SUPPLEMENT ARTICLE

Rotavirus Disease Burden and Impact and Cost-Effectiveness of a Rotavirus Vaccination Program in Kenya

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Background. The projected impact and cost-effectiveness of rotavirus vaccination are important for supporting rotavirus vaccine introduction in Africa, where limited health intervention funds are available.

Methods. Hospital records, health utilization surveys, verbal autopsy data, and surveillance data on diarrheal disease were used to determine rotavirus-specific rates of hospitalization, clinic visits, and deaths due to diarrhea among children <5 years of age in Nyanza Province, Kenya. Rates were extrapolated nationally with use of province-specific data on diarrheal illness. Direct medical costs were estimated using record review and World Health Organization estimates. Household costs were collected through parental interviews. The impact of vaccination on health burden and on the cost-effectiveness per disability-adjusted life-year and lives saved were calculated.

Results. Annually in Kenya, rotavirus infection causes 19% of hospitalizations and 16% of clinic visits for diarrhea among children <5 years of age and causes 4471 deaths, 8781 hospitalizations, and 1,443,883 clinic visits. Nationally, rotavirus disease costs the health care system $10.8 million annually. Routine vaccination with a 2-dose rotavirus vaccination series would avert 2467 deaths (55%), 5724 hospitalizations (65%), and 852,589 clinic visits (59%) and would save 58 disability-adjusted life-years per 1000 children annually. At $3 per series, a program would cost $2.1 million in medical costs annually; the break-even price is $2.07 per series.

Conclusions. A rotavirus vaccination program would reduce the substantial burden of rotavirus disease and the economic burden in Kenya.

An estimated 527,000 deaths are attributable to rotavirus each year, with most rotavirus-associated deaths occurring in sub-Saharan Africa and southern Asia [1]. Moreover, rotavirus is responsible for 25%–50% of all hospitalizations for diarrhea among children <5 years of age and represents a substantial economic burden in both developing and developed countries [2, 3]. Two safe, effective rotavirus vaccines are now available. However, the decision to introduce any vaccine requires local data on the disease and economic burdens to determine the benefits and cost-effectiveness of a vaccination program.

The objectives of this study were to estimate (1) the rotavirus disease burden among children <5 years of age in Nyanza Province in western Kenya, (2) the economic burden (medical and household) of rotavirus disease, and (3) the potential impact and cost-effectiveness of a national rotavirus vaccination program.

METHODS

Study setting. Bondo and Siaya are 2 districts in Nyanza Province that border Lake Victoria; Nyanza Prov-

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ince is one of the poorest provinces in Kenya [4]. A demographic surveillance system, which enumerates the population in part of each district 3 times per year, conducts surveys on incidence of disease syndromes, including diarrhea, and provides data on health care use [4]. In addition, surveillance for hospitalizations and clinic visits for rotavirus disease among children was performed at the 2 district hospitals and 6 clinics over 2 years, and economic data were collected for a subset of enrolled children at 2 hospitals and 3 clinics.

Disease burden. We estimated rates of death, hospitalization, and clinic visits due to any cause of diarrhea among children <5 years of age and then applied the prevalence of rotavirus disease detected through hospital and clinic surveillance to these rates to estimate rotavirus-specific rates of disease. To estimate the total number of deaths due to diarrhea among children, we used demographic surveillance system verbal autopsy data from the period 2002–2005 [4]. The symptom profiles of deaths coded as being caused by diarrhea and those coded as being caused by dehydration were similar (97% of deaths coded as being caused by diarrhea or dehydration had diarrhea listed as a symptom); thus, we used both codes to enumerate deaths. The proportion of all deaths due to diarrhea was then multiplied by the annual death rate among children <5 years of age in the demographic surveillance system (60 deaths per 1000 children) [5] to estimate the rate of death due to diarrhea.

To estimate the annual rate of hospitalizations for diarrhea, we used data from a survey during 2003–2005 that provided the total number of admissions at every hospital in Bondo District (Centers for Disease Control and Prevention [CDC], unpublished data). We extrapolated the national population census data from 1999 to calculate a rate of hospitalization for diarrhea in Bondo District. We assumed that rates of hospitalization for diarrhea in Bondo and Siaya Districts were comparable.

