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COST-EFFECTIVENESS OF ROTAVIRUS VACCINATION AND PREDICTORS OF DIARRHEAL DISEASE IN CHILDREN DURING A COMPLEX HUMANITARIAN EMERGENCY

BY
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An abstract of
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Abstract

COST-EFFECTIVENESS OF ROTAVIRUS VACCINATION AND PREDICTORS OF DIARRHEAL DISEASE IN CHILDREN DURING A COMPLEX HUMANITARIAN EMERGENCY

BY
Lisa M. Gargano, PhD

Background: A complex humanitarian emergency (CHE) involves a complete breakdown of authority that goes beyond the mandate or response capacity of any single country or United Nations agency. Diarrheal diseases are often a principal cause of morbidity and mortality in children under five during a CHE. Rotavirus causes up to 40% of diarrhea cases in Africa. Two vaccines for rotavirus are safe and effective in children. The goal of the first aim of this thesis was to assess if rotavirus vaccination would be cost-effective during a CHE. The goal of the second aim was to determine correlates of diarrhea disease in children under five in Somalia.
Methods: A cost-effectiveness analysis was performed comparing no vaccine, one-dose, or two-doses of rotavirus vaccine. A univariate sensitivity analysis was carried out to examine the extent to which the uncertainty in the variables affects our estimates. An incremental cost-effectiveness ratio (ICER) to compare no vaccination to one- or two-doses of rotavirus vaccine was performed. For aim two, data was from the 2005-2006 MICS3. The outcome was diarrhea among children under five in past two weeks. Variables included child's age, gender, vitamin A receipt, measles vaccination, polio vaccine, any vaccine, vaccine refusal, breastfeeding, maternal hygiene behaviors, and water treatment.
Results: Variables influencing the ICER most were vaccine effectiveness and access to outpatient and inpatient care. Rotavirus vaccination would avert up to 12,469 deaths and would save $71,124 in medical treatment costs. The base-case ICER was $17.76 per life saved. For aim two, in the unadjusted analysis, gender, age, measles/MMR vaccine, receipt of any vaccine, washing hands before feeding child, and washing hands after cleaning baby's bottom were all associated with diarrheal disease. The final model consisted of age, gender, receipt of any vaccine, and washing hands after cleaning baby's bottom. The kappa statistic for the model's ability to predict a case was 0.1304.
Conclusions: Rotavirus vaccination is a "very cost-effective" intervention, as defined by WHO as ≤ 1 per captia GDP (Somalia $220.30). Targeted interventions to prevent diarrheal diseases in children under five during a CHE should focus on vaccination and maternal hygiene behaviors.

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CHAPTER I: INTRODUCTION

Introduction and rationale

A complex humanitarian emergency (CHE) often involves a complete breakdown of authority that goes beyond the mandate or response capacity of any single country or United Nations (UN) agency.[1] Somalis constituted the third largest refugee group under the United Nations High Commissioner on Refugees (UNHCR) responsibility, with almost 1.1 million people at the end of 2011, three times as many as in 2004.[2] Diarrheal diseases are often a principal cause of morbidity and mortality in complex humanitarian emergencies. Rotavirus is the most common cause of severe diarrhea among infants and young children.[3] Children in the poorest countries account for 82% of rotavirus deaths with almost half (230,000) occurring in Africa.[4] Previous studies estimated that rotavirus infection occurs in 25%-40% of children hospitalized with diarrheal illness in Africa.[5] A recent study of the global burden of rotavirus reported that seven countries had a rotavirus-associated mortality rate among children under five years of age of greater than 300 deaths per 100,000 children annually (Sierra Leone, Niger, Angola, Afghanistan, Liberia, Somalia, and Mali), with all but one in Africa.[6] Despite two rotavirus vaccinations having been approved for use in 100 countries, only 28 use it in their routine immunization program. Rotavirus vaccination has not been administered during a CHE, despite the fact that diarrheal diseases are often a principal cause of morbidity and mortality in complex emergencies, especially among young children.

Purpose statement

The purpose of the thesis is to explore potential ways to decrease the under five mortality from diarrhea during a CHE.

Specific Aims

Aim 1: To examine the cost-effectiveness of rotavirus vaccination during a CHE

Aim 2: To determine the predictors of diarrheal disease among children under five years of age in Somalia, a country experiencing a protracted complex humanitarian emergency

Significance statement

It will be important to understand both the cost-effectiveness of rotavirus vaccination during a CHE and to understand specific factors that can predict diarrheal disease among Somali children in order to allocate limited resources to the most effective, and more importantly, appropriate interventions.

CHAPTER II: REVIEW OF LITERATURE

Complex humanitarian emergency

A CHE often involves a complete breakdown of authority that goes beyond the mandate or response capacity of any single country or UN agency.[1] This leads to the creation of refugees (those who leave their homeland) and internally displaced persons (IDPs). The end of 2011 considered 42.5 million people worldwide as forcibly displaced due to conflict and persecution. They included 15.2 million refugees and 26.4 million IDPs.[2] On average, 47% of all persons of concern were children under the age of 18 years, including 13% under the age of five.[2]

Infectious diseases continue to cause high levels of morbidity and mortality during a CHE. Measles in children has been shown repeatedly to be a major, and often the most important, cause of death in refugee and displaced children. However, through immunization campaigns this cause of mortality has been greatly reduced.[7] Today, diarrheal diseases are often a principal cause of morbidity and mortality in complex emergencies. Common pathogens, such as rotavirus and *Escherichia coli* are often important causes of diarrhea outbreaks, but *Vibrio cholerae* and *Shigella* species have also caused devastating outbreaks.

Rotavirus and rotavirus vaccine

Rotavirus is the most common cause of severe diarrhea among infants and young children.[3] It is a genus of double-stranded RNA virus in the family Reoviridae. The virus is transmitted by the fecal-oral route. It infects and damages the cells that line the small intestine and causes gastroenteritis. By five years of age, nearly every child in the world has been infected with rotavirus at least once.[8] However, with each infection, immunity develops, and subsequent infections are less severe; adults are rarely affected.[9,10] There are five subgroups of this virus,

referred to as A, B, C, D, and E.[11] Rotavirus A, the most common, causes more than 90% of infections in humans.

Where appropriate resources are available, rotavirus is usually an easily managed disease of childhood, but worldwide the World Health Organization (WHO) estimates that 527,000 children under the age of five years die of rotavirus each year[4] and almost two million more become severely ill.[12] Public health campaigns to combat rotavirus focus on providing oral rehydration therapy for infected children and vaccination to prevent the disease.[13]

In 2006, two vaccines against rotavirus A infection were shown to be safe and effective in children: 2 dose Rotarix by GlaxoSmithKline™ and 3 dose RotaTeq by Merck™.[14,15] Both are administered orally and contain attenuated live virus. Rotavirus vaccines are licensed in more than 100 countries, but only 28 countries have introduced routine rotavirus vaccination.[16] The incidence and severity of rotavirus infections has declined significantly in countries that have acted on the recommendation and have introduced the rotavirus vaccine into their routine immunization programs.[17] In Mexico, which in 2006 was among the first countries in the world to introduce rotavirus vaccine, the diarrheal disease death rates from rotavirus dropped by more than 65% among children aged two years and younger during the 2009 rotavirus season.[18] In Nicaragua, which in 2006 became the first developing country to introduce the rotavirus vaccine, investigators recorded a substantial impact, with rotavirus vaccine preventing 60% of cases against severe rotavirus and cutting emergency department visits in half.[19] In the United States, vaccination has reduced rotavirus-related hospitalizations by as much as 86% since 2006.[20] The vaccines may also prevent illness in non-vaccinated children by limiting exposure through reducing the number of circulating infections.[20]

