6 (n=16)	0.1 (n=8)	US$1.5	US$15,000
Age 3 -4.9	1.1	20%	0.22	1 (n=9)	0.6 (n=14)	0.4 (n=8)	0.6 (n=8)	0.1 (n=11)	US$1.3	US$72,000
	1.1	60%	0.66	0.9 (n=7)	0.7 (n=16)	0.4 (n=15)	0.4 (n=5)	0.4 (n=8)	US$3.1	US$56,000
Age 5 - 9.9	0.6	20%	0.12	0.6 (n=11)	0.8 (n=15)	0.5 (n=21)	0.3 (n=18)	0.1 (n=7)	US$0.9	US$92,000
	0.6	60%	0.36	0.8 (n=16)	0.7 (n=18)	0.6 (n=20)	0.2 (n=19)	0 (n=10)	US$0.6	US$21,000
Age > 10	0.4	20%	0.08	0.7 (n=15)	0.6 (n=18)	0.3 (n=20)	0.3 (n=16)	0 (n=7)	US$0.6	US$83,000
	0.4	60%	0.24	1 (n=10)	0.6 (n=9)	0.4 (n=18)	0.4 (n=22)	0 (n=9)	US$0.7	US$36,000

Table 5. Multivariate regression results from the probit models

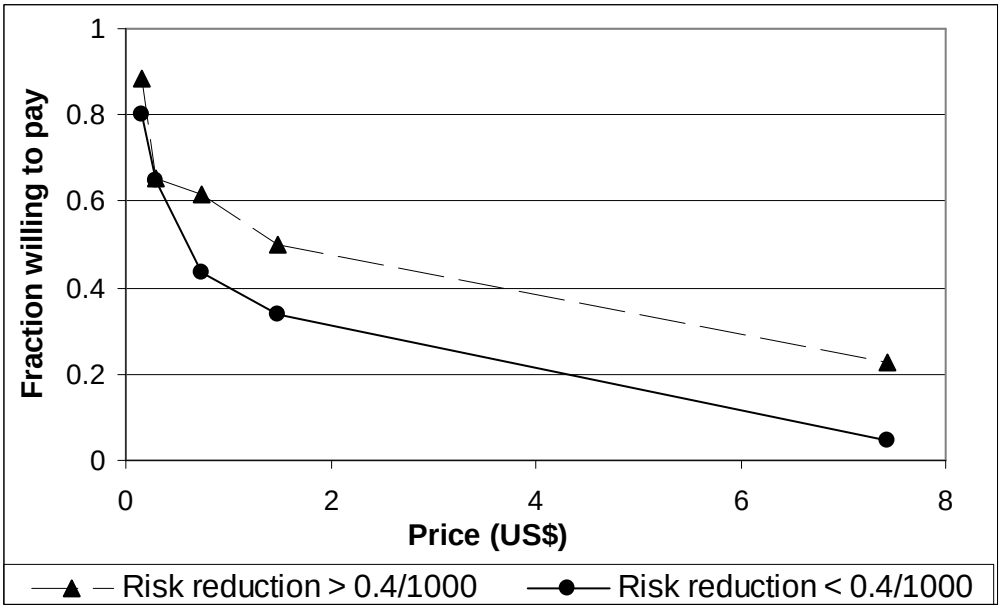
Model	1	2	3
T-statistic in parentheses			
Supplement price	-0.0036***	-0.0036***	-0.0036***
	(-6.9)	(-6.8)	(-6.9)
Male respondent	0.11	0.20	0.12
	(0.75)	(1.3)	(0.76)
Resident from ICDDR,B service area	-0.036	-0.041	-0.04
	(-0.21)	(-0.20)	(-0.20)
Received time to think for	-0.41***	-0.41***	-0.40***
Cholera vaccine experiment	(-3.7)	(-3.4)	(-3.4)
Respondent age		-0.011	
		(-1.5)	
Respondent older than 55 years			-0.25*
			(-1.7)
Risk reduction (annual*1000)	0.45**	0.32*	0.39**
	(2.6)	(1.9)	(2.3)
Education 1-5 yrs.	0.36**	0.35**	0.33**
	(2.2)	(2.1)	(2.0)
Education 6-10 yrs.	0.61***	0.53**	0.60***
	(3.0)	(2.5)	(2.8)
Education >10 yrs.	0.77***	0.71***	0.82***
	(3.0)	(2.7)	(2.9)
Log income per capita	0.31***	0.31***	
	(4.6)	(4.4)	
HH income quartile 2			0.30
			(1.6)
HH income quartile 3			0.36***
			(2.8)
HH income quartile 4			0.37**
			(2.0)
Youngest child is male	0.17	0.17	0.15
	(1.6)	(1.5)	(1.4)
Treats water		0.15	0.16
		(0.65)	(0.77)
Hindu respondent	-0.55*	-0.58**	-0.57**
	(-1.8)	(-2.0)	(-2.0)
Constant	-2.1***	-1.6**	-0.21
	(-4.7)	(-2.5)	(-1.2)
Log likelihood	-296	-297	-297
Average WTP per month	US$1.50	US$1.50	US$1.50
VSL estimate	US$22,000	US$16,000	US$19,000

