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Cost-Effective Analysis Of Rotavirus Vaccination In Dhaka, Bangladesh Using A Dynamic Model Of Rotavirus Transmission

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ABSTRACT

Background: Despite the global introduction of rotavirus vaccinations across countries, Rotavirus infections continue to be a leading cause of severe, dehydrating gastroenteritis in children under the age of 5 (Crawford et al., 2017). Bangladesh experiences an extremely high burden where rotavirus infections contribute to 6,000–14,000 deaths each year in children <5 years of age (Rahman et al., 2007). A cost-effective analysis can aid decision-makers in determining the pros and cons of introducing a rotavirus vaccination program in limited-resource countries.

Objective: A cost-effectiveness analysis was developed to evaluate the potential benefits of introducing rotavirus vaccination. The analysis performed aims to inform key decision-makers about the costs and benefits of introducing rotavirus vaccination in Bangladesh and help guide their decision on whether to implement such a program.

Methods: To better quantify vaccine impact and identify the optimal dosing schedule to improve vaccine performance as well as demonstrate the cost-effectiveness of rotavirus vaccines, previously developed, and validated mathematical models of rotavirus transmission for Dhaka, Bangladesh were used to project the potential impact of rotavirus vaccines over 10 years. Continuing to build off the previous modeling, identifying input parameters to include in the cost-effectiveness model was conducted. Extension of the developed rotavirus model for Dhaka, Bangladesh to include vaccines, run projected vaccination impact across different dosing schedules for ROTAVAC and ROTARIX vaccination programs, estimate moderate-to-severe and non-severe rotavirus annual incidence and organize the input variables for cost-effective analysis.

Results: The optimal dosing strategy across all schedules is shown to be 6/10/14. A 6/10/14 schedule of ROTARIX or ROTAVAC is the optimal strategy at a WTP threshold >=$200. However, the lower the WTP threshold is, no vaccination is the preferred method. Our findings highlight the value of Gavi's support for rotavirus vaccine introduction in Bangladesh.

Conclusion: A cost-effectiveness analysis is a useful tool for evaluating the potential benefits and costs of rotavirus vaccination because it enables decision-makers to compare the expected costs of a vaccination program with the expected health benefits. They can provide decision-makers with the information to understand the potential impact of the vaccine in terms of reducing the burden of rotavirus disease and associated costs, such as healthcare expenditures and lost productivity. It can also help to identify which vaccination strategies are cost-effective and prioritize limited resources towards the most efficient use of funds. Ultimately, a cost-effectiveness analysis can inform the policy decisions Bangladesh needs to jumpstart the implementation of rotavirus vaccination and ensure that resources are used in an effective way to improve public health outcomes.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Despite the global introduction of rotavirus vaccinations across countries, rotavirus infections continue to be a leading cause of severe, dehydrating gastroenteritis in children under the age of 5 (Crawford et al., 2017). These infections show significant morbidity and mortality within low- and middle-income countries, most notably within sub-Saharan Africa and South Asia. Together they account for more than 85% of global rotavirus deaths from 2000-2013 in children under the age of 5 (Tate et al., 2016). As the leading cause of severe diarrhea, it contributes to about 3% of all deaths among this population (Tanaka et al., 2007; Satter et al., 2017). Safe and effective WHO-prequalified rotavirus vaccines like ROTARIX (GSK) and RotaTeq (Merck) have been available globally for many years and are used in more than 98 countries around the world. In addition to these, several new rotavirus vaccines have attained national licensure -ROTAVAC, produced by Bharat Biotech, and ROTASIIL, produced by Serum Institute of India (Skansberg et al., 2020).

Although the introduction of the rotavirus vaccine is recommended by the WHO, many of these countries have yet to implement them into their national vaccine schedules. The decision to introduce new vaccines can be challenging due to various factors such as limited information about the disease burden, the cost of expanding cold chain equipment, and the uncertainty about the impact of vaccination in a particular context (Uddin et al., 2013). Insufficient funding also aids in compounding this problem. These factors make it hard for decision-makers to promote the adoption of new vaccines. One way to speed up the decision process is by conducting cost-effectiveness analyses that compare the costs and benefits of introducing new vaccines. This approach helps weigh the pros and cons of vaccine introduction and can assist these decision-makers in making informed choices.

With multiple rotavirus vaccines in existence, they have contributed to significantly decreasing the global burden of rotavirus infection, yet the effectiveness of licensed vaccines is moderate among low-income countries and continues to account for >200,000 deaths annually from rotavirus infection (Crawford et al., 2017). Delays in access to treatment result in staggering numbers, where impoverished and slum-dwelling individuals are affected most. Bangladesh experiences an extremely high burden where rotavirus infections contribute to 6,000–14,000 deaths each year in children <5 years of age (Rahman et al., 2007). Although they

have also made significant progress in reducing child mortality in recent years they still face many health challenges, including high rates of infectious diseases. Access to healthcare and vaccination programs remains limited in parts of the country, particularly in the rural areas.

It is crucial for lower-income countries to have a robust cost-effectiveness analysis in place to guide their decision-making process. In the case of Bangladesh, a cost-effectiveness analysis was developed to evaluate the potential benefits of introducing rotavirus vaccination. The analysis performed aims to inform key decision-makers about the costs and benefits of introducing rotavirus vaccination in Bangladesh and help guide their decision on whether to implement such a program.