Mortality, morbidity, and burden of rotavirus disease – developing countries

Burden of Rotavirus Disease

Africa

Children in the poorest countries account for 82% of rotavirus deaths with almost half (230,000) occurring in Africa.[4] Previous studies estimated that rotavirus infection occurs in 25%-40% of children hospitalized with diarrheal illness in Africa.[5] In Africa, rotavirus infection/disease occurs in 17% of infants less than 6 months of age, 75% of infants less than 12 months of age, and 83% of children under 18 months of age.[5] One study in eight sub-Saharan African countries found rotavirus in 40% of samples collected from hospitalized children.[21] There was a large range of rotavirus positive specimens from 29% in Tanzania to 52% in Ghana. The picture in northern Africa is similar with a range of rotavirus infections of 22% to 41% among children with acute gastroenteritis.[22] In South Africa, the mean rate of rotavirus among diarrheal patients was 24% among hospitalized children and 15% among children treated as outpatients.[23]

Middle East

Studies in the Middle East also show a high burden of rotavirus disease. There is a large regional variability (16%-61%) of rotavirus cases among acute gastroenteritis in children less than 5 years of age.[22]

Latin America

The burden of rotavirus was variable in Latin America from 2006-2007, the period before the introduction of rotavirus vaccine to some of the countries. The overall percent of hospitalizations for diarrhea among children aged less than 5 years who were rotavirus positive was 31.5%, with a range of 26%-47%.[24]

Mortality

Rotavirus-associated mortality rates among children aged less than five years varied among countries. One report from Guinea Bissau showed 3.4 rotavirus deaths per 100 infants per year.[25] Studies on country-specific rotavirus mortality among infants showed Nigeria at 80-90 deaths per day, Cameroon 50-60 deaths per day, and South Africa had 10-12 deaths per day.[4,23] A recent study of the global burden of rotavirus reported that seven countries had a rotavirus-associated mortality rate among children under five years of age of greater than 300 deaths per 100,000 children annually (Sierra Leone, Niger, Angola, Afghanistan, Liberia, Somalia, and Mali).[6] Annual mortality of among children under five years due to rotavirus in the Middle East and northern Africa varied from less than 10 per 100,000 (Israel, Kuwait, Bahrain, UAE, and Oman) to greater than 100 per 100,000 (Iraq and Yemen). In northern Africa (Egypt, Libya, Morocco, and Tunisia), the annual mortality among children under five years due to rotavirus ranged from 14 to 34 per 100,000.[22]

Morbidity - Hospitalization

Studies in South Africa and Kenya found that rotavirus is more common in hospitalized children than in outpatients.[23,26] In Egypt, two studies reported hospital admission rates due to rotavirus gastroenteritis among young children varied between 14% in southern Egypt and 45% at two government hospitals in the Nile River Delta.[22] Hospitalization rates were 39% among children under 2 years of age with rotavirus gastroenteritis in Iran and 31% among children younger than five years of age in Turkey.[22] Another Turkish study found that rotavirus gastroenteritis caused a significantly higher rate of hospital admission compared with non-rotavirus gastroenteritis (31% vs. 14%).[22] An Oman study estimated that by the age of five years,

one in 16 children will require hospitalization due to rotavirus.[22] In Venezuela, 85% of rotavirus hospitalizations occurred during the first year of life.[27]

Mortality and burden of rotavirus disease – Countries with experience of CHEs

There are limited studies of the burden of rotavirus in countries that have experienced complex humanitarian emergencies. One study in the Democratic Republic of Congo, a country long suffering from protracted conflict, found that of sampled acute gastroenteritis cases in children aged under 5 years, 76% were positive for rotavirus.[28] A study of two low-income communities in Karachi, Pakistan found that among children under 5 years with severe diarrhea 17% had rotavirus infection.[29] In Colombia, the number of cases related to rotavirus of any degree of severity is estimated to be 30% of all children by 2 years of age. The number of these cases that would require an emergency visit is 37% and 17% would require hospitalization.[30]

Economic burden of rotavirus disease

There are currently no studies on the economic burden of rotavirus disease during a CHE. We can look at studies done in developing countries for an estimate of the economic burden of rotavirus disease. A study in Ghana found that the annual national treatment costs for rotavirus ranged from $907,116 to $1,851,280 for outpatient clinic visits and from $701,833 to $4,581,213 for hospitalizations.[31] This leads to an estimated cost of $1.37 to $2.80 per outpatient visit and $15.70 to $101.81 per hospitalization. Another study from Uganda estimated that the total costs of rotavirus hospitalizations was $400,000 per year and $1.3 million per year for rotavirus outpatient and health center visits with the total economic burden of rotavirus disease for the healthcare system of $1.7 million per year or $1.19 per child under 5 years old.[32]

Cost-effectiveness analysis

Cost-effectiveness analysis (CEA) is a type of economic evaluation that examines both the costs and health outcomes of alternative intervention strategies. CEA compares the cost of an intervention to its effectiveness as measured in natural health outcomes (e.g., "cases prevented" or "years of life saved"). CEA results are presented in a cost-effectiveness ratio, which expresses cost per health outcome (e.g., cost per case prevented and cost per life year gained). CEA is generally used to either: compare alternative programs with a common health outcome, or assess the consequences of expanding an existing program.[33]

CEA is important for decision makers who are often faced with the challenges of resource allocation. Resources are scarce; therefore, they must be allocated judiciously. CEA is used to identify the most cost-effective strategies from a set of options that have similar results. These options have a common health outcome: the number of cases of a disease prevented by the vaccine compared with cost of vaccine and its administration. CEA can be used to identify the options that prevent the most cases at the least cost.[33]

Cost-effectiveness analysis for rotavirus vaccination

There have been several CEA studies of rotavirus vaccination impact in developing countries. A recent analysis of the impact of rotavirus vaccination in 72 Global Alliance for Vaccines and Immunizations (GAVI)-eligible countries found that using the WHO's cost-effectiveness threshold based on per capita gross domestic product (GDP), the vaccines were considered cost-effective in 68 of the 72 countries (~94%).[34] Under the base-case assumption (70% coverage), vaccinating one single birth cohort would prevent about 55% of rotavirus-associated deaths in the 72 GAVI-eligible countries. A 10-year routine rotavirus vaccination program would prevent 0.9-2.8 million rotavirus-associated deaths among children aged less

than 5 years in the poorest parts of the world, depending on the scale-up scenarios. Over the same intervention period, rotavirus vaccination programs would also prevent an estimated 4.5-13.3 million hospitalizations and 41-107 million cases of outpatient clinic visits in the same population.[34] In India, a rotavirus vaccination program would prevent 44,000 deaths, 293,000 hospitalizations, and 328,000 outpatient visits annually, which would avert $20.6 million in medical treatment costs. Even at $7 per dose, vaccination would be highly cost-effective.[35]

Mass vaccination campaigns

The goal of mass vaccination campaigns or supplementary immunization activities (SIAs) is to interrupt circulation of a disease by immunizing every child within a certain age range, regardless of previous immunization status. The idea is to capture children who are either not immunized, or only partially protected, and to boost immunity in those who have been immunized. This way, every child in the most susceptible age group is protected against the specific infection at the same time – instantly depriving the pathogen of the fertile seedbed on which its survival depends.[36] Mass campaigns are carried out when there is high potential for an outbreak. The cost of mass campaigns and supplementary immunization activities vary by country and disease. For oral polio vaccine (OPV), the UNICEF cost was US$0.128 in 2011.[37] Operational costs for one round of OPV SIAs varies from a low of US$0.17 per child in India to a high of almost US$0.60 per child in several African countries, with the average being US$0.20 for operational costs, not including the vaccine.[38] One study in India found that the total cost for a single round of oral SIA was US$0.48.[39] For measles, the average cost is US$1 but can also vary depending on country. In Somalia and South Sudan, the unit cost is much higher at about US$3 per child due to high operational costs, mainly logistics (Heather Papowitz, personal

communication, August 7, 2012). The cost of a nationwide measles vaccination campaign conducted in Afghanistan was estimated at $0.78 per child vaccinated.[40]

