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Projected health benefits and costs of pneumococcal and rotavirus vaccination in Uganda☆

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ABSTRACT

We determined impact and cost-effectiveness of pneumococcal and rotavirus vaccination programs among children < 5 years of age in Uganda from the public health system perspective. Disease-specific models compared the disease burden and cost with and without a vaccination program. If introduced, pneumococcal and rotavirus vaccine programs will save 10,796 and 5265 lives, respectively, prevent 94,071 *Streptococcus pneumoniae* and 94,729 rotavirus cases in children < 5 years, and save 3886 and 996 million Ugandan shillings ($2.3 and $0.6 million US dollars), respectively, in direct medical costs annually. At the GAVI price ($0.15/dose), pneumococcal vaccine will be cost-saving and rotavirus vaccine highly cost-effective.

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1. Background

Acute respiratory infections and diarrheal diseases are leading causes of childhood illness and death worldwide. Two of the most important vaccine-preventable pathogens in each disease group, *Streptococcus pneumoniae* and rotavirus, respectively, are together responsible for over 2 million deaths annually among children < 5 years of age globally [1–3]. In Uganda, *S. pneumoniae* accounts for approximately one-third of pneumonia and bacterial meningitis among children < 5 years [4–6]. Of all under-5 mortality in Uganda, 21% of deaths are due to pneumonia, of which 7% are caused by *S. pneumoniae* [4,7]. Rotavirus is the third major cause of mortality in children < 5 years in Uganda [7]. At Mulago National Referral Hospital in Kampala, 41% of all severe acute diarrheal admissions are attributable to rotavirus [8].

The availability of new vaccines, including conjugate vaccines against *S. pneumoniae* and live, orally administered rotavirus vaccines, represents a major opportunity to improve child health in Uganda. However, the decision to introduce a vaccine requires country-specific data on disease and economic burden to determine the health benefits and cost-effectiveness of a vaccination program. Introduction of pneumococcal conjugate vaccine in Uganda is anticipated in 2011 and rotavirus vaccine introduction in 2014. The objective of this study is to determine the potential impact and cost-effectiveness of national pneumococcal and rotavirus vaccination programs in Uganda. This analysis was conducted from the public healthcare system perspective to aid the Ugandan government and donor organizations in their decision of whether to introduce these vaccines into the national immunization program.

2. Methods

2.1. Overview of models

Disease-specific, decision-tree models were used to estimate the impact and cost-effectiveness of national pneumococcal and rotavirus immunization programs, respectively, by comparing the cost and burden of disease with and without such programs [9,10]. The models were created for use in developing country settings and estimate health outcomes and direct medical costs associated with pneumococcal and rotavirus disease for an annual birth cohort of 1.4 million followed for a 5-year period. Principle model inputs included disease burden, direct healthcare treatment costs, and

☆ The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention (CDC).

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vaccine coverage, efficacy, and cost. These models estimated the incremental cost-effectiveness ratio (cost per Disability-Adjusted Life Year (DALY) averted) expressed in 2008 inflation-adjusted Ugandan shillings (Ushs) and US dollars (USD) (1 USD = 1658 Ushs) and all future costs and DALY estimates were discounted at a rate of 3%. Only direct medical costs were included in the model.

2.2. Model inputs

2.2.1. Disease burden

Disease-specific burden was assessed both as number of events and DALYs, which quantify the number of years lost as the result of premature death and the number of years lived with disability [11]. DALY estimates included age weights and a discount rate of 3% [12].

Pneumococcal disease: Official WHO disease burden estimates of severe illnesses and deaths due to *S. pneumoniae* in children one month to < 5 years of age in Uganda were used to determine the number of *S. pneumoniae* events that occur annually [5]. These WHO estimates of severe cases and deaths in HIV-positive and HIV-negative children due to pneumococcal pneumonia, meningitis, and non-pneumonia, non-meningitis invasive pneumococcal disease (IPD) were derived using available data [5].

Rotavirus disease: Rates of death, hospitalization, and outpatient visits for any cause of acute diarrhea in children < 5 years were estimated, and then the prevalence of rotavirus detected through hospital surveillance was applied to these rates to estimate rotavirus-specific rates. We used the age distribution from hospitalized rotavirus cases at Mulago National Referral Hospital in Uganda for the age distribution of deaths, hospitalizations, and outpatient visits.

To enable the comparison of the rotavirus death rate from this analysis with other published estimates, we followed the WHO Child Health Epidemiology Reference Group (CHERG) method that assumes that the proportion of diarrheal hospitalizations due to rotavirus approximates the proportion of diarrheal deaths due to rotavirus [1,13]. To determine the diarrheal mortality rate, the total under-5 mortality rate in Uganda (138 per 1000 children) was multiplied by the estimated proportion of all deaths attributable to diarrhea in this age group (17%) [7]. To determine the rotavirus mortality rate, the diarrheal death rate was multiplied by the percent of stool specimens testing positive for rotavirus (41%) from diarrheal surveillance conducted at Mulago National Referral Hospital.