* indicates significance at the 10% level
** at the 5% level
*** at the 1% level

Table 5. Average marginal effects estimated from probit models dsfdsafdasfsdfsd

Model	1	2	3
Supplement price (increment $0.50)	-0.048 (.0071)	-0.049 (.0071)	-0.0048 (0.0072)
Male respondent (yes/no)	0.040 (0.059)	0.074 (0.059)	0.051 (0.059)
Resident from ICDDR,B service area (yes/no)	-0.012 (0.081)	-0.0014 (0.082)	-0.0038 (0.082)
Received time to think for cholera vaccine experiment (yes/no)	-0.16 (0.043)	-0.16 (0.046)	-0.16 (0.046)
Respondent age (increment 1 year)		-0.0047 (0.0032)	
Respondent older than 55 years (yes/no)			-0.094 (0.058)
Estimated risk reduction (1/10,000 annually)	0.018 (0.69)	0.0013 (0.068)	0.16 (0.068)
Education (increment 1 education category)	0.11 (0.035)	0.10 (0.035)	0.11 (0.037)
Log income per capita (increment 1 log unit)	0.12 (0.027)	0.12 (0.028)	
HH (increment 1 income quartile)			0.053 (0.22)
Youngest child is male (yes/no)	0.066 (0.042)	0.069 (0.045)	0.061 (0.044)
Hindu respondent	-0.21 (0.10)	-0.22 (0.10)	-0.22 (0.10)
Treats water (yes/no)		0.058 (0.090)	0.063 (0.085)

Figure 1. Willingness to pay for hypothetical nutritional supplement



Appendix 4. The development of a marginal cost per DALY function that better incorporates herd protection and herd immunity into cost utility analysis

DRAFT April 28, 2009

DO NOT CITE OR QUOTE

Introduction

As more and more new vaccines and other health interventions are developed, public health practitioners and international donor agencies face increasingly difficult decisions for investing limited resources to improve health in less developed countries. Health economists commonly use cost utility analysis to compare health improvement benefits (as expressed in non-monetary health utility units) and program costs of various interventions via a standardized methodology. Disability adjusted life years (DALYs) or quality adjusted life years (QALYs) are the two most common types of units used to quantify health improvements. The results of these analyses are commonly expressed as the cost per unit change in health utility (i.e. the cost per DALY/QALY saved).

It is commonly known that many health interventions, especially vaccination programs, provide indirect protection effects (i.e. herd protection). For example, when a school-age child receives an influenza vaccine, the child is less like to become ill when exposed (e.g., to infected classmates at school). Since this child is protected by the vaccine, she is also less likely to expose her family or her uninfected classmates to the disease. Thus, the child's vaccination indirectly

protects others from exposure to the disease. The aggregated effect of this reduction in exposure is herd protection.

This herd protection effect leads to a non-constant relationship between coverage and DALYs saved. Thus, the average cost per DALY depends on the coverage rate achieved. Especially for non-infant vaccination campaigns, it would be more informative to report a functional relationship between average cost per DALY and coverage in place of the point estimates or ranges that are commonly reported. It is also useful to define a marginal cost per DALY relationship, which examines the rate of change in cost per DALY as a function of coverage. This marginal cost per DALY function should be useful in targeting efficient coverage rates for vaccination programs. In a developing country context where budgets are extremely limited, these marginal considerations may help program planners to target interventions more efficiently to stretch limited resources. This appendix examines how to estimate cost utility functions rather than cost utility values to better demonstrate the impacts of herd protection for vaccination programs. I present both average and marginal cost functions, based on empirical herd protection relationships for cholera and influenza vaccination programs.

Background

There are many example of cost utility studies available in the literature; however, there appears to be little consensus about how to account for herd protection. Many cost utility analyses have omitted herd immunity effects entirely (Beutels et al., 2002; Beutels et al., 2007; Cook et al., 2008; Kim et al., 2009). Other analyses incorporate herd protection data from other sites for a pre-specified coverage rate (Armstrong et al., 2007; Lee et al., 2007; Lloyd et al., 2007; Jeuland et al., 2009). The pre-specified coverage rate usually represents universal coverage for a particular subgroup.[58] Many vaccination analyses are undertaken for infant vaccination programs,

[58]Both the Jeuland et al. and Cook et al. analyses examine three scenarios in which different groups receive vaccinations: 1) young children less than 5 years of age, 2) all children less than 14 years of age, and 3)

in which population coverage rates increase over time as successive cohorts of infants participate. Herd protection effects are then estimated as the coverage rates of young children gradually increases with time from the initiation of the vaccination program. Vaccination benefits are aggregated based on incidence reductions for both vaccine recipients and for non-recipients. By properly accounting for herd protection effects, the estimated cost per DALY saved may be reduced considerably. This is especially important when incidence is indirectly reduced for elderly age groups who may be most at risk from disease mortality (Lee et al., 2007; Lloyd et al., 2007).[59]

While cost utility analysis is the most common tool used to judge the economic attractiveness of vaccination programs, most of the published literature that examines how to target vaccinations in the presence of herd protection uses alternative frameworks. Epidemiologists and economists have used optimization models to examine the optimal distribution of vaccines given either a predetermined limitation in the number of vaccines available or an economic constraint. For example, Patel et al. (2005) examined the optimal allocation of influenza vaccines across age groups in the event of a shortage. They found that prioritization of vaccines for school-age children could maximize the number of cases and deaths avoided, even though the risk of death is greatest for elderly adults. This finding suggests that school-age children have the much greater capacity to spread influenza relative to other age groups.

Brito et al. (1991) examine the optimal tax or subsidy required to achieve a socially optimal vaccine coverage rate. They assume that 1) vaccines are 100% effective, 2) benefits are homogenous across the community, and 3) that costs vary across the community. They also prove

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universal vaccination of all age groups.