Success of mass vaccination campaigns

Measles – In 2008, the Kosi River floods in Bihar, India led to rapid displacement followed by rehabilitation of the affected population. A strategically planned activity of measles SIAs combined with vitamin A administration proved to be successful in maintaining coverage and preventing outbreaks and deaths due to measles. Vaccine coverage during the relief phase in camps reached 75% of 6 month through 14 year old children. In addition to measles and vitamin A, OPV was administered to children and tetanus vaccination to pregnant women.[41]

Polio –SIAs using OPV have been the key tool in the polio eradication efforts. National (NID) and sub-national (SNID) immunization days are conducted in an attempt to reach every household. Mop-up campaigns are then held to try to vaccinate those children not captured during the NID or SNID. Independent polio campaign monitoring is carried out to assess the quality and impact of SIAs. Real-time, independent monitoring data attempt to answer the question, "How many children did we reach with vaccine?".[42]

Measles during a CHE – A nationwide supplemental measles vaccination campaign conducted throughout 2002 in Afghanistan vaccinated 82% of the national target population (10,299,878 children aged 6 months through 12 years).[40] During March-August 2004, a region wide measles vaccination campaign targeting all children aged 9 months to 15 years was conducted in camps and neighboring communities in Darfur, Sudan. Approximately 93% of the accessible population and 77% of the total target population were vaccinated during the campaign. This effort appeared to have reduced the number of measles cases and deaths due to measles.[43] Measles campaigns

were conducted during June-August 2004 in the 10 refugee camps in eastern Chad with coverage ranging from 80%-92%.[43] Estimated measles vaccination coverage in Somalia was 46% in both 2010 and 2011 with only 20% in 2010 and 35% in 2011 of districts reporting ≥ 80% coverage.[44]

Predictors of diarrheal disease

Behavioral risk factors for diarrhea include poor nutritional status, micronutrient deficiency, and short duration of breastfeeding.[45,46] Inadequate hygiene behaviors are also a risk factor for diarrhea, these include feces around pit-hole/slab, feces seen in the compound, and no hand washing after cleansing child's feces.[45] Other behaviors that are a risk factor are using uncovered containers to transport drinking water and not using a home drinking water treatment.[45] Female children are more likely to suffer from diarrhea than male children.[47] Children in households' with low purchasing power, poor sanitation conditions, and mothers' who are under 19 years of age or of lower education are at an increased risk for diarrhea.[46,48]

Somalia context

Somalia has been without a central government since a military coup in 1991. Years of civil war followed, which has devastated much of the country's infrastructure, including its healthcare system.[49] Multiple attempts to restore the government since 1991 have been unsuccessful, and Somalia remains in protracted conflict, with a large population of IDPs with inadequate access to health and social services.[50] In 2011, Somalia was the third largest country of origin for refugees, with more than 300,000 people fleeing due to conflict, violence, drought, and famine.[2] Indicators of the collapse of the health system include child and maternal mortality rates being among the highest globally[51] and record low levels of routine child immunization coverage, which have remained at these levels for the past 20 years.[52] Somalia's routine immunization services, which are heavily supported by UNICEF and partner agencies, use both

fixed health facilities and outreach activities into communities to deliver vaccination. However, security problems and inadequate resources hamper coverage of these services. Inadequate infrastructure has resulted in repeated cholera outbreaks and further disruption of scarce resources and basic services.[53]

Conclusions

Rotavirus continues to be a major health issue in developing countries. Effective and safe vaccines exist to prevent rotavirus infection but their use in countries that are of the highest need remains poor. During a CHE, diarrheal disease is one of the leading causes of death for children under five. Mass campaigns provide an effective strategy to reach a large number of children during a CHE and are currently used to administer measles vaccination, providing a system to administer rotavirus vaccine. Somalia is a country that has been in a state of chronic conflict for decades with poor health and basic infrastructure making it prone to epidemics and diarrheal diseases, and serves as a model for health issues and potential application of interventions during a CHE.

CHAPTER III: METHODOLOGY

Introduction

The first aim of this thesis is a CEA of rotavirus vaccination during a CHE. The second aim of this thesis is to investigate the predictors of diarrheal disease in Somalia using UNICEF's Multiple Indicator Cluster Survey 3 (MICS3) which was carried out in 2005-2006.[54] We used Somalia as a model for CHE, since the country remains in conflict and experiences periodic drought and famine, both of which cause large population movement within Somalia and to neighboring countries of Kenya and Ethiopia, with majority immigrating to Kenya with resulting poor infrastructure to prevent diarrheal diseases.[2]

Aim 1: To examine the cost-effectiveness of rotavirus vaccination during a CHE

Procedures

Population

The study population for the CEA was the 2012 birth cohort in Somalia. GAVI reports this to be 424,594.[55]

Perspective

To be applicable to the broadest audience, a societal perspective is the most appropriate for the economic analysis.

Timeframe and Analytic Horizon

The timeframe for this analysis was two months. The Rotarix vaccine is recommended at 2 and 4 months of age but can be given as early as six weeks or as late as 14 weeks, six days. All doses must be given by eight months. As stated by Haddix *et al*., "the analytic horizon of a prevention-effectiveness study should extend over the time period during which the costs, harms, and benefits of the intervention are incurred".[56] The analytic horizon for this analysis is one year.

Costs

Cost estimates were obtained from several sources. We used GAVI Alliance price for the Rotarix of $2.50 per dose.[57] Operational costs were estimated from UNICEF at $3.00 per child (Heather Papowitz, personal communication, August 7, 2012). We used standardized WHO-CHOICE (CHOosing Interventions that are Cost Effective) to estimate the per diem costs of hospitalization and outpatient visits.[58] Somalia estimates were not available so we used the average of Ethiopia and Kenya, two neighboring countries where the majority of Somali refugees seek asylum. The cost of outpatient care was US$1.01. We multiplied the per diem cost by the average length of stay for a child hospitalized for rotavirus (3 days) to calculate the total cost of a hospital stay. The cost of one day of hospitalization (inpatient) was US$3.70 and the total cost of hospitalization for rotavirus was US$11.10.[58]

Vaccine Program Coverage and Effectiveness

For base case estimates and lower and upper limit of vaccination coverage, we used several data sources for measles vaccination coverage in Darfur, Sudan, Afghanistan, and refugee camps in Kenya.[40,43,59,60] Base case, and lower and upper limit estimates of vaccination effectiveness were obtained from a study done in El Salvador, which calculated both one and two dose effectiveness.[61] This study was selected because it was the only published study in a developing providing vaccine effectiveness after one-dose of rotavirus vaccine.

Data Analysis

Decision analysis model. The costs and benefit of implementing a rotavirus immunization program during a CHE were compared using Excel 2010 (Redmond, WA) (Figure 1). The model was analyzed under baseline scenario in order to determine the costs of different options: immunizing with one dose, two doses, or no vaccination. Key variables used in the model were

varied using univariate sensitivity analysis. In this model, the current practice of no vaccination is compared with a vaccination program in which either one or both doses of Rotarix are given. With any immunization program, some children may not receive vaccination (less than 100% coverage), and because vaccine efficacy is less than 100% against rotavirus diarrhea, some vaccinated children also will become ill (Figure 1). The model inputs include disease burden, rotavirus prevalence, vaccine coverage, vaccine effectiveness, cost of vaccine administration, price of the vaccine, outpatient costs, inpatient costs, percent who receive outpatient care, and percent who receive inpatient care. We did not consider in direct costs such as time lost to parents or transportation costs.

