Impact and cost-effectiveness of an injectable rotavirus vaccine candidate compared to oral rotavirus vaccines

While current live, oral rotavirus vaccines (LORVs) are reducing severe diarrhea in all settings, they are not as effective in places with the highest burden. Alternative approaches are in advanced stages of clinical development, including *injectable* next-generation rotavirus vaccine (iNGRV) candidates, which have the potential to better protect children against disease, be combined with existing routine immunizations, and be even more affordable than the current LORVs. Another new approach is *oral* NGRV (oNGRV) candidates that include a dose administered at birth followed by two infant doses, and one such candidate has shown preliminary evidence of higher efficacy than current LORVs in trials. PATH conducted a series of studies to better understand the real public health value of iNGRVs and help inform decisions by international agencies, funders, vaccine manufacturers, and countries. As part of this work, PATH conducted an impact and cost-effectiveness analysis examining multiple rotavirus vaccine options and strategies. (Manuscript has been submitted to a peer-reviewed journal.)

Key takeaways

- Currently available LORVs remain a good investment for countries.
- Vaccination programs with an iNGRV would save billions of US dollars compared to current LORV vaccination programs and prevent an additional 200,000 rotavirus deaths over 10 years.
- A standalone iNGRV is likely cost-effective in the majority of low- and middle-income countries (LMICs) and a hypothetical vaccine that combines an iNGRV with a diphtheria-tetanus-pertussis (DTP)-containing vaccine (iNGRV-DTP) into one formulation is likely cost-effective in all LMICs and is cost-saving in many. This remains true even if the iNGRV has a similar efficacy to current LORVs.

Background

Rotavirus causes about one-third of child deaths due to diarrhea globally and millions of hospitalizations each year.[1] Accessing the required care can be challenging in many LMICs, making rotavirus vaccination critical to saving children's lives. To date, more than 110 countries worldwide have introduced LORVs in their national immunization programs.[2] The globally available LORVs have similar clinical efficacy and are reducing severe disease and deaths where introduced.[3] However, their efficacy is lower in high-burden settings. Many scientists think vaccines delivered orally are less effective when children are malnourished or have other competing pathogens in their gastrointestinal track. iNGRVs are expected to provide superior efficacy in high-burden settings because they bypass the child's gut. Clinical trials are ongoing to determine whether they are more effective than current LORVs.

The currently available LORVs and NGRV candidates differ in terms of route of administration, presentation, efficacy, price, and immunization schedule, among other attributes. A market with multiple vaccine options helps ensure stable vaccine prices and sustainable supply.

PATH conducted a modeling study to assess the potential impact and cost-effectiveness of different rotavirus vaccination strategies (Table 1) in 137 LMICs. The study compared hypothetical iNGRVs and oNGRVs with varying levels of efficacy to the current LORVs to determine scenarios that could bring the highest value in terms of health impact and cost implications. Co-administration strategies, where an LORV is given alongside an iNGRV, were also explored as a way to increase efficacy in the event that iNGRVs do not show superior clinical protection.

Methods

PATH used UNIVAC, a validated impact and cost-effectiveness model, to project the costs and benefits of the different vaccines and strategies over a 10-year period starting in 2025. The model incorporated vaccine-specific attributes from documented sources such as efficacy*, price**, and product presentation, as well as other relevant data such as disease burden, vaccine coverage, and healthcare costs.

* Efficacy levels used in the analysis for iNGRV and oNGRV remain hypothetical as clinical trials continue to evaluate their efficacy.

** iNGRV pricing inputs were based on an anticipated global access price for one iNGRV candidate that is lower than current LORV public sector prices.

Table 1. Vaccine strategies analyzed.

Vaccine option *compared to no vaccination*		Efficacy assumptions
Standalone		
A	ROTAVAC®*	Base
B	ROTASIIL®*	Base
C	ROTARIX®*	Base
D	oNGRV	Moderately higher
E	iNGRV	Substantially higher
F	iNGRV-DTP combination	Substantially higher
Dh	oNGRV	Substantially higher
Ee	iNGRV	Comparable to base
Fe	iNGRV-DTP combination	Comparable to base
Co-administration		
G	iNGRV co-administered LORV	Substantially higher
H	iNGRV co-administered oNGRV	Substantially higher
I	iNGRV-DTP combination co-administered LORV	Substantially higher
J	iNGRV-DTP combination co-administered oNGRV	Substantially higher
K	LORV + 1 dose iNGRV	Substantially higher

* Currently available LORVs are assumed to provide similar impact.

Results

Vaccine impact

The results from this analysis predict substantial impact in averted cases, hospitalizations, and deaths across all rotavirus vaccine options included in the study (Figure 1). An iNGRV with higher efficacy compared to the currently available LORVs would prevent an additional 200,000 rotavirus deaths over 10 years. Additionally, vaccination programs with an iNGRV would save between US$1 to 15 billion compared to current LORV vaccination programs over 10 years, with even higher savings with an iNGRV-DTP combination (Figure 2). Rotavirus vaccines, regardless of type, are projected to prevent millions of rotavirus cases and billions in healthcare costs.

Figure 1. Estimated impact of rotavirus vaccines in 137 LMICs over 10 years.