[59]It is important to note that herd protection effects may be detrimental for some diseases if vaccine protection wanes with age and if the disease is more serious for adults than children, such as the varicella vaccine M. Brisson and W. J. Edmunds (2002), 'The cost-effectiveness of varicella zoster virus (VZV) vaccination in Canada', Vaccine 20: 1113-1125, M. Brisson and W. J. Edmunds (2003), 'Economic Evaluation of Vaccination Programs: The Impact of Herd-Immunity', Medical Decision Making 23: 76-82..

that compulsory vaccination is always non-optimal compared to a tax/subsidy scheme. Francis (1997; 2004) expands upon this work by incorporating a common mathematical model of epidemic disease spread, the susceptible-infected-recovered or SIR model. This dynamic model is applicable to epidemic disease spread, for which prevalence increases until the number of susceptible individuals is offset by the number of recovered (i.e. immune) individuals. At this point, prevalence begins to decline back to zero. Unlike Brito, Francis assumes that both vaccine costs and benefits are homogenous across the community. Francis solves for a threshold prevalence such that 1) when prevalence is below the threshold, no one is vaccinated and 2) when prevalence is above the threshold, everyone is vaccinated. Francis also examines a static equilibrium for which an optimal price is derived. Boulier et al. (2007) also employ the SIR model, but focus on how SIR parameters impact the optimal coverage rates. They also assume homogenous vaccine benefits and costs in the community. The optimal coverage rate depends primarily on the infectiousness of disease.

Methodology

Empirical herd protection data is available for both cholera and influenza vaccination programs. The relationships between coverage and community incidence reduction for cholera and influenza vaccination programs are shown in Figure 1. The community incidence reduction represents the combined impacts of direct and indirect vaccination protection across the entire community. Thus, it represents a weighted average of incidence reductions for vaccinated and unvaccinated subgroups. The cholera data corresponds to reported herd protection from a 1985 cholera vaccination trial conducted in Matlab, Bangladesh (Clemens et al., 1990; Longini Jr. et al., 2007). The influenza data is taken from an article that examines the optimal vaccine distribution across age groups to protect against pandemic influenza similar to the 1968–1969 A (H3N2) Hong Kong influenza pandemic (Patel et al., 2005). It is important to note that the cholera data are based on observed results from a community vaccination trial that targeted

children and adult females while the influenza data are based on stochastic optimization simulations. In other words, the cholera data are based on actual uptake rates, while the influenza data are taken from scenarios in which vaccinations are optimally distributed across age groups. Non-optimized influenza vaccination would probably result in considerably reduced herd protection effects.

The protection-coverage relationships shown in Figure 1 are quite similar. The rate or change in community incidence reduction is slightly greater for influenza, but differences are never greater than 10%. According to the models, it should be possible to achieve at least 80% reductions in community incidence with coverage rates of less than 50%, even though neither vaccine is 100% effective. Further increases in coverage from 50% to 100% would result in minor changes in community incidence, as shown by the near horizontal trajectory of the functions in Figure 1.

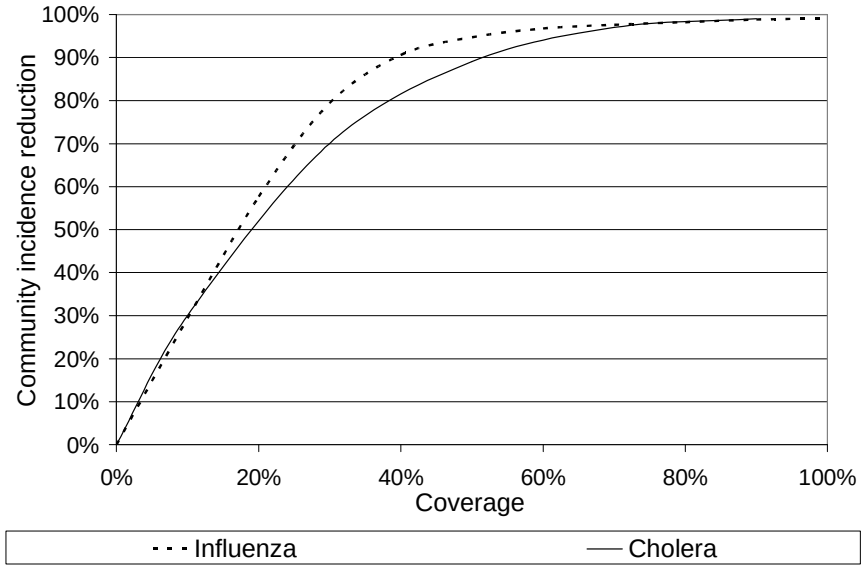

Figure 11. Community average herd protection as functions of cholera and influenza vaccination coverage rates (cholera data is from Longini et al. 2007; influenza data is from Patel et al. 2005)

The cost per DALY saved depends on a number of considerations, including disease incidence, vaccine effectiveness, case fatality rate, life expectancy, fixed and marginal costs of vaccination, and herd protection. I first develop a generalized model that is flexible enough to deal with a number of population subgroups that may be heterogeneous in incidence, case fatality rate, life expectancy or in herd protection impact. Assume that a population can be subdivided into n homogeneous subgroups, each with baseline incidence INC^0_i for $i = 1$ to n. After the initiation of a vaccination program, the incidence in subgroup i (INC_i) depends on the joint coverage rates of the individual subgroups based on a series of functions, V_i.

(1) For each i=1 to n, $INC_i = INC^0_i \cdot V_i (COV_1, COV_2, \ldots COV_n)$

where V_i translates observed vaccination coverage rates into expected incidence rates by subgroup.

The changes in incidence rates can be used to calculate the number of cases avoided through vaccination. This number of cases avoided must then be converted into saved DALYs by subgroup. The total number of saved DALYs incorporates both reductions in morbidity (years of life lost to disability, YLD_i) and mortality (years of life lost, YLL_i). The number of life years saved per case avoided for subgroup i is estimated via eq. 2 where CFR_i is the case fatality rate for subgroup i and LE_i is the average remaining life expectancy for subgroup i.