METHODS

Overview

To better quantify vaccine impact and identify the optimal dosing schedule to improve vaccine performance as well as demonstrate the cost-effectiveness of rotavirus vaccines, previously developed, and validated mathematical models of rotavirus transmission for Dhaka, Bangladesh was used to project the potential impact of rotavirus vaccines over 10 years. These models allowed for a better understanding of the importance of seasonal variations in birth rate and meteorological factors on temporal patterns of rotavirus infection (Asare et al., 2022). The models were able to simulate rotavirus incidence in the absence of vaccination while accounting for the changing patterns in rotavirus epidemiology, a baseline that can be used to evaluate future vaccine impact (Asare et al., 2022). Continuing to build off the previous modeling, we looked at identifying input parameters to include in the cost-effectiveness model. Extension of this developed rotavirus model for Dhaka, Bangladesh to include vaccines, allows us to run projected vaccination impact across different dosing schedules to estimate moderate-to-severe and non-severe rotavirus annual incidence and organize the input variables for the cost-effectiveness mode to then run the model.

An investigation of the comparative cost-effectiveness of the different rotavirus vaccine dosing schedules was conducted. Using simulations from dynamic models of rotavirus transmission, as well as best-estimated model parameters from the pre-vaccination model fit to Dhaka. Sampling from a range of parameters determining vaccine effectiveness, different model

simulations were generated for the considered dosing schedules. The generated moderate-to-severe and non-severe rotavirus cases will be used as input for the cost-effectiveness analysis model.

Dynamic Model Description

To simulate the dynamics of rotavirus infection in Bangladesh an adapted version of a SIRS-like model developed by Pitzer et al was used. (2022) fitted to observed RVGE (Rotavirus Gasteroentisis) cases. The boxes in the model indicate various model states and the lines indicate rates of movement between the compartments (Pitzer et al., 2022). The red lines show individuals who fail to respond to the first vaccine dose and the dark and light blue lines show the movement of individuals who respond to the first and second doses of the vaccine, respectively (Pitzer et al., 2022). The original model assumed that individuals are born into the maternal class (M), which is equal to the annual birth rate (B) (Pitzer et al., 2022). It shows infants are protected by maternally acquired immunity, which gradually wanes over time, making them fully susceptible to first infection. These individuals are subject to primary infection at a certain rate and move to the I1 compartment. Infected individuals in the model remain infectious for an average period and only a fraction of them develop severe RVGE. After primary infection, individuals gain temporary immunity to reinfection that wanes over time, making them susceptible to secondary infection at a reduced rate. Individuals with their second infection have their infectiousness lowered and are less likely to develop severe RVGE. They recover at a faster rate and enter the R2 compartment, which provides temporary immunity that wanes over time, making individuals partially immune and susceptible to subsequent infections that are mostly mild or asymptomatic (Pitzer et al., 2022). A proportion of infected individuals could still develop severe RVGE, and infectiousness is reduced by a factor. Recovered individuals are transferred to the temporary immune compartment, and this immunity also wanes over time, upon which individuals return to the partially immune susceptible compartment (Pitzer et al., 2022).

Those vaccinated and responding to each vaccine dose are transferred from either the maternal immunity or susceptible or recovered compartments where the vaccine is administered to the next recovered compartment (Pitzer et al., 2022). Waning of vaccine-acquired immunity is also incorporated. Vaccinated individuals who failed to seroconvert (red lines) remain in their

current state and for those who respond to the vaccine, the vaccine offers temporary protection against rotavirus infection and wanes at a rate ωv (same for both doses) was assumed (Pitzer et al., 2022). After the waning of vaccine-acquired immunity, vaccinated individuals either become susceptible after the first dose or after the second dose, and individuals who responded to both doses of the vaccine remain protected and enter the next protected compartment (Pitzer et al. 2022).