Finally, the rate of clinic visits for diarrhea was determined using a health utilization survey performed in August 2005 (CDC, unpublished data) [6]. In brief, a selection of households in Bondo District was asked about episodes of diarrheal illness in children <5 years of age for which care was sought during the previous 2 weeks. This information was combined with extrapolated data from the 1999 national census to calculate the annual rate of clinic visits for diarrhea in the study area.

To determine the proportion of each of these diarrheal outcomes (death, hospitalization, and clinic visits) that were attributable to rotavirus, we multiplied these rates by the percentage of rotavirus-positive children based on active diarrheal surveillance in Bondo and Siaya Districts. To enable comparison of the rate of death due to rotavirus disease from this study with other published estimates, we followed the World Health Organization (WHO) Child Health Epidemiology Reference Group method, which assumes that the proportion of hospitalizations for rotavirus diarrhea approximates the proportion of deaths due to rotavirus diarrhea [1, 2]. From May 2005 through May 2007, children <5 years of age who presented with diarrhea (⩾3 loose stools in a 24-h period lasting ⩽5 days) at 1 of 2 district hospitals or 6 clinics were enrolled, and stool specimens were tested for rotavirus with use of an enzyme immunoassay (Rotaclone; Meridian Diagnostics) [7]. During this 2-year study period, 198 (19%) of 1027 hospitalized children and 22 (16%) of 134 children enrolled at 6 study clinics tested positive for rotavirus.

Because our study was performed in one of the poorest provinces in Kenya and rates of diarrhea and health care access vary widely in Kenya, we could not directly estimate national burden from our data. Thus, we used data from the 2003 Kenya Demographic Health Survey [8] to estimate the province-specific likelihood that a child will have diarrhea (any cause) during a 2-week period and that the child would seek medical care for that episode. Using the ratio of each province-specific likelihood to the Nyanza-specific likelihood as a multiplier, we adjusted the rates of hospitalizations and clinic visits for rotavirus disease in our study in each province and nationally. Rates of death due to rotavirus diarrhea were adjusted using province-specific, all-cause, postneonatal mortality rates among children <5 year of age.

Disease burden was assessed both as the number of events and as the disability-adjusted life-years (DALYs), which quantify the number of years lost as the result of premature death and the number of years lived with disability [9]. Estimates of DALYs included age weights and a discount rate of 3% [10].

Health care costs. We used standardized WHO Choosing Interventions that are Cost Effective (WHO-CHOICE) estimates of the per diem cost of hospitalization and clinic visits in Kenya [11]. We multiplied the per diem cost by the median duration of hospital stay for a child hospitalized with a diarrheal illness in the surveillance system (5 days) to calculate the total cost of a hospital stay. We added costs of medication and diagnostic tests that were obtained by a review of records of 218 children with diarrhea at the 2 district hospitals and at 3 of the 6 clinics. For medications prescribed to ⩾10% of children, the typical prescribed course was determined by record review, and the cost was based on the wholesale cost of drugs through the Mission for Essential Drugs and Supplies [12]. The cost of each medication was weighted by the proportion of children to which it was prescribed, and the total cost was summed over all medications. Household costs were collected through interviews with parents that inquired about costs of transportation; previous treatments for this episode of diarrhea; expenses incurred during the current visit for food, medicine, and tests; and the estimated income lost while caring for their child.

All costs were expressed in 2007 US dollars. WHO-CHOICE estimates were inflated from 2000 US dollars using the US Consumer Price Index for medical care [13]. All other costs were collected in the local currency and were converted to US dollars with use of 2007 exchange rates.

Cost and effectiveness of a rotavirus vaccine program. We calculated the impact of a live attenuated, monovalent human rotavirus vaccine administered orally at 2 and 4 months of age [14] and concurrently with the diphtheria, tetanus, and pertussis vaccine (DTP) doses 1 and 2. Vaccine efficacy against hospitalization and death due to rotavirus disease was assumed to be 85%, based on data from Latin America [15]; these data more closely approximate the impoverished setting in Kenya than do other available data from Europe. A vaccine efficacy of 78% (the mean efficacy for severe [85%] and any [70%] rotavirus gastroenteritis) was used for outpatient visits. One-dose efficacy was assumed to be 50% of that of a full course. Vaccine coverage and timing estimates were based on province-specific DTP doses 1 and 2 coverage estimates from the 2003 Kenya Demographic Health Survey [8]. Because children who die of diarrhea may come from a disadvantaged subset of children with lower vaccination coverage, we conservatively assumed that vaccine coverage of children who die was 10% less than the vaccine coverage of children who do not.