(2) YLL_i saved per case = $(CFR_i / 0.03 \cdot (1 - \exp(-0.03 \cdot LE_i))$

The number of life years saved per death avoided is greater for younger subgroups, which have more life years remaining. However, these future life years are discounted at a 3% rate, which reduces differences across age groups. The number of years lost to disability, YLD_i, is calculated based on the disability caused by disease. These calculations depend on the duration of illness, DUR_i, and severity weight, W. Severity weights depend on the disutility caused by disease; illnesses that completely incapacitate sufferers have larger weights than those with minor symptoms. Acute illnesses that cause long term disability (e.g., blindness or paralysis) tend to have larger estimates of YLD_i per case.

(3) YLD_i saved per case = $(1 - CFR_i) \cdot DUR_i \cdot W$

Since neither cholera nor influenza tend to cause long term disability, consideration for long term disability is omitted from eq. 3. The total DALYs saved per case avoided is the sum of YLL_i and YLD_i.

(4) $DALY_i$ saved per case avoided = $(YLL_i + YLD_i)/ (1 + 0.03)^t$

The total number of DALYs saved is equal to the number of cases avoided multiplied by the average DALYs saved per case. This can be calculated as a function of coverage based on

(5) $$Total\ DALYs = \sum_{i=1}^{n}[DALY_i \cdot POP_i \cdot INC_i^0 \cdot (1 - V_i(COV_1, COV_2, ..., COV_n))]$$

where POP_i is the population of group i and $1 - V_i(COV_1, COV_2, ..., COV_n)$ represents the change in incidence inclusive of direct and herd protection effects.

The cost per DALY saved is calculated by dividing the total cost of the intervention by the total number of DALYs saved. The accounting of costs depends on the perspective taken (e.g., government, insurance provider, social). If the government or insurance provider perspective is taken, the cost calculation should subtract expected treatment expenditure savings from total costs of the vaccination program. If the social perspective is used, one should add recipient time and travel costs to receive vaccinations as well as subtract private treatment savings. This analysis takes the public health care provider perspective and subtracts public treatment savings from total costs to calculate a net public cost. This net public cost is expressed non-parametrically as

(6) $Cost = C(COV_1, COV_2, \ldots, COV_n) -$

$$PWF \cdot \sum_{i=1}^{n} COI_i \cdot POP_i \cdot [INC_i^0 \cdot \{1 - V_i(COV_1, COV_2, ..., COV_n)\}]$$

where $COIi$ is the average public COI per case avoided, PWF is the present worth function, which discounts future public treatment cost savings over the duration of vaccination protection, and $C(COV_1, COV_2, \ldots, COV_n)$ is a cost function. The average cost per DALY saved is eq. 6 divided

by eq. 5 as shown below. Note that the average cost per DALY may be negative if the public treatment savings exceed the cost of providing vaccinations.

(7) $$\text{DALYCOST}(COV_1, COV_2, \ldots, COV_n) = [\text{C}(COV_1, COV_2, \ldots, COV_n) - \sum_{i=1}^{n} COI_i \cdot POP_i \cdot (INC_i^0 \cdot (1 - V_i(COV_1, COV_2, ..., COV_n))] \; / \; \sum_{i=1}^{n} DALY_i \cdot POP_i \cdot INC_i^0 \cdot (1 - V_i(COV_1, COV_2, ..., COV_n))$$

Rather than reporting a function, most authors report point values for vaccination programs. However, eq. 7 would only be independent of coverage if 1) there is no herd protection, 2) the marginal cost per vaccination delivered is constant, and 3) there are no fixed costs. In general, all three of these conditions would rarely be met. The cost function may have a fixed cost component and either an increasing or decreasing variable cost component, depending on advertising requirements, population density and other considerations. The herd protection functions shown in Figure 1 indicate exponentially decreasing returns to scale with regard to incidence reduction. This herd protection function impacts both the public COI savings and saved DALYs components of equation 7.

The marginal cost per DALY saved can be calculated by taking a partial derivative of eq. 7 with respect to coverage by subgroup. It can also be numerically approximated by specifying a small change in coverage (by subgroup) and measuring the corresponding changes in program costs and DALYs saved that result.

Given a portfolio of various types of vaccinations and a fixed budget, the maximum number of DALYs saved would be achieved if the marginal cost per DALY saved were approximately equal across interventions and subgroups. This could be accomplished using numerical optimization, but that approach is not the focus of this appendix. When considering a portfolio of interventions, the following considerations should be included in marginal cost per DALY calculations by disease and by subgroup: 1) relative differences in the number of DALYs saved per case avoided, $DALY_i$ 2) expected baseline incidences, INC_i^0 3) relative differences in

herd protection impacts, $V_i(\cdot)$ and 4) relative differences in the costs of vaccine provision and distribution .

Thus, diseases with large disability impacts per case, high baseline incidences, large herd protection effects, and low vaccination costs would be targeted. The herd protection effects ($\delta Vi(\cdot) / \delta COVi$) are likely to express the greatest changes as functions of coverage. According to Figure 1, the marginal herd-protection-induced changes in incidence are likely to decrease considerably as coverage increases. In contrast, the number of *DALYi* and INC_i^0 are constants. The marginal cost of vaccination may vary with coverage, but this variation is likely to be small relative to the expected variation in herd protection.

Results

In this section, I present empirical simulations based on literature estimates of parameters. The primary purpose of this chapter is to examine DALY calculations as functions of coverage in consideration of herd protection effects. A number of important parameters for cholera and influenza vaccination programs are summarized in Table 1. These parameters are either taken from literature estimates or assumed.