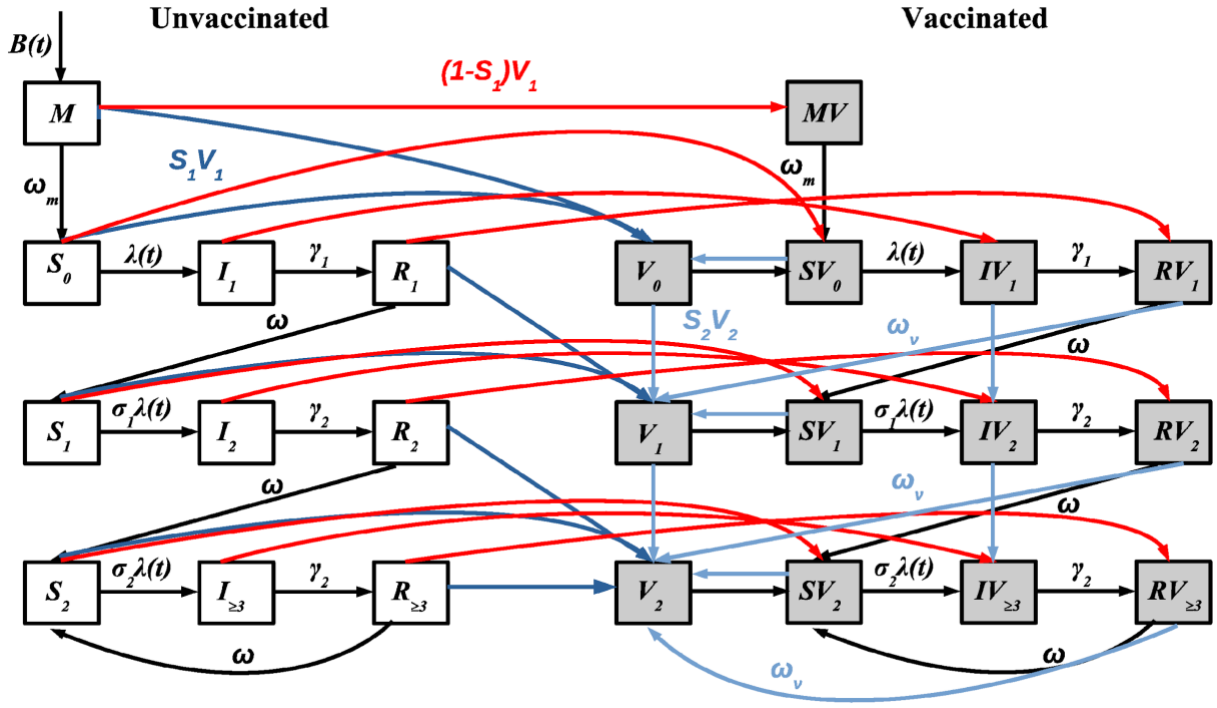

Figure 1. Model Structure

Cost-Effectiveness Decision Tree

A cost-effective decision tree was developed to estimate incremental costs, health outcomes, and cost-effectiveness associated with a rotavirus vaccination program using model predicted RVGE cases from the dynamical model. The estimates developed for this decision tree used a generalized model populated with country-specific data. The output is country-specific providing different vaccination strategy comparisons over time including uncertainty. Costs and health outcomes were analyzed using a public health perspective.

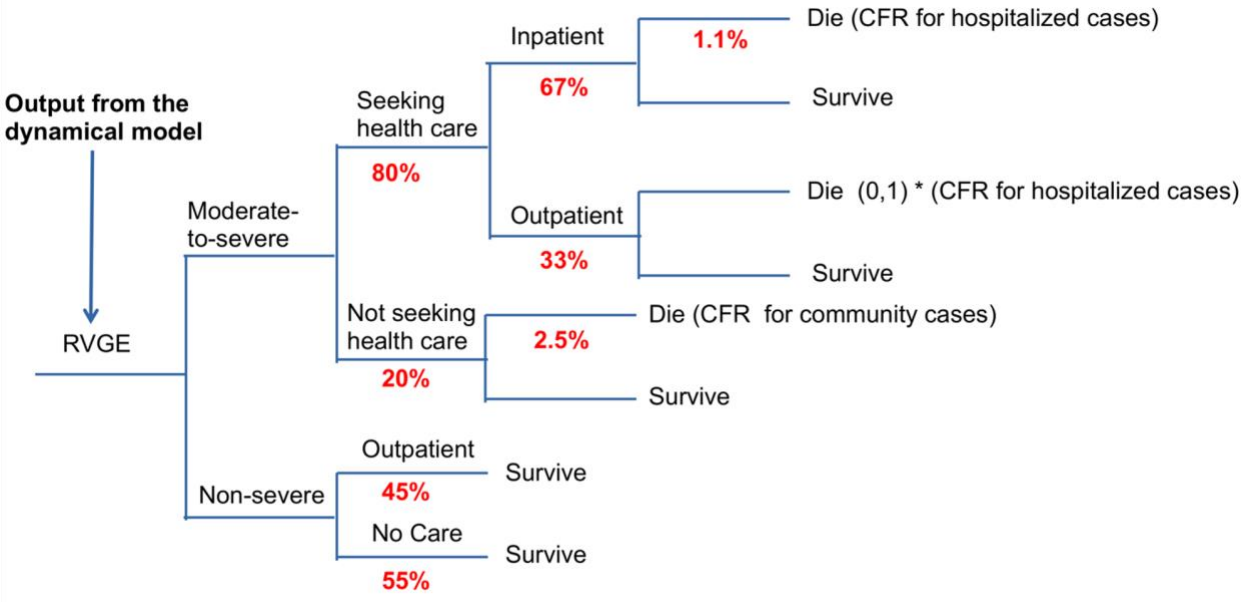

Figure 2. Cost-Effective Decision Tree

RVGE cases were classified as either moderate-to-severe or non-severe. Non-severe cases either received treatment in an outpatient setting and survive or received no treatment care and survive. Moderate-to-severe cases not seeking healthcare either die or survive and cases seeking care either received inpatient treatment or outpatient treatment. Moderate-to-severe cases receiving inpatient treatment either die or survive. Moderate-to-severe cases receiving outpatient care either die or survive.

Dynamic Model Fitting

Previous parameter estimates fitted 23 years of weekly age-stratified rotavirus surveillance data from Dhaka Hospital using a maximum likelihood framework. Estimates used are obtained from the best-fit model determined previously (Asare et al. 2022). This model was able to predict the observed increase in annual seasonal epidemics of rotavirus (see Appendix, Table 5). Building off the previous model (Asare et al., 2022), Bangladesh-specific input data of vaccines and rotavirus health-related outcomes, as well as their associated costs, were used to calculate disease and economic burden. Three vaccination dosing schedules were included with no vaccination used as the baseline. The model included 6/10, 6/10/14, and 6/10/40 weeks dosing schedules.

Estimates of healthcare-seeking behavior and hospitalizations for Moderate-to-severe and non-severe rotavirus cases were based on an averaged estimate across multiple Bangladesh-specific published papers regarding cases of children <5 years of age. DALY calculation estimates for both Moderate-to-severe and non-severe cases were based on published data from Pecenka et al., 2017. The average length of stay for both case severity types was based on published data from Kumar et al., 2020.