Vaccination costs included administration costs, vaccine price, and expected losses from waste (10%). Administration costs were estimated to be ~$1.06 per course with use of the WHO Global Immunization Vision and Strategy costing model [16]. Our analysis included a range of price estimates ($1–$20) for a full course (2 doses).

Model overview. A Microsoft Excel–based model was used to estimate the impact and cost-effectiveness of a national rotavirus immunization program by comparing the cost and burden of rotavirus disease with and without such a program [3]. Principle model inputs included rotavirus disease incidence, health care treatment costs, vaccine coverage and timing, and the cost and effectiveness of rotavirus vaccine.

Cost-effectiveness. Incremental cost-effectiveness ratios (ICERs), expressed as cost per DALY averted and cost per life saved, were calculated by dividing the incremental cost by the difference in the DALYs (or deaths) with and without vaccine. Incremental cost was calculated by subtracting the medical cost savings of prevented cases from the cost of a vaccination program.

ICERs were calculated for a range of vaccine prices ($1–$20 per course) and for the price at which vaccination would meet particular cost-effectiveness criteria in terms of cost per DALY averted. These criteria include cost neutrality, in which the medical costs saved were equal to the cost of vaccination, and 3 standardized thresholds of cost-effectiveness: (1) the World Bank standard for highly cost-effective interventions in developing countries of an ICER ⩽$227 per DALY averted (converted to 2007 US dollars) [17], (2) the World Bank standard for low-income countries (such as Kenya) of an ICER ⩽$166 per DALY averted (converted to 2007 US dollars) [17], and (3) the WHO threshold for a very cost-effective intervention of the cost per DALY less than the country's per capita gross domestic product [18]. The 2006 per capita gross domestic product for Kenya was $580 [19].

Sensitivity analysis. One-way sensitivity analyses were performed by separately varying incidence and costs of rotavirus-associated death, hospitalization, and outpatient visits by ±25% from the base-case estimate. Because the rate of outpatient visits in this population was particularly high, an outpatient visit rate of 75% less than baseline was also examined. In addition, vaccine efficacy was varied from 60% to 100%. The cost of vaccine was assumed to be $3 per course in the sensitivity analysis.

RESULTS

Rotavirus disease burden in Nyanza Province. Annually, diarrheal illnesses result in 842 deaths and 550 hospitalizations per 100,000 children <5 years of age in the study area. Hospital surveillance found that 19% of hospitalizations for diarrhea are attributable to rotavirus. By applying this proportion to the rates of death due to diarrhea and hospitalization for diarrhea, we estimated that rotavirus causes 164 deaths and 107 hospitalizations per 100,000 children per year. By 5 years of age, 1 of 122 children will die of rotavirus diarrhea and 1 of 187 children will be hospitalized. Finally, using the health utilization survey in Bondo District, we estimated that the annual rate of clinic visits for diarrhea is 109,000 per 100,000 children per year in this area. Clinic-based surveillance found that 16% of clinic visits for diarrhea are attributable to rotavirus, and the annual rate of clinic visits for rotavirus diarrhea is ~18,000 visits per 100,000 children. By 5 years of age, almost every child will have sought care for rotavirus diarrhea (Table 1).

Rotavirus disease burden in Kenya. Extrapolating the data from Nyanza Province, we estimated that 68 deaths, 132 hospitalizations, and 21,800 clinic visits per 100,000 children aged <5 years annually in Kenya are attributable to rotavirus diarrhea. Nyanza Province had the highest rotavirus-associated mortality rate (164 deaths per 100,000 children). The estimated rotavirus-associated mortality rates of the other provinces were 49%–84% less than the rate in Nyanza Province and ranged from 52 deaths per 100,000 children per year in Central Province to 84 deaths per 100,000 children per year in Western Province. Rates of hospitalization for rotavirus diarrhea ranged from 150 hospitalizations per 100,000 children per year in Nairobi to 240 hospitalizations per 100,000 children per year in Coast Province. In all provinces except Central Province, every child will have visited an outpatient clinic for rotavirus diarrhea

Table 1. Rotavirus Disease Burden in Nyanza Province, Kenya, 2007

Variable	Rate of diarrhea, episodes per 100,000 children per year	Percentage of children positive for rotavirus	Rate of rotavirus diarrhea, episodes per 100,000 children per year	Cumulative 5-year risk
Death	842	19	164	0.0082 (1:122)
Hospitalization	550	19	107	0.0054 (1:187)
Clinic visit	109,200	16	17,800	0.89 (1:1)

by 5 years of age. In Central Province, only 40% of children will have visited an outpatient clinic for rotavirus diarrhea by 5 years of age (Table 2).