These cholera vaccination parameters are based on endemic infection rates and common treatment practices in the rural Matlab, Bangladesh area. The influenza vaccination parameters are taken from the United States. The infection rate and herd protection parameters are based on an influenza pandemic similar to the 1968 Hong Kong influenza pandemic, while the treatment and vaccination costs are estimated based on existing practices for influenza in the United States. Note that treatment costs for pandemic influenza likely exceed those for common influenza, but pandemic-specific data are not available.

The populations under consideration for both programs are assumed to be 1,000,000 people. The fixed costs of the programs are assumed to be about US$0.10 per person or US$100,000 in total (Lauria et al., 2009). The marginal cost per influenza vaccination in the

United States is assumed to be US$60, based on a consultation cost of US$50 and a vaccine procurement cost of US$10 (Jordan et al., 2006). This is much greater than in Bangladesh where delivery cost is estimated at US$0.50 per dose and procurement cost is estimated US$0.60 per dose. The total cost is estimated to be US$2.2 for two doses of cholera vaccine (Jeuland et al., 2009).

The costs of these vaccination programs could be partially offset by the public savings from treating fewer cases of illness at public clinics. The public cost of treating cholera in Bangladesh is estimated at US$20 per case based on operating costs at a non-profit hospital in Matlab, Bangladesh (Poulos et al., 2008). Influenza treatment cost per case is estimated at US$25, assuming that 27% of infected patients would seek treatment at an average cost of US$125 per outpatient case in American hospitals (Jordan et al., 2006).

The attack rate for the 1968-69 Hong Kong influenza pandemic was about 34%, resulting in about 340 cases per 1,000 persons in one year (Patel et al., 2005). Incidence rates were consistent across age groups. The cholera incidence rate is based on a passive surveillance study conducted at the Matlab hospital (Deen et al., 2008). Cholera incidence is greater for young children age 1-5 years than for school-age children or adults. The average annual incidence across age groups is about 1.6 cases per 1000 persons. The average durations per illness are assumed to be 7 days for influenza and 3 days for cholera. The DALY weight is 0.27 for influenza, which is based on the value for malaria and other febrile diseases. The DALY weight for cholera is assumed to be 0.105, which corresponds to the weight for diarrheal disease ((WHO), 2003). A cholera-specific weight is not available from the WHO; it is likely that cholera is more severe than other types of diarrheal disease.

The influenza case fatality rate is a weighted average of the mortality rates observed for the 1968-69 Hong Kong influenza pandemic (Patel et al., 2005). The influenza mortality rate is greater for elderly adults (2%) than for other adults (0.3%) or children (0.025%). The cholera case fatality rate is assumed to be 1% because it is usually possible to reduce cholera case fatality rates

below 1% at hospital (Ryan et al., 2000). However, it is unlikely that all cholera patients would arrive at hospitals for treatment. The remaining life expectancy is based on life expectancy tables for Bangladesh and for the United States. The remaining life expectancies reported in Table 1 represent weighted averages of the age-specific case fatality rates, incidences and life expectancies across age groups. The average remaining life expectancy is greater for cholera fatalities because influenza deaths are concentrated among the elderly. Cholera deaths are more evenly spread across age groups with a slight concentration among children who are more likely to contract the disease.

These data can be used to calculate the average number of life years saved per case avoided (*YLL*) and the average number of disability years saved per case avoided (*YLD*). Since neither disease leads to long term disability, the number of life years saved are significantly greater than the number of disability years saved, $YLL > YLD$. For influenza, the average *YLD* saved per case avoided are about 0.005, compared to about 0.030 *YLL* per case. For cholera, the difference is even larger (about 0.001 YLD per case compared to 0.26 YLL per case). Overall, the number of DALYs saved per cholera case avoided are considerably greater for cholera (0.26) than for influenza (0.035). This would indicate that about 7.4 influenza cases would be approximately equal to one cholera case in terms of the number of DALYs saved.

Table 8. Cholera and influenza parameter inputs for DALY calculations

Variable	Cholera vaccination program parameters	Influenza vaccination program parameters
Literature estimated values		
Baseline annual incidence, INC^0, cases per 1,000 persons	1.6	340
Variable cost, *C*, US$	2.2	60
Herd protection coefficient, γ	5.1	6.6
Public COI per case- *PUBCOI*, US$	20	25
Duration of vaccine protection (years)	3	1
DALY weight, *W*	0.105	0.27
Case fatality rate, *CFR* (%)	1	0.3
Expected remaining life years, *LE*	52	12
Assumed parameters		
Population, *POP*	1,000,000	1,000,000
Fixed cost, *F*, US$	100,000	100,000
Length of illness (days)	3	7
DALY discount rate (%)	3	3
Present worth factor, *PWF*	2.58	1
Calculated parameters		
YLD saved per case	0.001	0.005
YLL saved per case	0.26	0.030
DALYs saved per case	0.26	0.035

The empirical relationships between coverage and incidence are approximately calculated from the data presented in Figure 1. It is possible to fit exponential functions to these relationships via transformed linear regression. The intercept is fixed such that the baseline incidence would be observed at zero coverage. The resulting functions are

(8) $\text{Cholera } V_c(COV_c) = INC_c^{\,0} \cdot \exp(-5.1 \cdot COV_c)$

(9) $\text{Influenza } V_f(COV_f) = INCf^{0} \cdot \exp(-6.6 \cdot COV_f)$

where COV_c and COV_f are included as the fractions of the total population receiving cholera or influenza vaccinations. These relationships suggest that the rates of decrease in incidence rates

decline exponentially as coverage rates increase. Thus, the greatest rates of change occur at low coverage rates.