Sensitivity analysis. Starting from the baseline scenario, univariate sensitivity analyses were carried out to examine the extent to which the uncertainty in the variables affects our estimates. During the time of a CHE, a SIA is often conducted. These are traditionally for measles[7], but will be assumed in this study to be conducted to rotavirus as well. Since vaccination coverage during an emergency SIA may not be complete, we conducted a sensitivity analyses on this variable.[44] Vaccine effectiveness of an oral antigen is dependent on many factors, such as access to presence of diarrhea at time of vaccination, nutritional status, and receipt of vitamin A so sensitivity analyses was performed on this variable as well.[62] Access to care, outpatient and inpatient, varies depending on mobility of target population, security, and presence of non-governmental and international governmental organizations. In addition to access to healthcare, access to clean water and sanitation can affect rotavirus disease burden. Since these services are uncertain during a CHE, we also performed sensitivity analysis on rotavirus disease burden.

Cost-effectiveness. Incremental cost-effectiveness ratios (ICERs) were expressed as cost per life saved.

Assumptions. Several assumptions were made for this analysis. The first is the proportion of diarrhea due to rotavirus is similar between general population in developing countries and CHE-affected population (40%). The second is that 90% of those who receive treatment will survive.[63] Thirdly, the severity of disease is the same regardless of vaccination status. Fourth, baseline rotavirus vaccine coverage is zero. Fifth, without treatment any sick child will die, most likely from complications of severe dehydration given the age of the cohort. Sixth, we assumed that all children will be vaccinated on time but all will not receive two vaccines. Finally, given the mobility of the population and security issues we assumed access to inpatient care is half that of outpatient care.

Aim 2: To determine the predictors of diarrheal disease in children under five in Somalia

Procedures

Data source

The Multiple Indicator Cluster Survey (MICS) survey tools are developed by UN Children's Fund (UNICEF) after consultations with relevant experts from various UN organizations as well as with interagency monitoring groups. UNICEF works closely with other household survey programs, in particular the Demographic and Health Surveys program, to harmonize survey questions and modules and to ensure a coordinated approach to survey implementation, with the objective to provide comparability across surveys and to avoid duplication of efforts. The survey questionnaires are modular tools that can be adapted to the needs of the country. MICS are typically carried out by government organizations, with the support and assistance of UNICEF and other partners. Technical assistance and training for the surveys is provided on questionnaire content, sampling and survey implementation, data processing, data quality, data analysis, and report writing and dissemination.[54]

The third round of MICS (MICS3), was carried out in over 50 countries in 2005-06, has been an important data source for monitoring the Millennium Development Goals with 21 MDG indicators collected through MICS3 (particularly indicators related to health, education and mortality). MICS3 was also a monitoring tool for other international goals including the World Fit for Children, the UN General Assembly Special Session on HIV/AIDS and the Abuja Declaration targets for Roll Back Malaria. In MICS3, as in the previous rounds, three model questionnaires were developed: a household questionnaire, a questionnaire for women aged 15-49 years, and a questionnaire for children under the age of 5 years (addressed to the mother or primary caretaker of the child).[54]

Participant selection

The target sample size for the Somali MICS3 was calculated as 6,000 households. For the calculation of the sample size, the key indicator used was the polio coverage among children aged 12–23 months. For the calculation, polio coverage was assumed to be 33 percent. The value of design effect was taken as a default of 1.75, percentage of children aged 0-4 years in the total population was taken as 3.6 percent, and the average household size was taken as 6 members per household. The resulting number of households from this exercise was 5776 households. The average cluster size in the Somali MICS3 was determined as 24 households, based on a number of considerations, including the budget available, and the time that would be needed per team to complete one cluster. Dividing the total number of households by the number of households per cluster, it was calculated that the selection of a total number of 250 clusters would be needed. In each region, the clusters (primary sampling units) were distributed to urban and rural domains, proportional to the size of urban and rural populations in that region. The design followed a 4 stage-sample approach. The first stage is the selection of the districts in each

of the 18 regions of the country selected using probability proportional to size. The second stage is the selection of the secondary sampling units that are defined as permanent and temporary settlements. The third stage is the selection of the cluster(s) within the settlement and the fourth stage is the selection of the households to be interviewed using the Expanded Program for Immunization random walk method.[64]

This analysis focused on the under-five child questionnaire. The questionnaire was administered to all mothers or caretakers for a child who lived with them and was under the age of five years. A separate questionnaire was administered for each eligible child.

Data Analysis

Outcome variable and covariate definitions

Cases were defined as having had diarrhea in the last two weeks. Diarrhea was determined as perceived by the mother or caretaker, or reported by her as the child having three or more loose or watery stools per day, or blood in stool.

Additional demographic and health-related covariates included gender; age (continuous); ever received vitamin A (yes/no); ever been breastfed (yes/no); ever received measles or measles-containing, like measles-mumps and rubella (MMR), vaccine (yes/no); ever received OPV (yes/no); ever received any vaccines (yes/no); ever refused vaccines (yes/no); treat water to make it safe for drinking (yes/no); use measures to prevent water contamination (yes/no); wash hands before feeding baby (yes/no); and wash hands after cleaning baby's bottom (yes/no) (Table 1).

For cases, treatments for diarrhea were also examined. These were: fluid made from a special packet (using local name for oral rehydration salts [ORS] packet solution) (yes/no);

government-recommended homemade fluid (yes/no); and pre-packaged ORS fluid for diarrhea (yes/no).

Statistical analysis

All analyses were performed using SAS version 9.2 (Cary, NC). The study sample dataset was weighted to produce national estimates. The weighted variable was 'chweight'. Descriptive analysis was performed using proc surveyfreq to assess variables among those with and without diarrhea as outcome variable. A validation dataset contained 50 observations with complete data was made to test the models. 'Proc surveylogistic' was used to obtain the crude odds ratios (cOR) of individual variables. Three different models were built using 'proc surveylogistic' to determine the model that would best predict diarrheal disease. Model 1 contained those variables that had a significant OR, which was determined a priori as $p <= 0.05$. Model 2 used a backward elimination process starting with all variables and removing those with the largest p-value, then re-running the model, this process was continued until only variables which were significant at the $p<=0.05$ level remained in the model. Model 3 used forward elimination, starting with the variable with the smallest p-value in the crude analysis, adding back one at a time. Using the Maximum Likelihood Estimate (MLE) Beta values for each model the validation dataset was then run through each model. A Kappa statistic was used as the primary measure to determine which model does the best at predicting the outcome. The Kappa statistic evaluates the accuracy of prediction relative to the accuracy that might have resulted by chance alone.[65,66] The closer to one the Kappa statistic is the better the model is at predicting the outcome. Once the model with the best fit was selected a Hosmer and Lemeshow Goodness of Fit test was performed to assess if there was any indication of two-way interactions. Finally,

variables that have been published to be important predictors of diarrheal disease in children were added back into the model to test if it would improve the fit of the model.

CHAPTER IV: RESULTS

Aim 1: To examine the cost-effectiveness of rotavirus vaccination during a CHE

Baseline scenario

Our analysis found that during a CHE, with a base case of 40% of children with diarrheal disease, of those 30% have rotavirus, with 40% accessing to outpatient case, 20% to inpatient care, receiving one dose of vaccine at 51% effectiveness and 70% coverage: there would be 8,367 deaths averted (36%), 7,215 outpatient visits averted (35%), and 3,638 inpatient visits averted (36%). This baseline scenario would save $7,349 in outpatient costs and $40,381 in inpatient costs (Table 2). Assuming a $2.50 per dose price, the healthcare plus vaccination program would cost $210,687. The ICER was $9.20 (Figure 2).