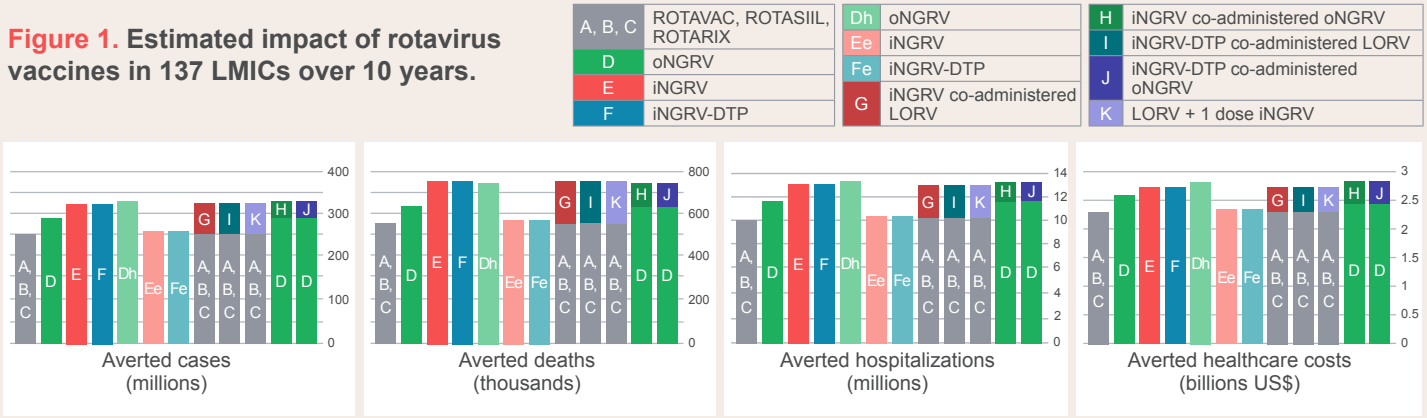
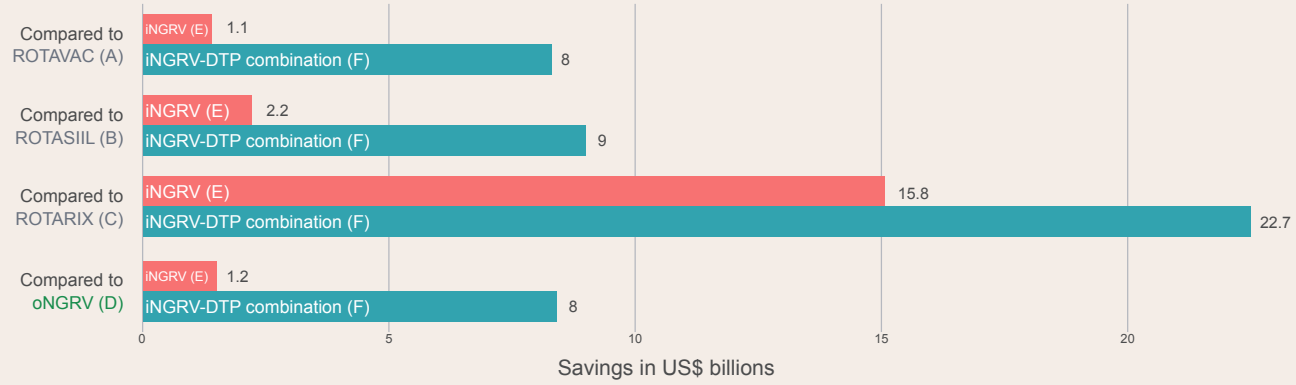


Figure 2. Vaccination program savings over 10 years in 137 LMICs using iNGRV standalone or iNGRV-DTP combination instead of LORV options.



Cost-effectiveness

Vaccine cost-effectiveness is measured by examining the cost to avert one lost year of healthy life, known as a disability-adjusted life-year. This analysis used the willingness to pay threshold of half of each country's gross domestic product per capita to evaluate cost-effectiveness across 137 LMICs.

The results showed that the most cost-effective option is an iNGRV-DTP combination vaccine, which is likely cost-effective in all LMICs and cost-saving in many. A second option is a standalone iNGRV, which is likely cost-effective in 84 percent of LMICs. This result remains true even if the iNGRV has similar efficacy to current LORVs. Co-administration strategies with a standalone iNGRV and an LORV are likely not cost-effective. However, an iNGRV-DTP combination vaccine co-administered with an oNGRV, ROTAVAC, or ROTASIIL is likely to be cost-effective in the majority of LMICs.

Conclusions

Currently available LORVs remain a good investment for countries. A standalone iNGRV is likely to be cost-effective and cost less than LORVs in the majority of LMICs at both higher or equivalent efficacy levels and is expected to provide a substantial public health impact. An iNGRV-DTP combination vaccine, should it be developed in the future, was the least costly and most cost-effective option evaluated.

These results contribute to PATH's broader effort to evaluate the public health value of iNGRVs. These findings may help guide investment decisions by donors and vaccine developers, influence new clinical trial designs and endpoints, accelerate development of an iNGRV-DTP combination vaccine, or help inform global policy guidance and national vaccine introduction decision-making in the future.

References

1. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*. 2016;388(10053):1459-1544.
2. International Vaccine Access Center. Johns Hopkins Bloomberg School of Public Health. VIEW-hub—Current vaccine introduction status. Available at: https://view-hub.org. Accessed September 2021.
3. Patel MM, Parashar US, eds. Real World Impact of Rotavirus Vaccination. *The Pediatric Infectious Disease Journal*. 2011;30(Suppl 1).