Economic burden in Nyanza Province. We reviewed hospital records for 94 children <5 years of age who were hospitalized for treatment for diarrhea. The majority (84%) of children sought care before going to the hospital. The median duration of a hospital stay for diarrhea was 5 days (range, <1 day to 23 days), and 80% of hospitalized children received intravenous fluids. A malaria smear was performed for more than half (53%) of the children. No other diagnostic tests or procedures were routinely performed. The median number of drugs prescribed was 7 (the most common were antimalarials, antibiotics, intravenous fluids, antipyretics, and multivitamins).

We reviewed clinic records for 124 children <5 years of age who presented at 1 of 3 clinics. Less than half (45%) of the children sought care before visiting the clinic. Three-quarters of the children received oral rehydration solution at the clinic. A malaria smear was performed for 21% of the children, but no other diagnostic tests or procedures were routinely performed. The median number of drugs prescribed was 4 (the most common were antipyretics, oral rehydration solution, antimalarials, and antibiotics).

The WHO estimates that the cost per bed per day in a primary care hospital in Kenya is $19.74 [11] (in 2007 US dollars), for a total cost of $98.70 for 5 days (median duration of hospitalization). The estimated total cost of the most frequently prescribed medications was $4.48 and for diagnostic tests was $0.50. Thus, the estimated total cost of a hospitalization for diarrhea was $103.68. The WHO estimates that the cost of a clinic visit is $5.31 (in 2007 US dollars). The estimated cost for medications was $1.42 and for diagnostic tests was $0.25, for a total cost for a clinic visit for diarrhea of $6.98 (Table 3).

To estimate household costs, parents were asked about costs incurred by the family as a result of their child's diarrheal illness. The median cost incurred by a family with a child hospitalized for diarrhea was $19.86. The largest single expenses were lost income and facility fees for the hospitalization. For a clinic visit, few expenses were incurred by families except for lost income. The median family cost of a clinic visit was $2.40, with a median of $1.50 in lost income. The median monthly household income of a family with a child hospitalized for diarrhea was $81, compared with $34 for families who brought their child to a clinic (Table 4).

Economic burden in Kenya. By extrapolation from Nyanza Province, in Kenya, hospitalizations for rotavirus disease cost $0.89 million per year (or $0.67 per child per year), and out-

Table 2. Input Adjustments: Rates of Mortality, Hospitalization, and Outpatient Visits Associated with Rotavirus Diarrhea among Children <5 Years of Age and On-Time Vaccine Coverage for Diphtheria, Tetanus, and Pertussis (DTP) Vaccine, by Province, Kenya, 2007

		Mortality		Hospitalization		Outpatient visit		On-time vaccine coverage, %	
Province	Birth Cohort	Cumulative 5-year risk (risk ratio)	Multiplier	Cumulative 5-year risk (risk ratio)	Multiplier	Cumulative 5-year risk of (risk ratio)	Multiplier	DTP dose 1[a]	DTP dose 2[b]
Nyanza	225,485	0.0082 (1:122)	1.0	0.0054 (1:187)	1.0	0.89 (1:1)	1.0	56	56
Central	116,079	0.0013 (1:760)	0.16	0.0024 (1:414)	0.45	0.40 (1:3)	0.45	89	91
Coast	111,729	0.0026 (1:392)	0.31	0.012 (1:83)	2.22	1.97 (1:1)	2.22	70	72
Eastern	203,815	0.0019 (1:539)	0.23	0.0072 (1:138)	1.34	1.19 (1:1)	1.34	70	76
Nairobi	53,050	0.0027 (1:369)	0.33	0.0075 (1:134)	1.38	1.23 (1:1)	1.38	91	85
North Eastern	61,743	0.0032 (1:315)	0.39	0.0067 (1:149)	1.25	1.11 (1:1)	1.25	12	12
Rift Valley	371,509	0.0019 (1:517)	0.24	0.0066 (1:151)	1.22	1.09 (1:1)	1.22	65	69
Western	178,590	0.0042 (1:239)	0.51	0.0067 (1:149)	1.25	1.11 (1:1)	1.25	65	69
All	1,322,000	0.0034 (1:296)	…	0.0066 (1:151)	…	1.09 (1:1)	…	68	75

[a] Administered at 2 months of age.
[b] Administered at 4 months of age.