If a two-dose program was implemented during a CHE with the same base case except for a 76% vaccine effectiveness for two doses, there would be 12,469 deaths averted (53%), 10,842 in outpatient visits averted (53%), and 5,421 inpatient visits averted (53%). This baseline scenario would save $10,951 in outpatient costs and $60,173 in inpatient costs (Table 2). The program would cost $347,897. The ICER was $17.18 (Figure 2).

Univariate sensitivity analysis

Given the uncertainty of variables during a CHE, we performed sensitivity analysis on several variables that could influence the cost-effectiveness of rotavirus vaccination. The univariate sensitivity analysis was first performed on one dose of rotavirus vaccine. At the base case scenario, the ICER for one dose was $17.76. We performed univariate sensitivity analysis on the disease burden of 21%, the ICER remained unchanged at $17.76. When our model was evaluated at the lower and upper limit of vaccine coverage for one dose, the ICER declined slightly to $17.74. When our model was evaluated at the lower limit of one-dose vaccine

effectiveness of 26%, the ICER rose to $40.29, whereas at the upper limit of one-dose vaccine effectiveness of 67%, the ICER decreased from $12.16. When our model was evaluated at the lower limit of access to outpatient care of 20%, the ICER was $13.07. At the upper limit of access to outpatient care of 50%, the ICER was $21.82. Lastly, when our model was evaluated at the lower limit of access to inpatient care of 10%, the ICER was $16.96. At the upper limit of access to inpatient care of 25%, the ICER was $18.35 (Figure 2). A one-dose strategy would cost between $197,491 and $376,171 and save between 25,117 and 47,841 lives (Table 3).

The univariate sensitivity analysis was next performed on two doses of rotavirus vaccine. At the base case scenario, with two doses the ICER was $17.19. We first evaluated the model for disease burden, the ICER remained relatively the same at $17.20. When our model was evaluated at the lower limit of vaccine coverage of 50% for two doses, the ICER remained the same at $17.18 also at the upper limit of 85% for two doses our ICER remained at $17.18. When our model was evaluated at the lower limit of two doses vaccine effectiveness of 64%, the ICER rose to $21.47, whereas at the upper limit of two doses vaccine effectiveness of 84%, the ICER decreased to $15.00. When our model was evaluated at the lower limit of access to outpatient care of 20%, the ICER decreased to $12.67. At the upper limit of access to outpatient care of 50%, the ICER rose to $21.11. Lastly, when our model was evaluated at the lower limit of access to inpatient care of 10%, the ICER was $16.45. At the upper limit of access to inpatient care of 25%, the ICER rose slightly to $17.72 (Figure 2). A two doses strategy would cost between $243,524 and $463,870 and save between 27,988 to 53,309 lives (Table 4).

Aim 2: To determine the predictors of diarrheal disease in children under five in Somalia

Characteristics of children under five with and without diarrhea

There were a total of 6,305 total observations with 1,232 of those having parental perception or report of diarrhea in the last two weeks. Table 5 shows the distribution of the variables by children who had diarrhea and those who did not. There was a significant difference in the distribution of gender ($p=0.012$) and age ($p<0.001$) in those children who had diarrhea vs. those who did not. There were significantly more children who did not have diarrhea who had ever received a measles/MMR vaccine compared to those who had diarrhea ($p<0.001$). There was a significant difference in the distribution of children who had ever received any vaccine and who diarrhea and those who did not ($p=0.001$). The distribution of washing hands before feeding the baby ($p<0.001$) and washing hands after cleaning the baby's bottom ($p<0.001$) were significantly different among children who had diarrhea and those who did not. There was no difference in distribution between children who had diarrhea and those who did not with regards to having ever received OPV, vitamin A, ever refused a vaccine, breastfeeding, measure to prevent water contamination, and treatment of water to make it safe for drinking.

Of those children who had diarrhea, 9.1% (7.5, 10.9) were treated with fluid from ORS packet, 9.4% (7.9, 11.1) were given the recommended homemade fluid, and 7.3% (5.9, 8.9) were treated with a pre-packaged ORS fluid (Table 6).

Model 1 – unadjusted ORs

The first model was built using those variables that had significant cORs (Table 7). The variables in the final model 1 were age, gender, ever received any vaccine, washing hands before feeding the baby, and washing hands after cleaning the baby's bottom (Table 8). This model was run using the MLE Beta distributions in Table 6 to test how robust it was in predicting either

observations in the validation dataset were cases or not. At a 20% cut-off, the Kappa statistic for model 1 was 0.0288 (Table 8).

Model 2 – backward elimination

The variables in the final model 2 were age, gender, ever received any vaccine, and washing hands after cleaning baby's bottom. This model was run using the MLE beta distributions in Table 6 to test how robust it was in predicting either observations in the validation dataset were cases or not. At a 20% cut-off, the Kappa statistic for model 2 was 0.1304 (Table 8).

Model 3 – forward elimination

The indicators in the final model 3 were age, gender, ever received any vaccine, and washing hands after cleaning baby's bottom. This model was run using the MLE beta distributions in Table 6 to test how robust it was in predicting either observations in the validation dataset were cases or not. At a 20% cut-off, the Kappa statistic for model 3 was 0.1304 (Table 8).

Final model

From these three models we selected the one that best predicts whether an observation in the validation dataset was a case or not. This was determined by the Kappa statistic. Models 2 and 3 were selected with a Kappa statistic of 0.1304. Once this model was selected, we assessed if there was any interaction. The Hosmer-Lemeshow Goodness of Fit test resulted in a p-value of 0.5737, indicating that there was no interaction. Other published reports have shown that breastfeeding,[45] vitamin A administration,[67] and hand washing before feeding the child[45] are all correlates of diarrheal disease in children. In order to try to improve the fit of our model, each of these variables was added back and retested on the validation dataset. None of the variables

alone or in any combination resulted in improved prediction ability and were therefore left out of the final model. The final model consisted of age, gender, ever received any vaccine, and washing hands after cleaning baby's bottom.

Summary

The first aim demonstrated that rotavirus vaccination would be cost-effective during a CHE. Sensitivity analysis showed that access to outpatient care, vaccine effectiveness, and access to inpatient care had the largest impact on the ICER, in both the one and two dose scenarios. The second aim demonstrated that important predictors of diarrheal disease in children under five in Somalia were gender, age, receipt of any vaccine, and washing hands after cleaning the baby's bottom.

CHAPTER V: DISCUSSION

Introduction

The purpose of this chapter is to provide an overall summary of the analysis of the CEA and modeling exercise. The results of the analyses will be used to draw conclusions about the value of using rotavirus vaccination during a CHE. In addition, results will be examined to assess what interventions should be targeted to decrease the likelihood of a child getting diarrheal disease. Furthermore, a discussion of the limitations and delimitations of the study and how they were addressed will be included. Finally, recommendations will be made for future interventions to decrease diarrheal disease in children under five during a CHE.