Parameter	Value	References
	Moderate-to-Severe	
Healthcare Seeking Behavior (95% CI)		
% Seeking Health Care	*0.74 (0.99 - 0.48)*	[9],[11],[12],[15]
% Not Seeking Health Care	*0.33 (0.56 - 0.09)*	[9],[11],[12],[15]
% Die Not Seeking Care	*0.07*	[12]
Hospitalization (95% CI)		
% Inpatient	*0.36 (0.66 - 0.08)*	[11],[15]
% Outpatient	*0.63 (0.92 - 0.34)*	[11],[15]
% Die Inpatient	*0.14*	[12]
% Die Outpatient	*0.79*	[12]
DALY Calculation	*0.25*	[11]
Average Length of Stay at Hospital (days)	*5*	[6]
Average Duration of Illness (days)	6 (2-10)	[12]
	Non-severe	
Healthcare Seeking Behavior (95% CI)		
% Outpatient	*0.28 (0.49 - 0.08)*	[5], [12], [16]
% Seeking No Care	*0.46 (0.78 - 0.14)*	[5], [12]
% Survive Outpatient	*0.86*	[12]
DALY Calculation	*0.19*	[11]
	Case Fatality Rates (95% CI)	
Hospitalized	0.0023 (0.0020-0.0025)	[3]
Community	0.0245 (0.0148-0.0403)	[3]

Table 1. Bangladesh-specific input parameters

Vaccine-related costs for ROTARIX (GSK) and ROTAVAC (Bharat Biotech) were obtained from a pricing table generated by UNICEF illustrating awarded price per dose (in US$) per product per supplier per calendar year, based on a multi-year supply agreement for both Gavi and non-Gavi support (UNICEF Supply Division, 2021). Gavi, the Vaccine Alliance provides support for vaccines in low- and middle-income countries (LMICs) through mechanisms like vaccine procurement and health system strengthening. A study conducted by Sarker et al., 2023

published data regarding vaccine and inpatient/outpatient related treatment costs for rotavirus infection including vaccine wastage rate. Case fatality rates for hospitalized and community rates were obtained by published estimates from Asare et al., 2022.

Vaccine type	Cost (Gavi)	Cost (Non-Gavi)	References
ROTAVAC	1.1500	2.0000	[19]
ROTARIX	2.0500	5.1600	[19]

Table 2. Vaccine costs, Gavi and Non-Gavi support (UNICEF Supply Division, 2021)

Parameter	Value (95% CI)	References
delivery cost per dose	0.8 (0.1-2)	[1], [3]
Treatment Costs		
average inpatient treatment cost (provider + household)	62.62 (31.31-125.24)	[14]
average outpatient treatment cost (provider + household)	3.27 (1.64-6.54)	[3]
average informal cost per treatment	1.17 (0.59-2.34	[3]
vaccine wastage rate (%)	5	[3]

Table 3. Vaccine and treatment-related costs input parameters.

Dosing Schedules

6/10, 6/10/14, and 6/10/40 week rotavirus dosing schedules are used for comparison in research for the cost-effectiveness of rotavirus vaccination campaigns in low-income countries, they represent different vaccination schedules that have been used in clinical trials for various, currently licensed, rotavirus vaccines. By comparing the cost-effectiveness of these different schedules, researchers can determine which schedule provides the best balance of protection and affordability in low-income countries. Distribution of age for vaccines dosage (months) is found in Appendix (Table 4).

Schedule (weeks)	No. Doses	Age for Vaccine (months)
No Vaccine	0	
6/10	2	2, 3
6/10/14	3	2, 3, 4
6/10/40	3	2, 3, 9

Table 4. Model Parameter Dosing Schedules

After fitting and scaling, the model was used to simulate rotavirus infection cases from 2025 to 2034 in Bangladesh under these three dosing schedules, both Moderate-to-Severe (MS) and Non-severe (NS) cases.

Incremental Cost-Effectiveness Model Inputs

The model inputs for no vaccine (baseline) included cases, deaths, years of life lost (YLLs), years of life lost due to disability (YLDs), disability-adjusted life years (DALYs), and treatment costs. Under the 6/10, 6/10/14, and 6/10/40 dosing schedules, model inputs included cases averted, deaths averted, YLLs averted, YLDs averted, DALYs averted, % DALYs averted, averted treatment costs, % of cases + deaths + treatment costs averted, cost of vaccination, and net costs. These estimates were input for both ROTARIX and ROTAVAC-specific parameters as well as separate estimates were generated for Gavi and non-Gavi support for each.

RESULTS

The model output consisted of 10-year data from 2025 to 2034, consisting of three dosing schedules (6/10 weeks, 6/10/14 weeks, and 6/10/40 weeks) with no vaccination (novacc) as our baseline. The data is for both moderate-to-severe (MS) and non-severe (NS) cases. Each year consists of 400 simulations sampled from the model parameters. A box plot time series was generated for this data (Appendix: Fig. 5 & Fig. 6), for both Moderate-to-Severe (MS) and Non-severe (NS) cases.

Over a 10-year period across both MS and NS cases, the 6/10/14 week dosing schedule consistently illustrated an overall lower incidence of cases compared to all other dosing schedules. MS cases under the 6/10 dosing schedule during a 10-year span from 2025 to 2034, with an incidence per 100,000, started at around an average of 416 cases and is estimated to reach around 457 cases. The 6/10/40 dosing schedule starts at about an average of 333 cases and over time reaches about 362 cases. 6/10/14 dosing schedule illustrates the lowest incidence in cases over time starting at an average of around 292 to about 318 cases. For NS cases, this trend follows, however, the incidence per 100,000 is much higher. For a 6/10 dosing schedule, cases average from 4537 in 2025 to 4607 by 2034. Under the 6/10/40 dosing schedule, cases average starting from 3816 cases to 3790 cases. The 6/10/14 dosing schedule illustrated the lowest

incidence of cases, averaging 3640 cases, estimated to reach 3624 cases. Further analysis was conducted to further illustrate this.

Model input estimates also listed various willingness-to-pay (WTP) thresholds and the corresponding rotavirus vaccination schedule that is considered cost-effective at each threshold. Estimates show that at a WTP threshold of $0, there is no vaccination (novacc), while at a threshold of $200, the 6/10/14 dosing schedule is cost-effective. The 6/10/14 schedule becomes cost-effective at a WTP threshold of 0.25 times the GDP (gross domestic product). As the WTP threshold increases, the cost-effective vaccination schedule shifts to 6/10/14 and remains so until the threshold reaches $2000 or 4 times the GDP.