The total cost, public COI savings, and DALYs saved are shown as functions of coverage rates in Figures 2 and 3 for cholera and influenza vaccination programs. The total cost functions have intercepts at the fixed costs of vaccination and increase at a constant marginal cost per vaccination. The public COI savings are small relative to total costs for both diseases. For cholera, public treatment cost savings are not even sufficient to cover the fixed costs of the vaccination program, even at 100% coverage. Since the number of DALYs saved and public COI savings are linear projections of the changes in incidence rates, the shapes of these functions are similar to the herd protection curves shown in Figure 1. Thus, while total costs increase linearly, public COI savings plateau at higher coverage rates. The public COI savings are greater as a percentage of total costs for influenza vaccination than for cholera vaccination.

For both vaccination programs, there are rapid increases in the numbers of DALYs saved for coverage rate increases from 0-30%. The DALY functions appear to plateau at coverage rates greater than 50%, such that additional vaccinations result in very small changes in DALYs. This is because incidence rates have already been reduced to almost zero at 50% coverage.

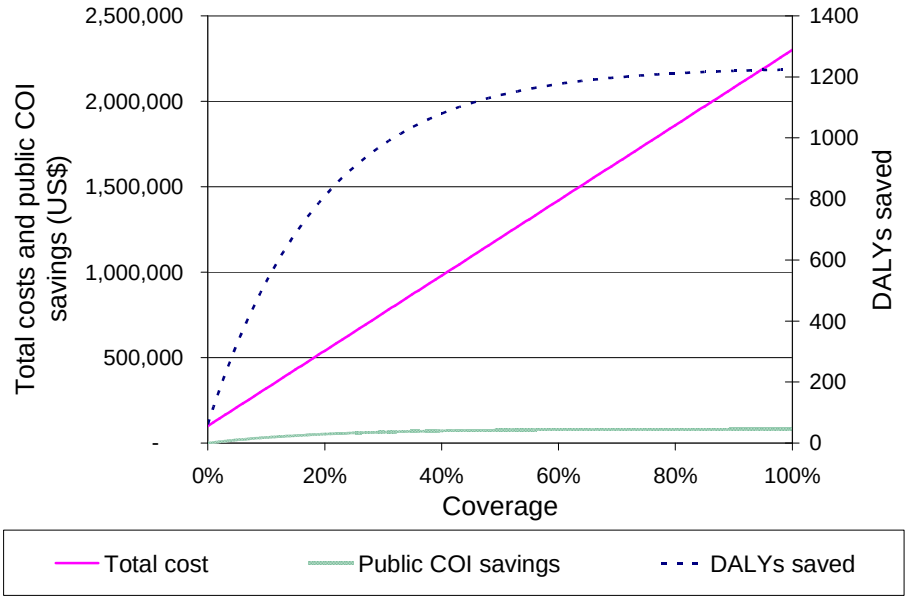

Figure 12. DALYs saved, total costs, and public COI savings as functions of coverage for cholera vaccination

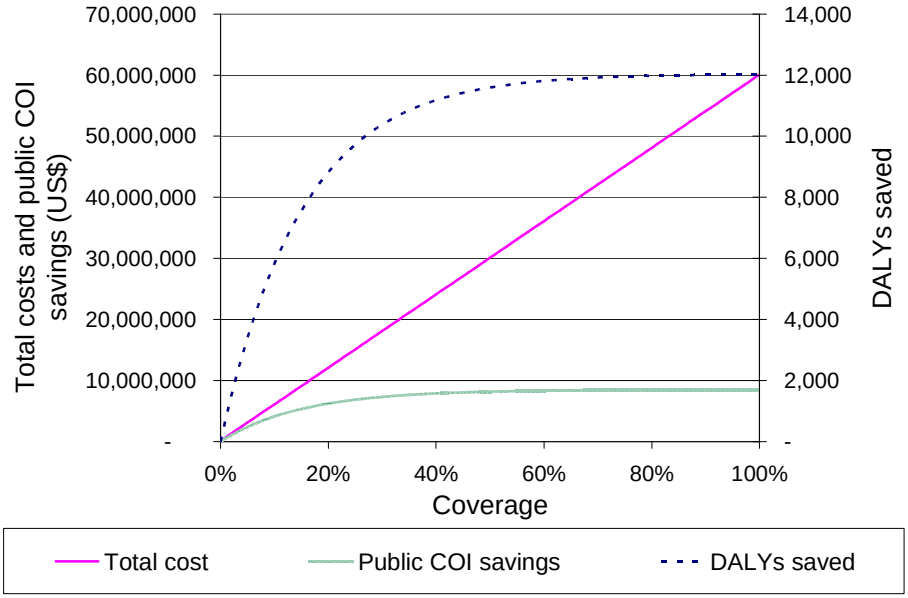

Figure 13. DALYs saved, total costs, and public COI savings as functions of coverage for influenza vaccination

The average net costs per DALY with and without consideration for herd protection are shown in Figures 4 and 5 for cholera and influenza respectively. Without herd protection, the

average net costs per DALY decline to asymptotic values as coverage rates increase. The average net cost per DALY is very high at low coverage rates because fixed costs must be absorbed by the small fraction of the population that is vaccinated. As coverage increases, the net costs per DALY decrease to asymptotic values of about US$3,000 per DALY for cholera vaccination in Matlab and about US$8,000 per DALY for vaccination against pandemic influenza in the United States.

With consideration of herd protection, the average net costs per DALY are much more variable as functions of coverage. For cholera, the average net cost per DALY decreases at very low coverage rates because of the impact of fixed costs (i.e. because the average cost per vaccination is very high at low coverage rates). At coverage rates greater than 5%, the average net cost per DALY increases as coverage increases due to the diminishing returns of herd protection. The average net cost per DALY for cholera vaccination increases from US$600 at 15% to US$1,800 at 95%.

