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Cost-effectiveness of norovirus vaccination in children in Peru

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ABSTRACT

Background: With candidate norovirus (NV) vaccines in a rapid phase of development, assessment of the potential economic value of vaccine implementation will be necessary to aid health officials in vaccine implementation decisions. To date, no evaluations have been performed to evaluate the benefit of adopting NV vaccines for use in the childhood immunization programs of low- and middle-income countries.

Methods: We used a Markov decision model to evaluate the cost-effectiveness of adding a two-dose NV vaccine to Peru's routine childhood immunization schedule using two recent estimates of NV incidence, one for a peri-urban region and one for a jungle region of the country.

Results: Using the peri-urban NV incidence estimate, the annual cost of vaccination would be $13.0 million, offset by $2.6 million in treatment savings. Overall, this would result in 473 total DALYs averted; 526,245 diarrhea cases averted; 153,735 outpatient visits averted; and 414 hospitalizations averted between birth and the fifth year of life. The incremental cost-effectiveness ratio would be $21,415 per DALY averted; $19.86 per diarrhea case; $68.23 per outpatient visit; and $26,298 per hospitalization. Using the higher jungle NV incidence rates provided a lower cost per DALY of $10,135. The incremental cost per DALY with per-urban NV incidence is greater than three times the 2012 GDP per capita of Peru but the estimate drops below this threshold using the incidence from the jungle setting. In addition to the impact of incidence, sensitivity analysis showed that vaccine price and efficacy play a strong role in determining the level of cost-effectiveness.

Conclusions: The introduction of a NV vaccine would prevent many healthcare outcomes in the Peru and potentially be cost-effective in scenarios with high NV incidence. The vaccine cost-effectiveness model could also be applied to the evaluation of NV vaccine cost-effectiveness in other countries in resource-poor settings, where NV incidence rates are expected to be higher.

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1. Introduction

Diarrhea remains one of the largest causes of preventable death and disability among young children in low- and middle-income countries [1]. Prior to the introduction of vaccines against rotavirus, 1.4 billion children younger than five years of age developed diarrhea annually in these settings [2]. Of those, 123.6 million required medical care, and nine million were hospitalized [2]. While rotavirus vaccination has had an impact in terms of reducing child mortality, diarrhea remains a significant contributor to medical costs and morbidity in resource poor settings [3]. Interventions targeting the major etiologies of diarrhea in the children most susceptible to diarrhea-associated morbidity should accelerate the declining burden of disease.

Peru is a rapidly developing country with a current population of 30 million [4]. In 2009 it added a two-dose monovalent oral vaccine against rotavirus to its national immunization schedule, achieving annual national vaccine coverage rates of 95% and 86% for the first and second doses, respectively [5]. However, diarrhea-associated child morbidity in this setting remains significant [6]. Current evidence indicates that NV has become the number one cause of viral gastroenteritis in young children in Peruvian communities, with over 70% of children in peri-urban communities experiencing between one and eight episode of NV diarrhea in the

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first two years of life [6]. In the wake of Peru's successful rotavirus vaccine implementation, NV has also been associated with over a third of cases of diarrhea in young children seeking hospital care for diarrhea [7]. This makes it one of the predominant pathogens in medically attended pediatric diarrhea cases, which can translate into substantial costs [8].

The development of an NV vaccine has been complicated in the past by the lack of a NV cell culture system, the heterogeneity of NV strains, and a lack of knowledge about cross strain immunity or the duration of protection conferred by NV infection. However, with the successful application of virus-like particle (VLP)-based vaccine technology for the highly effective Gardasil and Cervarix vaccines for human papillomavirus infections and precancerous lesions, there is promise that this same approach could be used as a template for NV vaccine development. Expression of the NV capsid proteins in eukaryotic cells leads to the spontaneous assembly of VLPs, which have been shown to be immunogenic when delivered parenterally, orally, or intranasally [9]. In 2011, a human trial of intranasally delivered, VLP-based vaccine against the prototypic Norwalk virus demonstrated 47% effectiveness against the vaccine strain [9]. Multivalent candidate vaccines against NV are currently under development, and other vaccine approaches include multivalent alpha-virus replicon particles (VRPs), that allow formation of NV VLPs, edible vaccines that deliver VLPs, P particle based vaccines, and polyvalent NV P domain glutathione S-transferase complexes [10].

With candidate NV vaccines in a rapid phase of development [11], assessment of the potential economic value of vaccination will be necessary to aid health officials in implementation decisions. Although previous analyses have found NV vaccines to be potentially cost-effective for outbreaks and in children younger than five years old in high-income countries [12,13], no evaluations have evaluated the benefit of adopting NV vaccines for routine use in the childhood immunization programs of low- and middle-income countries. Here, we evaluate the cost-effectiveness of incorporating a vaccine against NV into the Peruvian national immunization schedule. A full-scale introduction of the vaccine is assumed and compared with a status quo scenario in which there is no national NV vaccination. Our model provides a useful template for evaluating the potential economic benefit of NV vaccine implementation in other resource-limited countries following the implementation of rotavirus vaccines at high coverage rates.