	6_10_schedule	6_10_14_schedule	6_10_40_schedule
Cases Averted (thousands)	3 (0.720-4)	4 (2-5)	4 (0.859-5)
Deaths Averted	146 (42-279)	214 (89-357)	197 (50-346)
YLLs Averted (thousands)	4 (1-8)	6 (2-10)	5 (1-10)
YLDs Averted (thousands)	0.030 (0.004-0.086)	0.043 (0.010-0.111)	0.040 (0.006-0.109)
DALYs Averted (thousands)	4 (1-8)	6 (2-10)	5 (1-10)
Percent DALYs Averted	41 (11-68)	60 (24-82)	55 (13-80)
	ROTAVAC		
Averted Treatment Costs (thousands)	770 (214-1374)	1149 (455-1702)	1060 (255-1661)
Percent Cases & Deaths & Treatment Costs Averted	41 (11-68)	60 (24-82)	55 (13-80)
Cost of Vaccination (thousand)	1078 (1077-1079)	1616 (1615-1618)	1616 (1615-1618)
Net Costs (thousands)	308 (-296.839-864)	467 (-85.278-1161)	557 (-45.820-1360)
	ROTARIX		
Averted Treatment Costs (thousands)	785 (219-1351)	1155 (468-1689)	1065 (263-1648)
Percent Cases & Deaths & Treatment Costs Averted	41 (11-68)	60 (24-82)	55 (13-80)
Cost of Vaccination (thousand)	1248 (1246-1249)	1871 (1869-1873)	1870 (1869-1872)
Net Costs (thousands)	463 (-104.900-1028)	716 (182-1403)	806 (222-1607)

Table 5. Key model outputs for ROTAVAC and ROTARIX under each dosing schedule

Under the 6/10, 6/10/14, and 6/10/40 dosing schedules, cases, deaths, YLLs, YLDs, and DALYs averted do not change in effectiveness across schedules for ROTAVAC and ROTARIX implemented vaccines. However, averted *costs* related to both treatment and vaccination differ compared against each dosing schedule for both ROTAVAC and ROTARIX. It is observed that the 6/10 dosing schedule is least costly compared to the 6/10/14 and 6/10/40 schedules, providing thousands in projected savings.

Although this dosing schedule resulted in the least expensive vaccination schedule for both ROTAVAC and ROTARIX, further analysis was performed to understand the consistency

of this finding and illustrate the probability of highest net benefit and WTP for a DALY averted (2025$USD) for each vaccine across all dosing schedules. A cost-effectiveness plane was also constructed to illustrate the incremental costs associated with each schedule for DALYs averted in the thousands. For each analysis, 2 results were produced to illustrate vaccination implementation with Gavi support and non-Gavi support. Vaccine implementation across all analysis was shown to provide the highest net of benefits with Gavi-support. Figure 3. Below illustrates the analyses performed with Gavi-support.

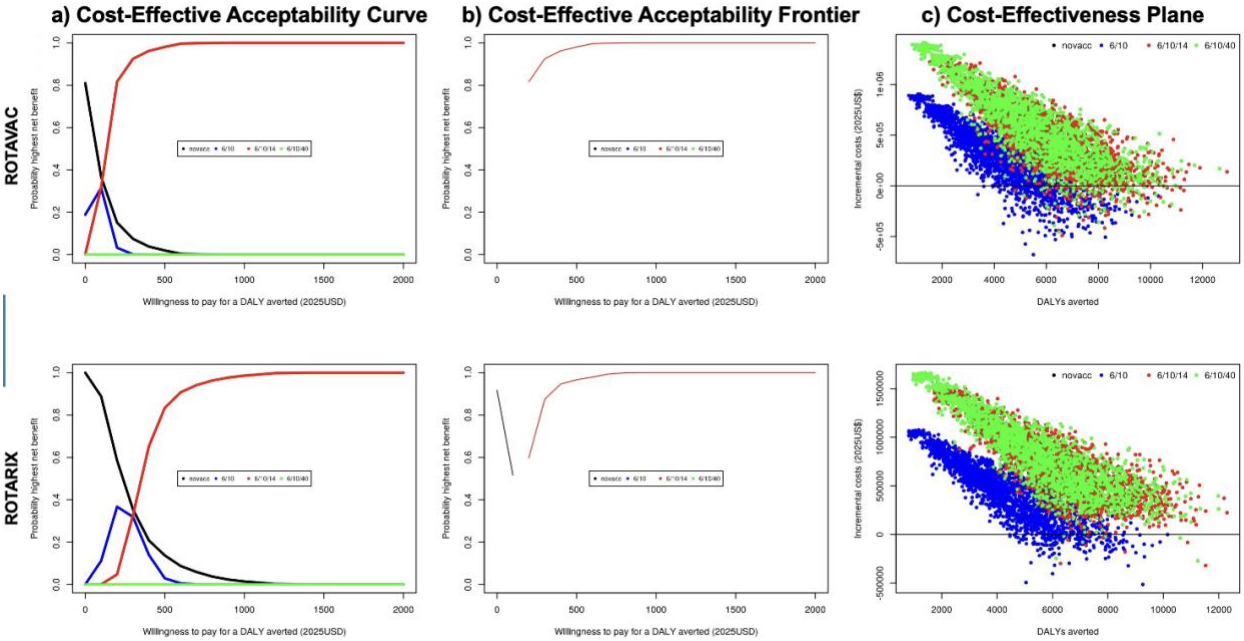

Figure 3. CEAC, CEAF, and Cost-Effectiveness Plane for ROTAVAC and ROTARIX under Gavi support

The upper and lower left panel (Figure 3) illustrates a Cost-Effectiveness Acceptability Curve (CEAC) for ROTAVAC and ROTARIX under Gavi support. Illustrated here is the probability of the highest net benefit of these vaccine treatments under the various dosing schedules are cost-effective at different WTPs for DALYs averted (2025$ USD). The baseline (novacc) drops considerably after the WTP passes $100 across all scenarios. The 6/10 dosing schedule increases at a WTP of around $100, then considerably drops as it reaches $300. The 6/10/40 dosing schedule does not show any probability of benefit compared. The 6/10/14 dosing schedule consistently shows the probability of the highest net benefit across both vaccine treatments. This illustration allows decision-makers to choose between the different rotavirus treatments based on cost-effectiveness.