These increasing costs per DALY are demonstrated more clearly by the marginal cost per DALY function. The marginal net cost per DALY is independent of fixed costs and increases exponentially based on the shape of the herd protection function. The marginal net cost per DALY increases from about US$500 at 10% coverage to about US$900 at 20% coverage to about US$40,000 at 80% coverage for cholera vaccination. Thus, it would cost about 80 times more to achieve a marginal increase of one saved DALY at 80% coverage than at 10% coverage.

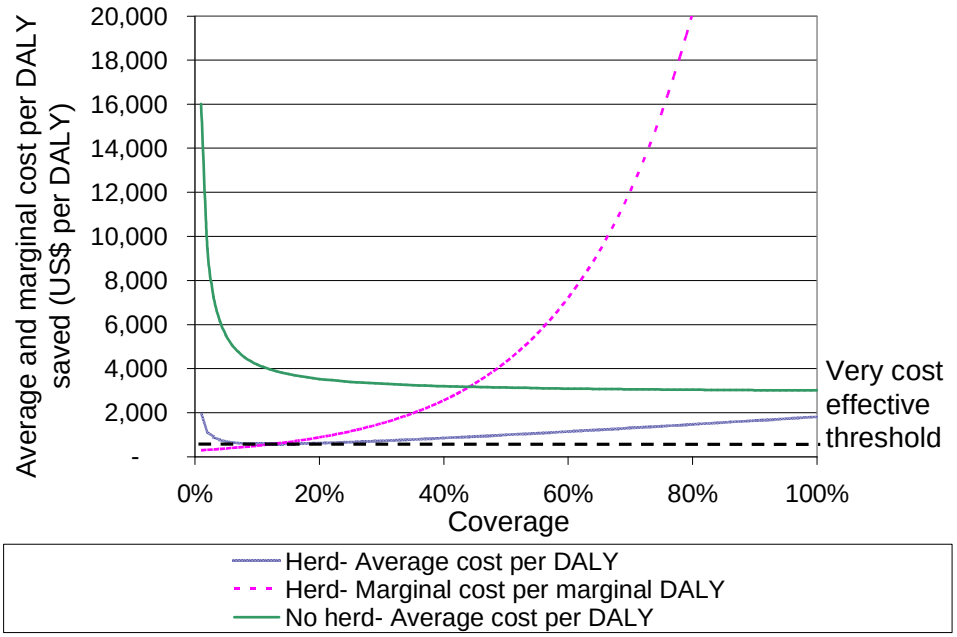

Figure 14. Average and marginal cost per DALY for cholera vaccination

The trends in the average net cost per DALY and marginal net cost per DALY functions are similar for influenza vaccination. The average net cost per DALY increases from about US$1,300 at 15% coverage to about US$4,000 at 95% coverage for influenza vaccination. The marginal net cost per DALY increases from about US$1,300 at 15% to about US$380,000 at 80% coverage, a 300-fold increase.

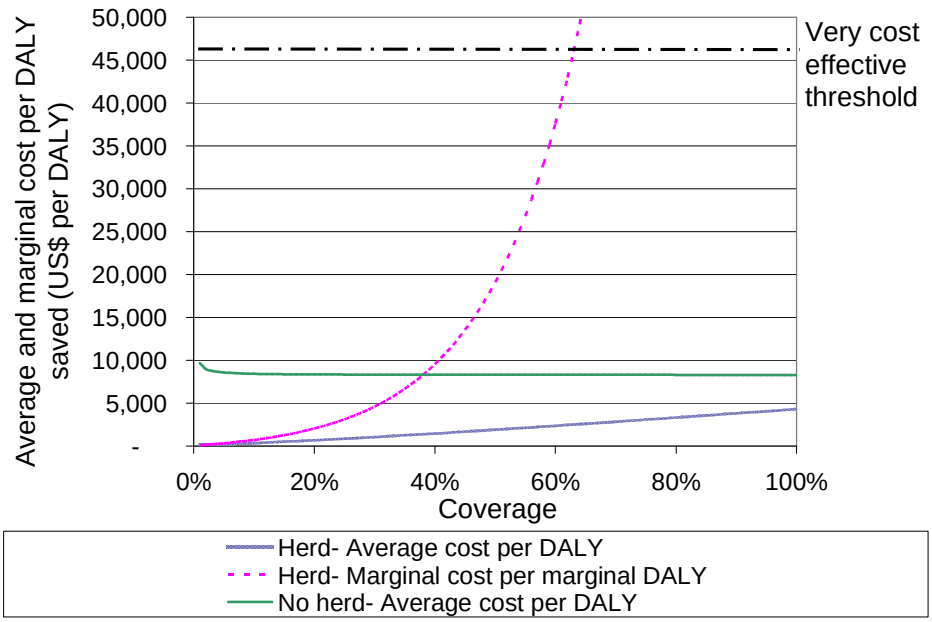

Figure 15. Average and marginal cost per DALY for influenza vaccination

The average and marginal net cost per DALY functions can be compared to commonly used thresholds for cost-effective interventions. According to the World Bank, a 'very cost-effective' intervention has a net cost per DALY ratio less than per capita GDP. A 'cost-effective' intervention has a ratio less than three times per capita GDP (Jeuland et al., 2008). Note that the average GDP per capita is much greater in the United States (about US$ 46,000) than in Bangladesh (about US$ 510).