Aim 1: To examine the cost-effectiveness of rotavirus vaccination during a CHE

Summary and Conclusions

A rotavirus vaccination program would have substantial health benefits for children during a CHE. At base case parameter of 70% coverage and 51% effectiveness for one dose or 76% effectiveness two doses, the cost per life saved would be cost-effective. A one-dose strategy would cost between $197,491 and $376,171 and there would be between 25,117 and 47,841 lives saved with a cost per life saved ranging from $13 to $40. A two doses strategy would cost between $243,524 and $463,870, there would be 27,988 to 53,309 lives saved with a cost per life saved ranging from $12.76 to $21.49. Given the absence of other strategies to prevent rotavirus infection and the fact that oral rehydration therapy (ORT) is widely used to reduce deaths, there was no obvious alternative intervention which vaccination can be compared. However, when looking at the MICS data for Somalia, the context of the CEA, assuming each child with diarrhea was only given one form of ORT, only 26% of children received this life saving therapy. Findings from these analyses agree with findings from previous CEA for rotavirus vaccine

introduction into developing countries, including those who have confronted CHEs that rotavirus vaccine would be highly cost-effective.[30,32,68,69]

Unlike in other studies,[70,71] the variable influencing most the ICER in the sensitivity analysis was vaccine effectiveness and access to outpatient care. However, changes in vaccine coverage did not have a substantial impact on cost-effectiveness estimates in the sensitivity analysis, which is a similar finding to a CEA of rotavirus conducted for Uganda.[32]

According to the World Health Organization, a cost-effective intervention is that where the ICER is less than three times the per capita GDP while a very cost-effective intervention is one where the ICER is less than one the per capita GDP.[72] The present study shows that vaccinating against rotavirus during a CHE may be very cost-effective since the ICER of $17.76 for the base scenario is lower than the Somali, our example country, per capita GDP (US$ 220.30 in 2009).[73] Rotavirus vaccination may also very cost-effective in neighboring countries of Ethiopia and Kenya, where the majority of Somali refugees fled during the 2011 famine, where the per capita GDP are US$ 739.00 and US$344.60, respectively.[73]

This analysis shows that rotavirus vaccination during a CHE would be cost-effective across a wide range of vaccine coverage even either the one or two dose strategy. It is worth highlighting the fact that measles vaccinations campaign is standard procedure during a CHE. If rotavirus vaccinations were given during these measles campaigns, the additional cost would only be cost of vaccine which would decrease the cost per life saved and increase the cost-effectiveness. Given the poor hand washing practices found in the MICS for Somalia and the long time needed to cause significant health behavior changes, providing an intervention in conjunction with measles vaccination for a major cause of morbidity and mortality among the

most vulnerable in CHEs, becomes an ethical consideration in addition to a cost-benefit consideration.

Limitations and Delimitations

As with any modeling exercise, the necessary simplification of a complex reality implies limitations that must be considered in the application of the results. Since there is almost no surveillance data that would specify the etiology of diarrhea during a CHE we had to estimate the disease burden. We did not take into account the effects of herd immunity of rotavirus vaccination, which may lower disease burden. The model also did not consider possible vaccine side effects, including intussusception that might become apparent with large-scale implementation of the vaccine. However, they were not observed in the clinical trials of Rotarix.[74,75] Given the probable high burden of rotavirus disease in CHE, even if these were to occur they are very unlikely to significantly alter the cost-effectiveness of the vaccine. The range of vaccine effectiveness was estimated from El Salvador and may not be a true estimate of the coverage that can be achieved in Somalia during a SIA. Given the high rates of diarrhea, the vaccine effectiveness may be on the lower end of the range. It has been observed with oral polio vaccine, another live vaccine, among populations with high burden of diarrhea, malnutrition, and other medical conditions such as TB and HIV,[32] the vaccine effectiveness is lower. A decrease in vaccine effectiveness would increase the CEA.

Aim 2: To determine the predictors of diarrheal disease in children under five in Somalia

Summary and Conclusions

This analysis sought to develop a model to predict diarrheal disease among children under five in Somalia, a country that has faced decades of conflict and has faced many CHE with the aim of giving more focus to what interventions are implemented during a CHE. Our final model showed

that age, gender, hand washing after cleaning child's bottom, and receipt of any vaccine. Similar to this analysis, a number of studies have shown that age and gender are significant predictors of diarrheal disease.[45,47,48] We also demonstrate that receipt of any vaccine is also a significant predictor of diarrheal disease in both the unadjusted analysis and in our prediction model. The unadjusted analysis also showed that measles/MMR vaccine and receipt of any vaccine are significantly correlated with a decrease risk of diarrheal disease, pointing to the importance of vaccination not only for disease-specific prevention but secondary disease prevention as well. Both measles and polio vaccines have been shown to decrease morbidity and mortality from diarrhea.[76-78] A number of studies revealed that poor maternal care giving behaviors, including hygiene behaviors related to sanitation contribute to the leading killers of children under five, including diarrheal disease.[79] Interventions to improve hygiene behaviors were reported to reduce diarrhea morbidity by nearly 45%.[80,81] There are also studies done on the risk factors for diarrheal disease that have attempted to describe the relationship between parental behavior and the occurrence of childhood diarrhea. They suggested that maternal practices related to hygiene, breastfeeding, food preparation, and health care are important determinants of diarrheal disease incidence.[79] Unlike other studies we did not find that breastfeeding significantly decreased the risk of diarrheal disease in the unadjusted analysis nor did it resulted in any additional precision of the model to predict diarrhea.[45,82] Vitamin A supplementation was not significantly associated with diarrheal disease in the unadjusted analysis nor did it result in any additional precision of the model to predict diarrhea which is in contrast to previously published studied showing that vitamin A plays a role in the prevention of diarrheal disease.[67,82,83] Neither measures taken to prevent contamination of water or treating water to make it safe for drinking are significantly associated with diarrheal disease in our analysis, which is in agreement with different studies

which showed that availability of improved water sources will not reduce diarrhea morbidity, without a change in behavior that affects hygiene practice.[79]

Limitations and Delimitations

The findings in this report are subject to several limitations. This reported used Somalia as a model of a country that has experienced CHEs and therefore may not be generalizable to other CHEs. Missing data in the dataset may have decreased the precision of our estimates. In addition, only observations with complete data were selected for the validation dataset that may have decreased the overall representativeness of the models. None of the three models developed in this report had a high level of agreement. One reason could be that only the children under-five survey was used in this analysis. Including other factors from either the women aged 15-49 year or household survey, such as maternal age and education and purchasing power of household may improve fit of model.

IMPLICATIONS AND RECOMMENDATIONS

The ability to illustrate the cost-effectiveness of a rotavirus vaccination program during a CHE adds another layer of evidence that the money spent on such a program would be a good investment. In an economy in which governmental agencies are under increased scrutiny, the ability to demonstrate economic responsibility justifies programmatic funding.

In 2009, UNICEF and WHO published a report on diarrhea that included a package of key diarrhea prevention and treatment interventions to reduce diarrhea morbidity and mortality. The complete package included improved access to safe water, community-wide promotion of sanitation, routine rotavirus and measles vaccination, vitamin A supplementation, and promotion of breastfeeding, and treatment with ORS and zinc.[82] The data presented here support this report that hygiene behavior interventions and vaccination may serve to reduce diarrhea during a CHE.

However, the changing behaviors take time and not possible to change immediately in a CHE. This reinforces the importance of the CEA analysis for rotavirus vaccination during a CHE, particularly during the acute phase to prevent child mortality.

The number of CHEs has been on the rise, leading to a record number of people, particularly children under five years, at risk for infectious diseases. Diarrhea remains a leading cause of mortality among children under five years in low-income countries, some of these countries are at risk for experiencing or have had a CHE. These data may serve to further reduce diarrhea mortality by showing that rotavirus vaccination serves to reduce mortality and is cost-effective and what the predictors of diarrhea are which may help focus interventions during a CHE. The reduction of child mortality is one of the fourth United Nations' Millennium Development Goals, decreasing child mortality during a CHE will aid in reaching this goal.