A Cost-Effectiveness Acceptability Frontier (CEAF) shown in the upper and lower middle panels of Figure 3 was also used to illustrate the probability that rotavirus vaccine treatment under these scenarios is cost-effective at different WTP thresholds. The CEAF was constructed by plotting the incremental costs for WTP for DALYs averted (2025$ USD) and the incremental probability of the highest net benefit. The CEAF estimations consider the uncertainty in the estimates of costs and outcomes. Under the baseline (novacc), the WTP threshold is at about $200, anything more than that the 6/10/14 dosing schedule becomes the cost-effective option. No data is shown for the 6/10 and 6/10/40 dosing schedules as 6/10/14 is the preferred strategy relative to 6/10 and 6/10/40.

Figure 3 illustrates a cost-effectiveness plane that compares the costs and health outcomes (in DALYs averted) of the various dosing schedules in the upper and lower right panels. These graphs depict cost-effectiveness across the ROTAVAC and ROTARIX vaccine programs with Gavi support. The points on the plane that fall below $0 in incremental costs, indicate these dosing schedules are not cost-effective at a certain point. The 6/10 dosing schedule is shown to be the least expensive option but also provides the least benefit. The 6/10/40 option is highly effective yet is the most expensive dosing schedule to implement. The 6/10/14 dosing schedule produced high health benefits (DALYs averted) while also significantly saving on costs compared.

DISCUSSION

Rotavirus is one of the leading causes of severe diarrhea in children <5 years of age worldwide, and it can be fatal if left untreated. Bangladesh is one of the countries where rotavirus infection is prevalent, and it has a significant impact on child mortality rates. In 2016, Bangladesh applied to Gavi, the Vaccine Alliance, for support to introduce rotavirus vaccination in the country (Zaman et al., 2021). The plan was to introduce the ROTARIX vaccine into the routine immunization program by 2018, as reported in a study by Zaman et al. in 2021. Gavi provides financial support to eligible countries for vaccine introduction and covers the cost of the rotavirus vaccine and a one-time grant to cover introduction costs. This support is essential for low-income countries like Bangladesh, as it helps to make vaccines more affordable and accessible to the population.

Although this application has been submitted, the introduction of rotavirus vaccines in Bangladesh has been delayed due to a lack of many aspects of infrastructure and the need to expand and upgrade facilities to support the planned expansion in the whole country (Zaman et al., 2021). In addition, various other challenges pose obstacles to the implementation of the rotavirus vaccine in Bangladesh. These included limited time, resources, and funding due to competing priorities with issues such as the measles-rubella vaccination campaign planned for late 2019 (Zaman et al., 2021). The measles outbreak in the country began to surge around the time when Gavi approved Bangladesh's application for rotavirus vaccination (Zaman et al., 2021). The overall readiness of Bangladesh's Expanded Program on Immunization (EPI) and the lack of a realistic introduction timeline has further contributed to the significant delay in the implementation of the rotavirus vaccine in the country.

As of now, the vaccine introduction has not yet begun. To evaluate the impact of vaccination on reducing the burden, a comparative cost-effectiveness analysis was conducted to identify the optimal dosing schedule to improve vaccine performance as well as demonstrate the cost-effectiveness of rotavirus vaccines with the use of previously developed and validated mathematical models of rotavirus transmission for Dhaka, Bangladesh. We also obtained information on the potential costs for healthcare-seeking behavior, treatment costs as well as other related costs to simulate an introduction of the rotavirus vaccine through Bangladesh's National Immunization Program. This analysis aimed to help guide key decision-makers on whether to introduce rotavirus vaccination in the country or not.

Our initial time series boxplot of both moderate-to-severe cases and non-severe show 6/10/14 dosing schedule illustrating the lowest incidence of cases across all dosing schedules however modelling resulted in the 6/10 dosing schedule across vaccination programs to be least costly, this is understandably so as this schedule requires only 2 vaccination doses compared to 3. To investigate this further, analysis showed that rotavirus immunization of ROTAVAC or ROTRIX on a 6/10/14 week dosing schedule is shown to have the high net benefit across different vaccination treatments. However, the lower the WTP threshold of $200 is, the no vaccination (novacc) is the preferred method. This is comparable to Bangladesh paying 0.25 times the GDP per person. This indicates that the cost of implementing any of the vaccination strategies is too high relative to the expected benefits at this threshold and that resources would be better spent elsewhere. The optimal dosing strategy across all schedules is shown to be

6/10/14. A 6/10/14 schedule of ROTARIX or ROTAVAC is the optimal strategy at a WTP threshold >=$200. However, the lower the WTP threshold is, no vaccination is the preferred method. Our findings also highlight the value of Gavi's support for rotavirus vaccine introduction in Bangladesh.