Table 3. Estimated Medical Costs of Rotavirus Diarrhea, Kenya, 2007

Cost	Hospitalization, US$	Clinic visit, US$
Facility[a]	98.70[b]	5.31
Medication	4.48	1.42
Diagnostic test[c]	0.50	0.25
Total	103.68	6.98

[a] Based on the World Health Organization Choosing Interventions that are Cost Effective estimates (adjusted for 2007 US dollars).
[b] $19.74 per day for 5 days (median duration of stay for hospitalization for diarrhea).
[c] Estimate based on technician time.

patient visits for rotavirus disease cost $9.9 million per year (or $7.47 per child per year). The total economic burden of rotavirus disease for the health care system in Kenya is $10.8 million per year or $8.14 per child <5 years of age.

Vaccine impact. Rotavirus disease causes an estimated 4471 deaths, 8781 hospitalizations, and 1,443,883 outpatient visits annually in Kenya, resulting in a loss of 105 DALYs per 1000 children per year. On-time vaccination for DTP doses 1 and 2 ranged from 12% in North Eastern Province to 91% in Nairobi and Coast Province (Table 2). The introduction of rotavirus vaccine nationally at these province-specific coverage levels would prevent 2467 deaths (55%), 5724 hospitalizations (65%), and 852,589 clinic visits (59%) annually and would avert the loss of 58 DALYs per 1000 children (Table 5).

The introduction of a vaccination program would also save ~$0.58 million (65%) in hospital costs and ~$5.9 million (59%) in clinic costs, for a total of $6.4 million (60%) in medical costs averted. The medical costs averted per child would be $4.87 (Table 5).

Cost-effectiveness. The medical break-even price is $2.07 for the full vaccine course, including administration costs and waste. At a price of $2.07 per course, the costs of vaccination would equal the costs prevented. Below this price, vaccination would result in cost savings to the health care system. On the basis of the criterion for cost-effectiveness in developing countries of an ICER of ~$227 per DALY, the maximum vaccine price in Kenya could be $9.26 per course to be cost-effective at this threshold. If an ICER of $166 per DALY was established as the standard for determining cost-effectiveness in low-income countries, the vaccine could cost up to $7.35 per course. Finally, with use of the standard of cost per DALY less than the per capita gross national income, the maximum vaccine price could be $20.31 per course and remain a good value (Figure 1*A*). The cost per death averted ranged from cost savings, if the vaccine was priced at $1 per course (Figure 1*B*), to a net cost of $17,723, if the vaccine was priced at $20 per course.

Sensitivity analysis. At a price of $3 per course of vaccine, the results were most affected by the rate of rotavirus-associated clinic visits, the cost of a clinic visit, and the vaccine efficacy against clinic visits. A 25% change in the outpatient visit rate resulted in a 23%–25% change in the medical cost per child and a 70% change in the ICER. Similarly, a 25% change in the medical cost of a clinic visit resulted in a 23%–25% change in the medical cost per child and a 70% change in the ICER. By contrast, a 25% change in the rotavirus-associated mortality rate resulted in a 7%–11% change in the ICER. Reducing vaccine efficacy against clinic visits from 78% to 60% resulted in a 67% decrease in the ICER. If a vaccine price of $1 per course was assumed, the vaccine would be cost-saving under all of these scenarios. If rates of outpatient visits were lowered to only 25% of the base-case scenario, the ICER would increase to $85 per DALY averted and the medical cost per child would decrease to $1.55 (Table 6).

