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Impact and cost-effectiveness of rotavirus vaccination in Bangladesh

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ABSTRACT

Introduction: Diarrheal disease is a leading cause of child mortality globally, and rotavirus is responsible for more than a third of those deaths. Despite substantial decreases, the number of rotavirus deaths in children under five was 215,000 per year in 2013. Of these deaths, approximately 41% occurred in Asia and 3% of those in Bangladesh. While Bangladesh has yet to introduce rotavirus vaccination, the country applied for Gavi support and plans to introduce it in 2018. This analysis evaluates the impact and cost-effectiveness of rotavirus vaccination in Bangladesh and provides estimates of the costs of the vaccination program to help inform decision-makers and international partners.

Methods: This analysis used Pan American Health Organization's TRIVAC model (version 2.0) to examine nationwide introduction of two-dose rotavirus vaccination in 2017, compared to no vaccination. Three mortality scenarios (low, high, and midpoint) were assessed. Benefits and costs were examined from the societal perspective over ten successive birth cohorts with a 3% discount rate. Model inputs were locally acquired and complemented by internationally validated estimates.

Results: Over ten years, rotavirus vaccination would prevent 4000 deaths, nearly 500,000 hospitalizations and 3 million outpatient visits in the base scenario. With a Gavi subsidy, cost/disability adjusted life year (DALY) ratios ranged from $58/DALY to $142/DALY averted. Without a Gavi subsidy and a vaccine price of $2.19 per dose, cost/DALY ratios ranged from $615/DALY to $1514/DALY averted.

Conclusion: The discounted cost per DALY averted was less than the GDP per capita for nearly all scenarios considered, indicating that a routine rotavirus vaccination program is highly likely to be cost-effective. Even in a low mortality setting with no Gavi subsidy, rotavirus vaccination would be cost-effective. These estimates exclude the herd immunity benefits of vaccination, so represent a conservative estimate of the cost-effectiveness of rotavirus vaccination in Bangladesh.

1. Introduction

Diarrheal disease is one of the leading causes of child mortality globally, and rotavirus is responsible for more than a third of those deaths [1–3]. While there is some variation in global mortality estimates by source, rotavirus mortality has fallen dramatically over the past two decades. In 2000, the number of deaths due to rotavirus disease was estimated to be 518,000 per year in children under five years of age. In 2013, this number decreased to 215,000 rotavirus deaths per year in children under five years of age. Of these deaths, 121,000 occurred in Sub-Saharan Africa and 89,000 occurred in Asia. As many as 2700 of these deaths are estimated to occur in Bangladesh [2,4]. While deaths are an important component of rotavirus burden, there are additional health and economic consequences due to rotavirus disease.

Currently, there are two World Health Organization (WHO) prequalified rotavirus vaccines available globally to help reduce the burden of rotavirus disease. These two vaccines are Rotarix® (manufactured by GlaxoSmithKline), administered as a two-dose schedule, and RotaTeq® (manufactured by Merck & Co., Inc.), administered as a three-dose schedule. According to WHO recommendations, rotavirus vaccines should be introduced into every country's national immunization program, particularly those where diarrhea is a leading cause of child death. Consistent with this recommendation, more than 80 countries have introduced

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rotavirus vaccination [5]. Gavi, the Vaccine Alliance also supports rotavirus vaccination by subsidizing the cost of vaccination in eligible countries [6]. Despite the WHO recommendation, Gavi support and large declines in global mortality, substantial mortality, morbidity, and economic burden due to rotavirus disease remain [7].

Bangladesh has played a leading role in building the evidence base for rotavirus vaccination, as well as other interventions to combat diarrheal disease (i.e., oral rehydration salts) [8,9]. In 2016, Bangladesh applied for Gavi support for rotavirus vaccination and plans to introduce vaccination in 2018. This analysis evaluates the impact and cost-effectiveness of rotavirus vaccination in Bangladesh and provides estimates of the costs of the vaccination program to help inform decision-makers in Bangladesh and international partners.

2. Materials and methods

This analysis examines the cost-effectiveness of a routine infant rotavirus vaccination program in Bangladesh compared to no vaccination. We examine nationwide introduction of a two-dose rotavirus vaccine beginning in 2017. Benefits and costs are examined from the societal perspective over ten successive birth cohorts. Costs and benefits are discounted at 3% per annum. All monetary units are adjusted to 2016 USD. Key outputs of the analysis include: deaths averted; disability adjusted life years (DALYs) averted; cases averted; inpatient visits averted; outpatient visits averted; informal "visits" averted; and health costs averted as a result of rotavirus vaccination. Additional outputs include total cost of vaccination program and cost/DALY averted.