Our study has an important limitation that potentially impacts the estimated cost-effectiveness and should be further researched. This limitation is that our estimates of disease burden (% die not seeking care, % die inpatient, % die outpatient) for moderate-to-severe cases and (% survive outpatient, %s survive no care) were based on data from a cohort of children in Bangladesh experiencing diarrheal disease, which might not reflect the specific burden of *rotavirus* disease in Bangladesh. This highlights the importance of obtaining primary cost data on hospitalization, outpatient visits, and treatment of rotavirus in Bangladesh, which would enable a more accurate valuation of the economic burden of the disease.

A cost-effectiveness analysis is a useful tool for evaluating the potential benefits and costs of rotavirus vaccination because it enables decision-makers to compare the expected costs of a vaccination program with the expected health benefits. They can provide the decision-makers with the information to understand the potential impact of the vaccine in terms of reducing the burden of rotavirus disease and associated costs, such as healthcare expenditures and lost productivity. It can also help to identify which vaccination strategies are most cost-effective and prioritize limited resources towards the most efficient use of funds, especially considering the major setbacks Bangladesh faces when vaccine introduction begins. Ultimately, a cost-effectiveness analysis can inform the policy decisions Bangladesh needs to jumpstart the implementation of a rotavirus vaccination program and ensure that resources are used in the most effective way to improve their public health outcomes.

APPENDIX

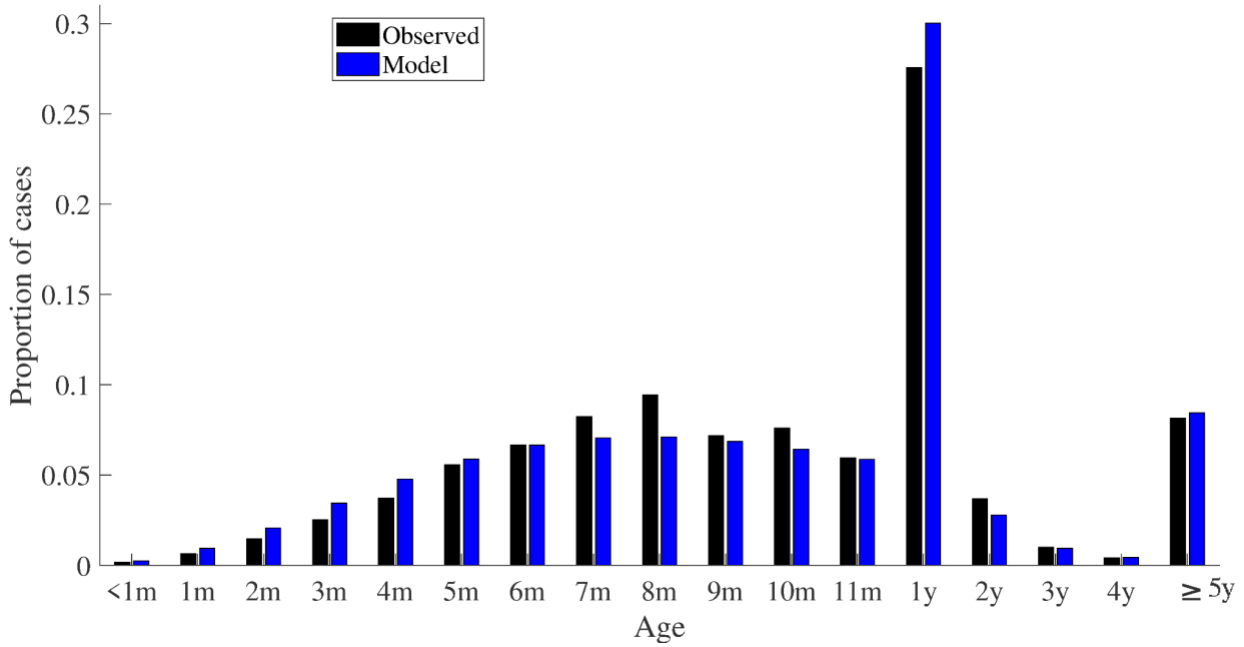

Figure 4. Age Distribution of Cases

Parameter	Estimate	Term
	Pre-Vaccination Model Estimates	
***R*0**	*26.2 (25.9–26.4)*	basic reproductive number
1/*ωm* (weeks)	*28.7 (28.6–29.1)*	duration of waning maternal immunity
***d*3**	*3.60 × 10−4*	proportion of subsequent infections that are severe
h	*0.051*	proportion of severe diarrhea cases reported
***b*1**	*0.114 (0.107–0.130)*	amplitude of annual seasonal forcing
***ϕ*1 (weeks)**	*5.7 (5.4–8.6)*	annual seasonal offset
***b*2**	*0.047 (0.045–0.050)*	amplitude of biannual seasonal forcing
***ϕ*2 (weeks)**	*32.5 (32.3–32.8)*	biannual seasonal offset
***b*dtr**	*0.367 (0.361–0.372)*	scaling parameter for diurnal temperate range (dtr)
***b*wpre**	*0.244 (0.175–0.481)*	scaling parameter for water presence (wpre)
	Model Parameters Describing Vaccine Effectiveness	
SC	*50-90%*	vaccine response rate (same for each dose)
wv	*3-60 (months)*	duration of vaccine-induced immunity

Table 6. Previous Estimated Model Parameters fitted to data from Dhaka, Ernest et al. 2022.