DISCUSSION

Every year in Kenya, rotavirus diarrhea causes an estimated 4500 deaths, 8800 hospitalizations, and 1,444,000 clinic visits among children <5 years of age and costs Kenya almost $11

Table 4. Societal Costs of Rotavirus Diarrhea, Kenya, 2007

Variable	Hospitalization, median 2007 US$ (IQR) (*n* = 94)	Clinic visit, median 2007 US$ (IQR) (*n* = 124)
Cost		
Total	19.86 (11.70–30.50)	2.40 (4.05–1.65)
Previous treatment	0 (0–0.60)	0 (0)
Transportation	1.57 (0–4.50)	0 (0–0.15)
Facility fees	4.80 (3.45–6.75)	0 (0)
Medications and tests	0.90 (0.30–1.95)	0 (0–0.15)
Other	2.25 (1.50–4.50)	0 (0–0.15)
Lost income	6.60 (2.55–10.72)	1.50 (0.75–3.00)
Monthly income	80.95 (44.97–152.90)	33.58 (14.99–74.95)

NOTE. IQR, interquartile range.

Table 5. Events in Children <5 Years of Age and Associated Medical Costs With and Without Rotavirus Vaccine and Averted by Vaccination and Cost of Intervention, Kenya, 2007

Variable	No vaccine	Vaccine	Averted events or cost (%)
No. of events			
Death	4471	2004	2467 (55)
Hospitalization	8781	3057	5724 (65)
Outpatient visit	1,443,883	591,294	852,589 (59)
DALYs	138,934	62,237	76,697 (55)
DALYs averted per 1000 children	…	…	58
Medical cost, US$			
Hospitalization	892,228	310,503	581,725 (65)
Outpatient Visits	9,874,884	4,012,315	5,862,569 (59)
Total	10,767,113	4,322,820	6,444,293 (60)
Averted per child	…	…	4.87
Cost of intervention, US$			
At $0 per course	…	1,180,162	…
At $1 per course	…	3,629,555	…
At $3 per course	…	8,528,340	…
At $5 per course	…	13,427,125	…
At $10 per course	…	25,674,088	…
At $20 per course	…	50,168,015	…

NOTE. DALYs, disability-adjusted life-years.

million. The bulk of the medical costs (92%) for rotavirus diarrhea in Kenya are from clinic visits, because every child in Kenya will visit a clinic by 5 years of age. Routine use of rotavirus vaccine at current coverage levels similar to those of DTP doses 1 and 2 and with timing similar to that of other childhood vaccines would avert ~2500 deaths (55%), ~5700 hospitalizations (65%), and ~853,000 clinic visits (59%) annually; overall, this is equivalent to 58 DALYs per 1000 children. At a price of $3 per course, a vaccination program would cost $2.1 million in medical costs annually.

If the vaccine is shown to be efficacious in ongoing studies in Africa, the GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunization) may substantially subsidize vaccine purchase for Kenya and other eligible countries. Kenya will contribute only $0.60 per course for the first 5 years of the vaccine program. Our study suggests that, even if Kenya pays up to $2.07 per course (medical break-even price), a rotavirus vaccination program would be cost-saving. However, the introduction of a program would still be considered to be a highly cost-effective intervention at higher prices of $7.35, $9.26, and $20.31 per course, according to the WHO and World Bank standards for cost-effective interventions. However, although a rotavirus vaccination program may be a good value at these prices, such a program may not be affordable, and there may also be other interventions that are better values.

Our national mortality estimate of 68 deaths per 100,000 children per year is lower than the WHO estimate for Kenya of 135 rotavirus deaths per 100,000 children per year [1] and than a recent assessment in Coast Province of 120 deaths per 100,000 children per year [20]. This latter estimate is more than twice the rate that we estimated for Coast Province (52 deaths per 100,000 children annually). Our results are more in line with the global estimate of 68 rotavirus deaths per 100,000 children per year [21]. However, all of these estimated rates fall within our range of 52 deaths per 100,000 children per year in Central Province to 164 deaths per 100,000 children per year in Nyanza Province, which is almost twice the global estimate. Of note, on-time coverage of DTP dose 2 in Nyanza Province, where rotavirus mortality is highest, is 56%, compared with 91% in Central Province, where rotavirus mortality is lowest. These differences in mortality rates and vaccination coverage within Kenya highlight the importance of identifying and increasing vaccine coverage in poor populations with the highest mortality rates to optimize national health impact.