To estimate the annual rate of rotavirus diarrheal hospitalizations, we used 2008 surveillance data from Mulago National Referral Hospital. The number of children < 5 years of age from Kawempe Division admitted to Mulago Hospital with severe diarrhea ($n = 334$) was divided by the total under-5 population living in Kawempe Division ($n = 66{,}912$) to estimate the rate of diarrheal hospitalization. To determine the rotavirus hospitalization rate, the diarrheal hospitalization rate was multiplied by the rotavirus detection rate (41%) from surveillance.

To estimate the annual rate of diarrheal outpatient visits, the total number of outpatient visits for acute diarrhea by children < 5 years of age in Uganda ($n = 554{,}200$) was divided by the total under-5 population ($n = 6{,}066{,}504$) [14]. To determine the rate of rotavirus diarrhea outpatient visit, the all-cause acute diarrhea outpatient visit rate was multiplied by the proportion of rotavirus diarrhea (41%) detected through surveillance.

2.2.2. Healthcare utilization

Data on healthcare utilization patterns in Uganda were unavailable and based on consultation with local medical officials. We assumed that 60% of hospital care in Uganda occurs in primary care hospitals, 30% occurs in secondary level hospitals, and 10% occurs in tertiary level hospitals and for outpatient care, 75% occurs in free-standing health center facilities and the remaining 25% occurs in hospital-associated outpatient clinics. We further assumed that 100% of meningitis cases are treated in hospital whereas 50% of pneumococcal pneumonia and 50% non-pneumonia, non-meningitis IPD cases are treated in hospital and that every case of pneumococcal pneumonia visits an outpatient clinic once whereas pneumococcal meningitis and non-pneumonia, non-meningitis IPD cases visit outpatient facilities twice. We assumed every rotavirus case will visit a healthcare facility only once for a diarrheal illness.

2.2.3. Healthcare costs

We used standardized WHO-CHOICE (CHOosing Interventions that are Cost Effective) estimates of the per diem cost of hospitalization and outpatient visits in Uganda [15]. We multiplied the per diem cost by the average length of stay for a child hospitalized with the illness of interest (pneumococcal pneumonia, pneumococcal meningitis, non-pneumonia, non-meningitis IPD, or rotavirus) in the surveillance system (6, 14, 6, and 2.5 days, respectively) to calculate the total cost of a hospital stay. For hospitalized children, we added medication and diagnostic test costs obtained by reviewing medical records of 33 children with pneumococcal disease and 50 children with rotavirus disease hospitalized at Mulago National Referral Hospital and enrolled in the surveillance program. For outpatient visits for rotavirus diarrhea, we assumed that all prescribed medications were administered orally and the average cost of only the medications orally administered to hospitalized children was used to estimate medication costs in the outpatient setting.

The medication costs for a course of each prescribed treatment including ancillary supplies for administration were determined using wholesale price data from local medical suppliers and interviews with pediatricians and pharmacists at Mulago Hospital. The costs of diagnostic tests were obtained from wholesale price lists and interviews with laboratory workers at Mulago Hospital. All hospitalized pneumococcal meningitis cases were assumed to have a lumbar puncture performed and all hospitalized rotavirus diarrhea cases were assumed to have a stool culture performed. We assumed that no diagnostic tests were performed at outpatient clinics.

2.2.4. Vaccine program

We calculated the impact of a 10-valent pneumococcal conjugate vaccine and a live-attenuated, monovalent human rotavirus vaccine administered at 6, 10, and 14 weeks and 6 and 10 weeks of age, respectively, and concurrently with the diphtheria, tetanus, and pertussis vaccine (DTP)-Hepatitis B (HepB) + *Haemophilus Inflenzae* type B (Hib). Vaccine coverage was based on DTP-HepB + Hib coverage estimates (3-dose coverage for pneumococcal vaccine (79%) and 2-dose coverage for rotavirus vaccine (83%)) from the WHO/UNICEF 2008 Joint Report Form [16]. We assumed that all children will be vaccinated on time. When determining the number of doses needed, a wastage rate of 10% was used for both models [9,10].

2.2.5. Effectiveness of pneumococcal and rotavirus vaccines

The 10-valent pneumococcal conjugate vaccine would be effective against 63% of circulating pneumococcal serotypes in Uganda [17]. Based on published studies, the vaccine efficacy for preventable serotypes against severe pneumococcal disease and death is 85% in HIV-negative children and 28% in HIV-positive children [18].

Rotavirus vaccine provides heterotypic immunity. Efficacy against rotavirus-associated hospitalization and death was assumed to be 50% based on clinical trial data from Africa [19]. No data specifying rotavirus vaccine efficacy against outpatient