2. Methods & data

We evaluated NV vaccine cost-effectiveness in a hypothetical cohort of children younger than five years of age in Peru. The evaluation used a five-year time horizon to estimate the incremental costs and health benefits of routine NV vaccine introduction compared with the status quo, where no NV vaccine was available, but rotavirus vaccination had been implemented at scale. We modeled the introduction of a vaccine against NV for the 2012 Peruvian birth cohort with an 85% vaccine coverage rate, which is similar to the scaled up rotavirus vaccine coverage rate in Peru in 2009 [1]. We reported costs in 2012 USD, and health effects as NV-associated diarrhea cases, outpatient visits, hospitalizations, deaths, and disability adjusted life years (DALYs) averted.

2.1. A Markov model for CEA

We constructed a probabilistic three-box Markov model for the Peruvian birth cohort using TreeAge Pro software [14]. The basic model included a healthy state (no diarrhea) and a sick state (having diarrhea) (Fig. 1). The third state was an absorbing state (cannot exit) for those that die. The model used a one-month time step for the Markov process and ran for 60 months until the cohort reached the end of the fifth year of life. The entire birth cohort began in the healthy state and had a probability of transitioning to the NV diarrhea state based on the one-month hazard of NV diarrhea. Those who weren't infected with NV were also subject to the background hazard of mortality, which was the mortality rate from all non-NV causes. In the NV diarrhea state, children could either die from the NV-attributable hazard of mortality or recover to the healthy state in the next time step. Children in the absorbing state entered through either NV mortality or background mortality. At each time step, children who did not transition out of the healthy state remained there until the next month and were subject to the same probabilities for subsequent time steps.

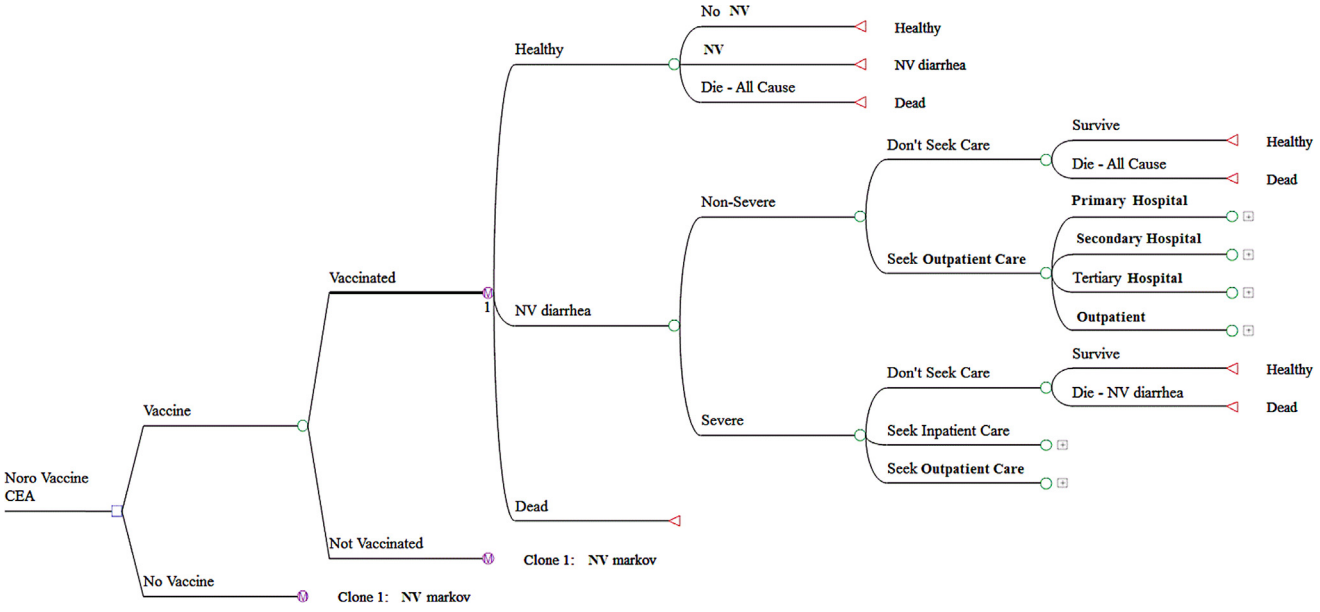

Fig. 1. Markov decision model for norovirus vaccination.
Abbreviations: CEA—Cost-effectiveness analysis; NV—norovirus.
Note: Several branches have been collapsed to fit the figure (denoted with plus sign). Nodes with an 'M' denote a Markov process.