Our rate of 132 hospitalizations per 100,000 children per year is considerably lower than the estimated global rate of 308 hospitalizations per 100,000 children [21] and than the rate in New Delhi, India, of 337 hospitalizations per 100,000 children per year [22]. Our hospitalization rate for Coast Province (240 hospitalizations per 100,000 children per year) is our highest rate for all provinces, but it is less than half the rate of hospitalization for Kilifi District Hospital in Coast Province (478 hospitalizations per 100,000 children per year) [20]. Of importance, a high rate of rotavirus-associated hospitalization and mortality in Kenya, as was seen in Coast Province, would make rotavirus vaccination even more cost-saving. Although the hos-

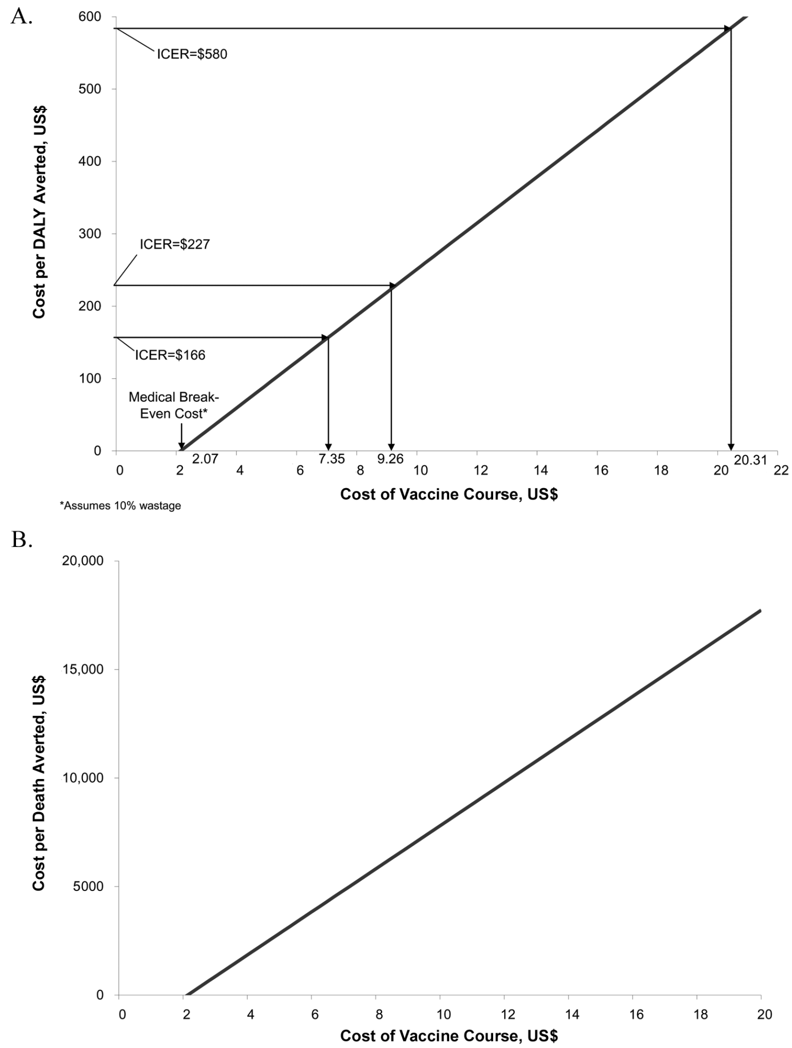

Figure 1. Cost-effectiveness of rotavirus vaccination per disability-adjusted life-year (DALY) averted *(A)* and per death averted *(B)*. The cost of a vaccine course includes an administration cost of $1.06 per course. ICER, incremental cost-effectiveness ratio.

pitalization rate was lower than expected because of the lack of access, our estimate that every child in Kenya visits an outpatient clinic for rotavirus diarrhea by 5 years of age is several times higher than the global estimate of ~1 of 7 children and is an important driver of our results. Of note, the global estimate of 1 of 7 children visiting a clinic for rotavirus diarrhea was derived from a single study in Chile [21, 23] and is likely not representative of rural Kenya. We also validated our data from the health utilization survey with a second survey of syndromes and health care–seeking behavior in the demographic surveillance system population; similar results were found, which suggests that clinics are indeed highly used for rotavirus diarrhea in Nyanza Province (CDC, unpublished data). If we reduced the rate of clinic visits in our model from every child visiting a clinic for rotavirus diarrhea to 1 of 4 children, the vaccine would still be considered to be a cost-effective intervention, with a cost of $85 per DALY averted. The difference in the use of hospitals and clinics likely reflects a lack of access to hospital care. Clinics tended to be used by rural, poor families, because the cost to a family of a clinic visit was lower than the cost to visit a hospital. This is reflected by our data showing that the median household income of families with children seen at clinics was less than half that of families with children seen at hospitals.