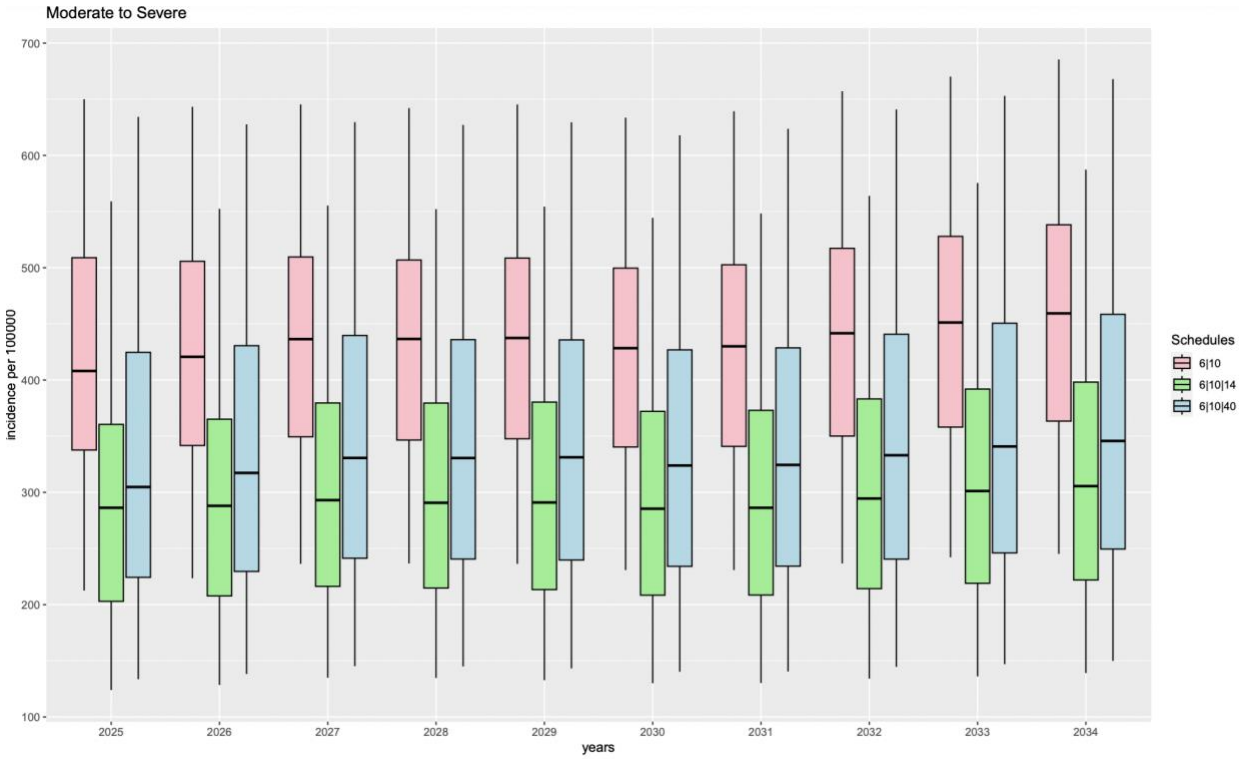

Figure 5. Time series boxplot for moderate-to-severe cases

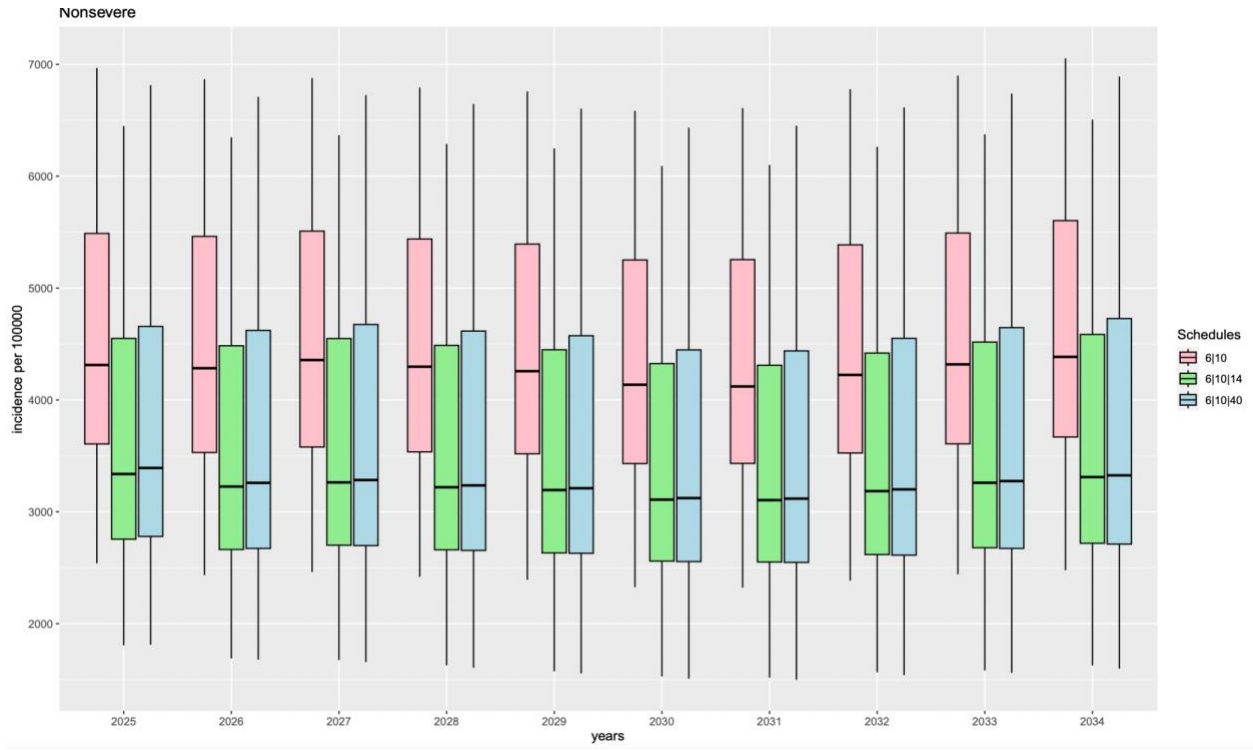

Figure 6. Time series boxplot for nonsevere cases

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