This analysis tracks disease events and costs in ten vaccinated cohorts over the first five years of their life. During this time, they may or may not get rotavirus disease. If they acquire rotavirus, it can be either non-severe or severe. In either case, treatment for rotavirus disease can be sought as an inpatient (facility-based setting) or as an outpatient (facility-based or informal setting). A facility-based setting could be a hospital or clinic and an informal setting could include a faith-based healer or the acquisition of oral rehydration salts. Non-severe disease results in recovery with or without informal or outpatient care. Severe disease results in recovery or death with or without informal or inpatient care.

2.1. Model

This analysis uses Version 2.0 of the TRIVAC model. This Excel-based model was developed by researchers from the London School of Hygiene and Tropical Medicine (LSHTM) with support from Pan American Health Organization's (PAHO's) ProVac Initiative. The model is designed to be used at the country-level to conduct cost-effectiveness analyses for three vaccines: Rotavirus vaccine, Pneumococcal conjugate vaccine, and *Haemophilus influenza* type b and provides a consistent and transparent framework for comparing the impact and cost-effectiveness of these vaccines [10]. The model has been widely used across the world to evaluate the cost-effectiveness of these vaccines [11–16]. The model input parameters include: demographics, burden of disease, vaccine schedule, vaccine efficacy, vaccine coverage, vaccine costs, health service utilization, and health service costs. More detail on input parameters and values is included below.

2.2. Demographic data

Data on the number of live births and life expectancy at birth were gathered from the United Nations Populations Division [17]. Infant and child mortality data in Bangladesh were taken from the United Nations Inter-agency Group for Child Mortality Estimation [18]. The annual rate of reduction in infant and child mortality over the 2005–2015 period was used to project infant and child mortality rates through 2026.

2.3. Disease burden

2.3.1. Incidence and severity

The incidence of rotavirus in the under-five population is estimated to be 10,000 cases per 100,000 children. This value is based on a systematic review and meta-analysis by Bilcke et al. [19]. It is also corroborated by Zaman et al. which found an incidence of rotavirus gastroenteritis of 9,500/100,000 person years in the control arm of a RotaTeq trial in Bangladesh and in Vietnam [8]. Platts-Mills et al. note that 13% of all cause *diarrhea* episodes were severe, and subsequent unpublished analysis indicates that 27% of rotavirus episodes were severe in the same study [20,21]. This is a conservative estimate of rotavirus severity relative to other studies in the region [8]. Severity is defined by the duration and number of loose stools; and duration of vomiting, dehydration, and fever.

2.3.2. Mortality

There is substantial divergence in rotavirus mortality estimates in Bangladesh. Some estimate fewer than 1000 deaths per year [3] while others estimate over 2700 deaths per year [4]. To account for this divergence, we examine a midpoint mortality scenario with 1850 deaths from rotavirus in children under five per annum prior to vaccination. We also include scenarios with 1000 and 2700 rotavirus deaths in children under five prior to vaccination. A more extensive set of disease burden parameters is included in Table 1.

2.4. Vaccine coverage and efficacy

Vaccine coverage is high in Bangladesh. DTP1 is 97% and the second dose is interpolated as 95.5% based on DTP3 coverage of 94% [24]. Vaccine efficacy for severe and non-severe disease in the first year following vaccination is 48% and 45.2%, respectively. Vaccine efficacy decreases by 36% per year.[1] These values are based on an unpublished analysis of a Rotarix® trial in Bangladesh [25]. We assume single dose efficacy is half that of the two dose course. We exclude any indirect benefit of vaccination, i.e. herd effects.

2.5. Vaccine price and delivery cost

We model the vaccine price using Gavi's projection of Bangladesh's co-financing shares as they increase over time. Using a Gavi price of $2.19 per dose results in a vaccine price for Bangladesh of $0.16 in 2017 and this increases by 15% a year to $0.55 by 2026 [26,27]. We compare this to a vaccine price of $2.19 per dose, without a Gavi subsidy. We assume an additional 3% and 2% of the vaccine cost for handling and delivery, respectively. We also assume 5% vaccine wastage.

We initially, and conservatively, estimated the delivery cost as $0.80 per dose. This estimate is an average cost per dose delivered across the relevant Expanded Program on Immunization (EPI) cost categories for 2017 in the 2014–2018 cMYP [28]. Rotavirus relevant expenditure categories include personnel; maintenance and overhead; short term training; information, education, communication (IEC) and social mobilization; disease surveillance; program management; other routine recurrent costs; vehicles; and other capital equipment. These costs were allocated to rotavirus vaccines and other vaccines on a per dose basis. New cold chain investments were allocated to rotavirus vaccines and other new vaccines by

[1] This is a relative decrease, not an absolute decrease.

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