Given pandemic influenza incidence rates in the United States, vaccination would be considered 'very cost effective' at any coverage rate based on the average cost per DALY functions (with or without accounting for herd protection). Using the marginal cost per DALY function instead of the average cost per DALY function, influenza vaccination would be considered 'very cost effective' at any coverage rate less than 60%. Thus, program planners could maximize coverage rates with little fear of misallocating resources; however, special effort should not be made to increase coverage beyond about 80%.

The cost effectiveness of vaccination against endemic cholera in Matlab, Bangladesh requires more careful consideration. The average cost per DALY is almost equal to the 'very cost effective' threshold at low coverage rates (10-30%). The marginal cost per DALY is less than the 'very cost effective' threshold at coverage rates less than 10% and less than the 'cost effective' threshold at coverage rates less than 30%. At 50% coverage, the marginal cost per DALY is three times greater than the 'cost effective' threshold. These findings demonstrate that the marginal cost per DALY calculation is highly sensitive to the coverage rate under consideration. While a cholera vaccination program can be considered 'cost effective' at low to moderate coverage, there should be little incentive to increase coverage rates beyond 50% based on the parameters included in this simulation.

Conclusions

This appendix examines the relationship between coverage rates and cost utility metrics in the presence of herd protection impacts. The calculations incorporate actual incidence-coverage relationships from epidemiological studies of endemic cholera in Bangladesh and for an influenza pandemic similar to the 1968-69 Hong Kong strain observed in the United States. Both epidemiological studies suggest an exponential relationship between vaccination coverage rates and reductions in disease burden, which infer that it is possible to achieve substantial reductions in incidences at modest coverage rates. These studies further show that increases in coverage beyond 30-50% have very little impact on disease burden because incidence rates have already been reduced considerably.

Cost utility metrics are useful for prioritizing across health interventions. When the average cost per DALY metric falls between the 'very cost effective' and 'cost effective' thresholds, but this does not guarantee that a vaccination program should be implemented. Financial resources for health interventions are likely to be extremely limited in many developing countries. There may be many interventions are considered 'cost effective', but for which funding

is unavailable. It is necessary to check if other health interventions that pass these thresholds may have more attractive ratios (Jeuland et al., 2008). With many 'cost-effective' options, it becomes especially important to consider the marginal cost per DALY as well as the average cost per DALY metrics. As shown in Figure 4, vaccination against endemic cholera in Matlab, Bangladesh is likely to fall between the 'very cost effective' and 'cost effective' thresholds based on average cost per DALY calculations. However, the marginal cost per DALY is almost certain to be excessive at any coverage rate greater than 50%. Thus, any vaccination portfolio would probably improve efficiency by diverting resources to other health interventions rather than try to boost cholera vaccination coverage rates beyond 50%.

These findings suggest that it might be more efficient to introduce more types of vaccines at lower coverage rates than to introduce a smaller number of vaccinations at high coverage rates. For example, given a refugee setting with limited resources, it might be better to introduce two vaccines at 50% coverage than to introduce a single vaccine at 100% coverage. If one endeavors to take advantage of herd protection, it is important to ensure that vaccines are distributed uniformly across an area. In a best case scenario, a program administrator would attempt to evenly split different types of vaccinations within households (i.e. half of the household members would receive vaccine A while the other half would receive vaccine B). This should better retard disease spread for both diseases relative to a program in which coverage rates vary widely from one neighborhood to the next.

Given a pandemic influenza strain that invades the United States, it may be 'very cost effective' to maximize vaccination coverage rates because disease prevalence is likely to be very high. In this situation, it is important to continue to provide vaccinations beyond 50% because the threat is so great. This situation may be similar to the provision of the low cost vaccinations included in the Expanded Programme of Immunization (EPI) already available in low income countries. Thus, it is important not to assume that all vaccinations should be provided at lower coverage rates, only vaccinations that are considered marginally cost effective.

Although I merged age groups to allow for better visualization of trends, it is also important to note that this approach should allow for efficient allocations of vaccinations across age groups. For example, Patel et al. (2005) report that the influenza mortality rate is much greater for elderly adults than for other groups. Thus, the number of DALYs saved per case avoided is greatest for elderly adults. However, the number of DALYs saved per case is only one important parameter (shown in eq. 7). Patel et al. also find that vaccination of children has a much greater impact on herd protection than vaccination of other groups. In the marginal calculations, this greater influence of herd protection from child vaccination relative to DALYs saved per case avoided for elderly vaccinations should be evident. In other words, the marginal cost per DALY saved for the child subgroup should be less than the marginal cost for the elderly subgroup across a range of coverage rates.

There are some limitations to the model developed in this chapter. First, the relationships between coverage rates and herd protection effects are not well-studied for many vaccines. Even in cases where linkages between herd protection and vaccination coverage are well established, differences across subgroups or across locations may not be well understood (e.g., it may not be known if adult or child vaccinations have greater impacts on herd protection for a particular vaccine). Second, it may be difficult to achieve the 'optimal' coverage rates calculated from the marginal cost per DALY analysis. It may be possible to introduce different pricing or rationing schemes to achieve these coverage rates, but there may be considerable uncertainty in predicting populations' responses to these policies.

In spite of these limitations, I believe this model should be useful. When incidence changes are converted to health utility units, the cost effectiveness of a particular intervention is heavily dependent on the coverage rate achieved. While herd protection is a well known attribute of vaccination and other health intervention programs, it is rarely rigorously considered in economic evaluations. This chapter develops a new method of accounting for herd protection in cost utility analysis and also demonstrates the need for better research in regard to the empirical

relationships between coverage and herd protection. I believe that the marginal cost per DALY metric is better suited for determining appropriate coverage levels and for targeting vaccinations across population subgroups in comparison to commonly used analyses.

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