The present study has several limitations. First, we assumed that the cost to treat a diarrheal illness due to rotavirus was equal to the cost to treat a nonrotavirus diarrheal illness. In addition, several cost inputs were derived from only a few facilities in Nyanza Province and may not be representative of Kenya overall. Nyanza Province is rural, and many families live by subsistence farming; thus, the estimated lost income may be lower and the travel costs may be higher than those for Kenya overall. Although we adjusted for the likelihood of seeking treatment for diarrheal illness in each province, we were

Table 6. Sensitivity Analysis to Examine the Impact of Rotavirus Disease-Associated Health Burden, Medical Cost, and Vaccine Efficacy on the Medical Cost Attributed to Rotavirus Disease and the Cost-Effectiveness of Vaccination

Variable	Input value	Medical cost per child, US$	Cost per DALY averted,[a] US$
Health burden[b]			
Mortality rate			
Low	6.2	NA	30
Base-case	8.2	NA	27
High	10.3	NA	25
Hospitalization rate			
Low	4.1	4.77	29
Base-case	5.4	4.87	27
High	6.8	4.99	25
Outpatient visit rate			
Very low	223	1.55	85
Low	668	3.77	46
Base-case	890	4.87	27
High	1113	5.99	8
Medical costs[c]			
Hospitalization			
Low	77.76	4.76	29
Base-case	103.68	4.87	27
High	129.60	4.98	25
Outpatient visit			
Low	5.24	3.77	46
Base-case	6.98	4.87	27
High	8.73	5.99	8
Vaccine characteristic[d]			
Efficacy against death			
Low	60	NA	38
Base-case	85	NA	27
High	100	NA	23
Efficacy against hospitalization			
Low	60	NA	29
Base-case	85	NA	27
High	100	NA	26
Efficacy against outpatient visits			
Low	60	NA	45
Base-case	78	NA	27
High	100	NA	6

NOTE. NA, not applicable.

[a] Incremental cost per DALY averted assumed a vaccine price of $3 per course and an administration cost of $1.06 per course.

[b] Input values are expressed as cumulative incidence per 1000 children by 5 years of age.

[c] Input values are expressed as US dollars.

[d] Input values are expressed as percentages.

unable to calculate this for hospitalizations and clinic visits separately. In rural areas, such as Nyanza Province, accessible clinics may be used relatively more frequently than hospitals, and therefore, we may have overestimated the rate of clinic visits and underestimated the rate of hospitalization nationally. Few estimates of rates of clinic visits for rotavirus diarrhea are available. Consistent with the approach by the WHO and others to estimate deaths due to rotavirus, we applied the proportion of hospitalizations for diarrhea due to rotavirus (19%) to the rate of death due to diarrhea, rather than the prevalence of rotavirus disease among in-hospital deaths, which was considerably lower (9%). The case-fatality ratio of rotavirus infection among hospitalized children may be low because of the relative ease of treatment for rotavirus infection (intravenous rehydration), compared with many bacterial infections, for which antibiotics may be needed. In this population, in which overall rates of diarrhea are high and access to hospitalization and intravenous rehydration is low, the case-fatality ratio of severe rotavirus diarrhea (relative to other pathogens) among children who do not receive medical attention is likely to be higher than it is for those who are hospitalized. Although we used a wide range of vaccine effectiveness in the model, the performance of a vaccine in an impoverished setting may be even lower. Finally, we did not consider any indirect effects that may increase vaccine impact.

On the basis of early promising results of vaccine trials in African and Asia, the WHO recently extended its recommendation for use of rotavirus vaccines to all countries worldwide [24]. Routine use of rotavirus vaccine could have a large impact on diarrhea-associated mortality and morbidity in Kenya, and priority should be given to improve on-time vaccination coverage in poorer provinces, such as Nyanza, where rotavirus burden is highest; introduction of the vaccine in such provinces would further increase the impact and cost-effectiveness. The reduced vaccine price through GAVI Alliance is available for 5 years, and although the retail cost is expected to drop during this time, competition for limited resources from other health interventions may mean that the nondiscounted price may no longer be affordable to Kenya, even if vaccination remains cost-effective. Thus, continued surveillance will remain critical to define the impact on disease burden after vaccine introduction in Kenya.

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