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Figure 1. Decision tree

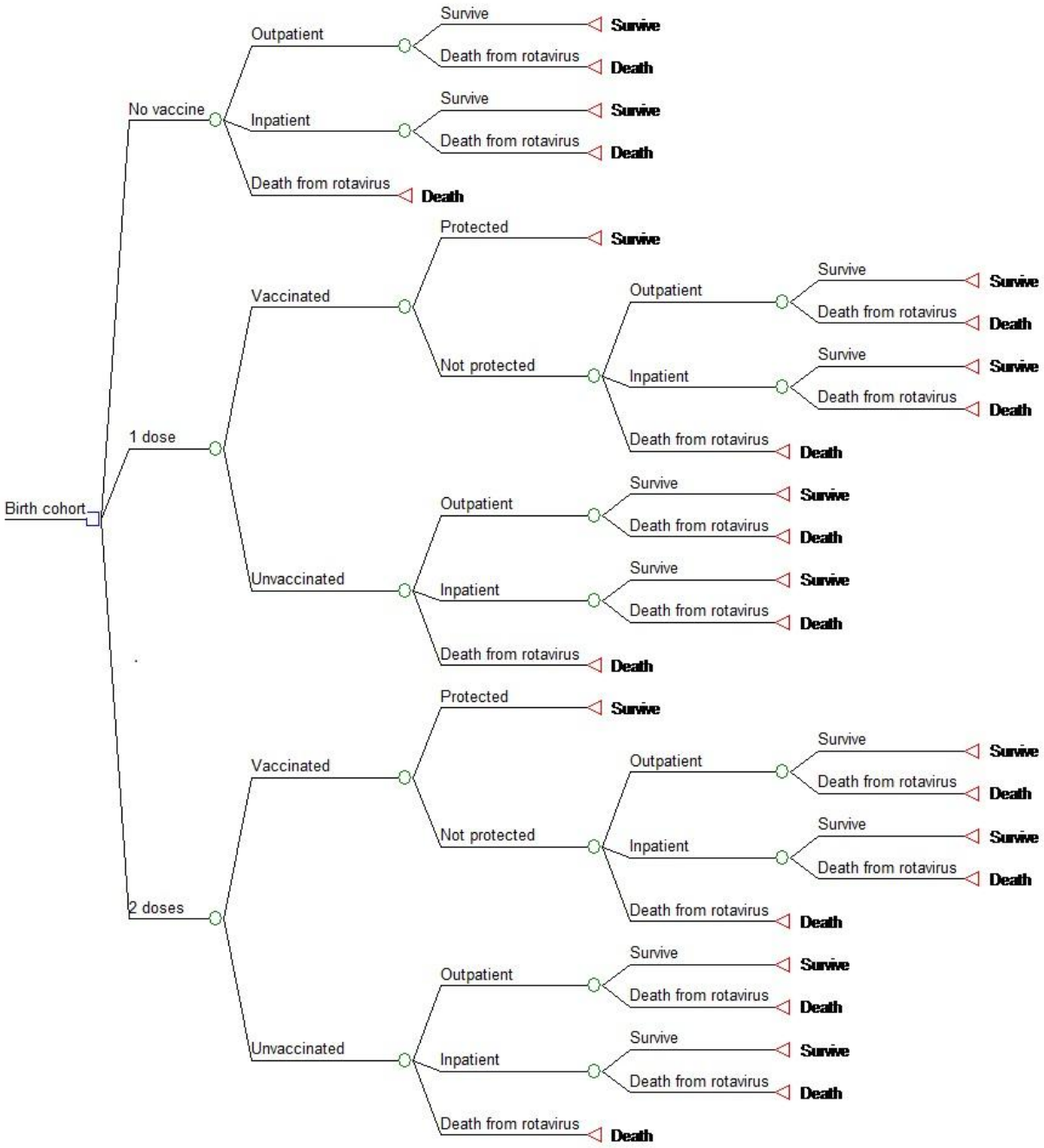


Table 1. MICS3 variable names and questions

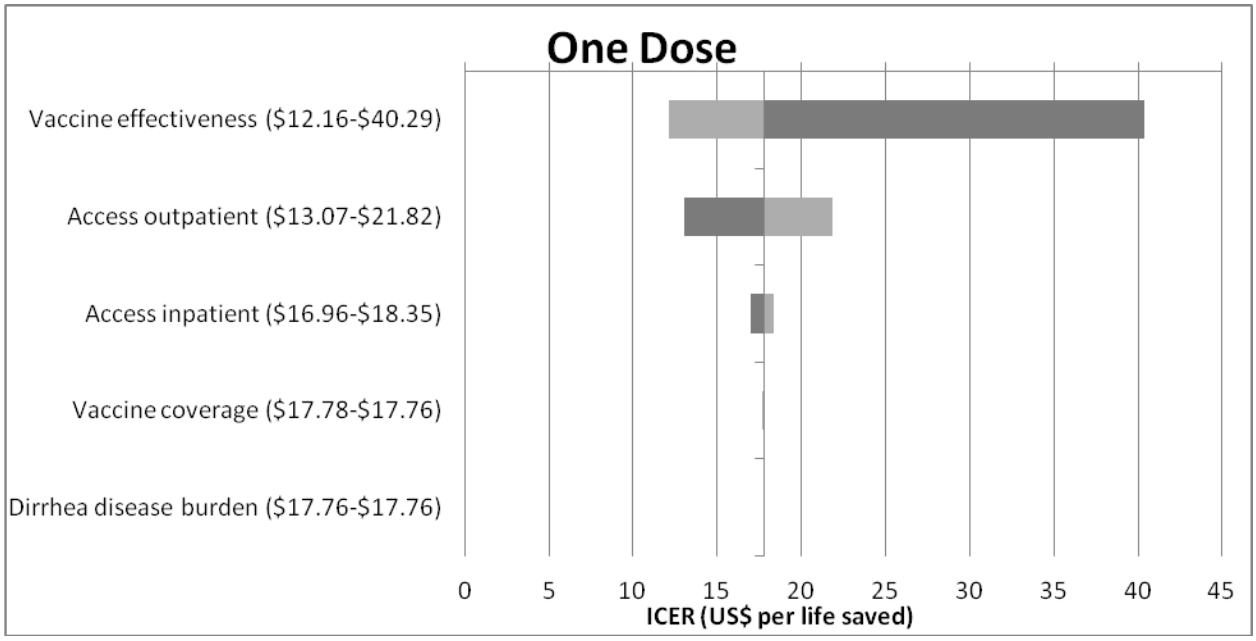
Survey	Variable Name	Variable Indicator/Question
Demographics	HL4	Gender
	UF11	Age
Vitamin A	VA1	Has (*name*) ever received a vitamin A capsule (supplement) like this one?
Breastfeeding	BF1	Has (*name*) ever been breastfed?
Illness	CA1	Has (*name*) had diarrhea in the last two weeks?
Immunization	IM10	Has (*name*) ever received any vaccinations to prevent him/her from getting diseases, including vaccinations received in a campaign or immunization day?
	IM12	Has (*name*) ever been given any vaccination drops in the mouth, to protect him/her from getting diseases – that is polio?
	IM17	Has (*name*) ever been given measles vaccination injections or MMR – that is a shot in the arm at the age of 9 months or older to prevent him/her from getting measles?
	IM18C	Have you ever refused to have (*name*) receive a vaccination to prevent diseases?
Water, Sanitation, and Hygiene	WS5	Do you treat your water in any way to make it safer to drink?
	WS5A	Do you take any measures to prevent contamination of your water?
	WS9AA	Do you wash your hands before feeding the baby?
	WS9AD	Do you wash your hands after cleaning the baby's bottom?

Table 2. Rotavirus-related events or costs with and without rotavirus vaccine and averted by vaccination (base case scenario)

	Without vaccine	With 1 dose	Annual averted events or cost (%)	With 2 doses	Annual averted events or cost (%)
No. of events					
Deaths	23,437	15,070	8,367 (36)	10,968	12,469 (53)
Outpatient	20,380	13,165	7,215 (35)	9,538	10,842 (53)
Inpatient	10,190	6,552	3,638 (36)	4,769	5,421 (53)
Medical treatment costs (US$)					
Outpatient	20,584	13,235	7,349 (36)	9,633	10,951 (53)
Inpatient	113,109	72,728	40,381 (36)	52,936	60,173 (53)

Figure 2. Tornado diagrams of univariate sensitivity analysis of rotavirus vaccination program during a CHE. Endpoints of each bar represent the incremental cost-effectiveness ratio (ICER) (cost per life saved) at the high (light grey) and low (dark grey) end of the ranges to the left of the bar. A) Sensitivity analysis for one dose, B) Sensitivity analysis for two doses

A



B

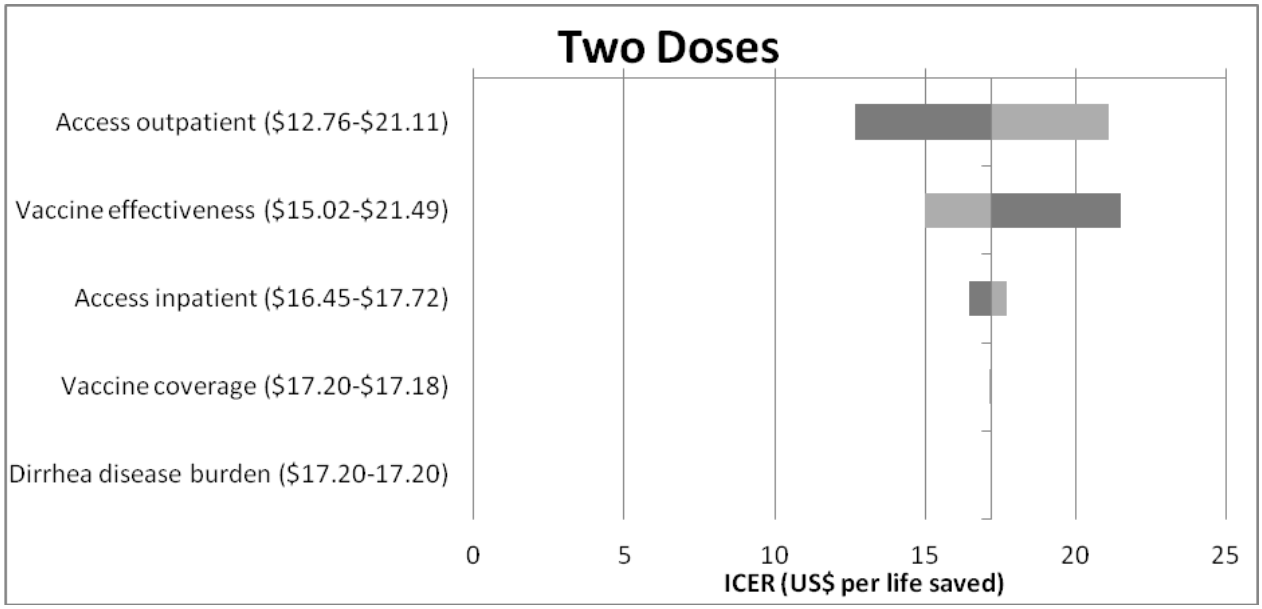


Table 3. Sensitivity analysis for one dose to examine the effect of diarrhea burden, vaccination coverage, vaccine effectiveness, and outpatient and inpatient care access on the cost-effectiveness of a rotavirus vaccination program

	Parameter value range, %	Base costs (US$)	Lower limit	Upper limit	Base lives saved	Lower limit	Upper limit
Diarrhea disease burden	21-30	282,128	197,491	376,171	35,881	25,117	47,841
Vaccine coverage	50-85	282,128	239,718	313,935	35,881	33,490	37,674
Vaccine effectiveness	26-67	282,128	305,524	267,155	35,881	31,779	38,506
Access outpatient	20-50	282,128	275,509	285,435	35,881	29,984	38,829
Access inpatient	10-25	282,128	245,762	300,307	35,881	32,933	37,355

Table 4. Sensitivity analysis for two doses to examine the effect of diarrhea burden, vaccination coverage, vaccine effectiveness, and outpatient and inpatient care access on the cost-effectiveness of a rotavirus vaccination program

	Parameter value range, %	Base costs (US$)	Lower limit	Upper limit	Base lives saved	Lower limit	Upper limit
Diarrhea disease burden	21-30	347,897	243,524	463,870	39,983	27,988	53,309
Vaccine coverage	50-85	347,897	286,695	393,795	39,983	36,420	42,654
Vaccine effectiveness	64-84	347,897	359,128	340,407	39,983	38,013	41,294
Access outpatient	20-50	347,897	343,081	350,306	39,983	35,690	42,128
Access inpatient	10-25	347,897	321,435	361,128	39,983	37,837	41,056

Table 5. Distribution of variables by presence or absence of diarrhea in last two weeks

	Diarrhea in last two weeks		No diarrhea in last two weeks		p-value
Variable	**Frequency**	**Percent**	**Frequency**	**Percent**	**95% CI**
Gender (male)	680	11.7	2586	40.2	0.012
Age (years)					
0	300	5.1	1044	16.0	
1	286	4.9	806	12.3	
2	272	4.8	985	15.5	
3	216	3.7	1090	17.0	
4	158	2.7	1140	18.1	<0.001
Breastfed (ever)	1185	20.3	4812	75.2	0.21
Vitamin A	401	7.2	1586	26.1	0.53
OPV (ever)	674	21.2	2555	75.1	0.32
Measles/MMR (ever)	255	8.2	1211	35.7	<0.001
Received any vaccines	701	13.0	2659	45.8	0.001
Ever refused vaccines	151	2.8	764	12.4	0.14
Wash hands before feeding child	429	6.6	2224	31.8	<0.001
Wash hands after cleaning child bottom	499	7.7	2742	39.2	<0.001
Measure to prevent contamination	616	12.6	2270	43.9	0.57
Treat water to make safe for drinking	363	6.5	1457	24.7	0.63

Table 6. Distribution of different treatments for diarrhea

Variable	Frequency	Percent	95% CI
Fluid from ORS packet	119	9.1	7.5, 10.9
Recommended homemade fluid	130	9.4	7.9, 11.1
Pre-packaged ORS fluid	93	7.3	5.9, 8.9

Table 7. Unadjusted odds ratios for potential predictors of diarrheal disease

Variable	**Unadjusted OR (95% CI)**	**p-value** *p≤0.05
Sex (male)	0.84 (0.74, 0.96)	0.011*
Age	0.82 (0.79, 0.86)	<0.0001*
Breastfed (ever)	0.79 (0.56, 1.12)	0.184
Vitamin A	0.97 (0.84, 1.11)	0.638
OPV (ever)	1.30 (0.82, 2.05)	0.269
Measles/MMR (ever)	1.46 (1.22, 1.75)	<0.0001*
Received any vaccines	0.80 (0.70, 0.92)	0.002*
Ever refused vaccines	0.85 (0.70, 1.04)	0.123
Wash hands before feeding child	1.49 (1.30, 1.71)	<0.0001*
Wash hands after cleaning child bottom	1.74 (1.52, 1.98)	<0.0001*
Measure to prevent contamination	1.03 (0.90, 1.19)	0.669
Treat water to make safe for drinking	1.04 (0.90, 1.19)	0.639

Table 8. MLE beta values and Kappa statistic for the three models

Model 1		**Model 2**		**Model 3**	
	MLE betas		**MLE betas**		**MLE betas**
Intercept	-1.5661	Intercept	-0.9524	Intercept	-0.9524
Age	-0.2948	Age	-0.2256	Age	-0.2256
Gender	-0.3947	Gender	-0.2144	Gender	-0.2144
Receive any vaccine	-0.3947	Receive any vaccine	-0.3897	Receive any vaccine	-0.3897
Washing hands before feeding the baby	0.1655	Washing hands after cleaning baby's bottom	0.5704	Washing hands after cleaning baby's bottom	0.5704
Washing hands after cleaning baby's bottom	0.4857				
Kappa statistic	0.0987		.1304		.1304