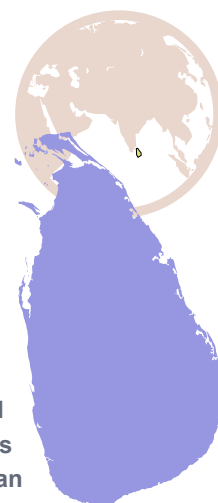


Sri Lanka stakeholder preferences for a new rotavirus vaccine candidate

Comparing an injectable vaccine candidate with oral rotavirus vaccine options



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 vaccines (iNGRVs), 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, which may have higher efficacy than current LORVs. PATH conducted a series of studies to understand the real public health value of iNGRVs to help inform decisions by international agencies, funders, vaccine manufacturers, and countries. This included a feasibility and acceptability study with **national stakeholders** and **healthcare providers** in Ghana, Kenya, Malawi, Peru, Senegal, and Sri Lanka to assess their preferences for different hypothetical rotavirus vaccine options. This brief provides an overview of the study results, with a focus on Sri Lanka. No **healthcare providers** were interviewed in Sri Lanka as LORVs have not yet been introduced there. However, the results from other countries are included here as they may be relevant to other new vaccine introductions or switches in a Sri Lankan context.^{1,2}

Key takeaways across all countries

- ◆ For **national stakeholders**, vaccine delivery considerations were the most important preference drivers, followed by efficacy and cost.
- ◆ Nearly half of the **national stakeholders** preferred a standalone iNGRV with higher efficacy over current LORVs despite reservations about adding new injections to the vaccination schedule. Almost all **healthcare providers** strongly opposed adding another injectable to the schedule, though they were not given information about vaccine efficacy so it is unclear if a higher efficacy iNGRV would impact this preference.
- ◆ Both **national stakeholders** and **healthcare providers** strongly preferred an equally high-efficacy neonatal oNGRV over a standalone iNGRV.
- ◆ **National stakeholders** and **healthcare providers** were highly supportive of a hypothetical vaccine that combines an iNGRV with a diphtheria-tetanus-pertussis (DTP)-containing vaccine over all LORV options, including a neonatal oNGRV, due to ease of delivery.

Background

Rotavirus causes about one-third of child deaths due to diarrhea globally and millions of hospitalizations each year.³ Accessing the required care can be challenging in many low-resource settings, making rotavirus vaccination critical to saving children's lives. To date, more than 110 countries worldwide have introduced LORVs in their national immunization programs.⁴ While they are reducing severe disease and deaths in all populations,⁵ oral vaccines are typically less effective in high infant mortality settings compared to low infant mortality settings.⁶

iNGRV candidates, designed to be given on the same schedule as LORVs, are expected to provide superior efficacy in high-burden settings because they bypass the child's gut. Many scientists think vaccines delivered orally are simply less effective when children are malnourished or have other competing pathogens in their gastrointestinal tract. They also could be available at a lower price. Other alternatives are oNGRV candidates that include a birth dose, and one such candidate has shown preliminary evidence of higher efficacy than current LORVs in trials.

While these NGRVs are still being evaluated in advanced clinical studies, it is important to consider **national stakeholders'** views on attributes that may impact policy decisions and delivery, as well as perceptions of **healthcare providers** who administer vaccines. Understanding preferences for different rotavirus vaccine options, and the drivers behind them, can help to inform future research and development efforts.

Sri Lanka experiences a rotavirus mortality rate of less than 1 child per 100,000 younger than five years of age,⁷ which is considered in the low range globally. The country has not yet introduced rotavirus vaccine into their national immunization program, due to low rotavirus disease burden and other more urgent child health priorities, and is no longer eligible for support from Gavi, the Vaccine Alliance.⁴ However, rotavirus vaccine is available in the private market in Sri Lanka. Given Sri Lankan **healthcare providers'** lack of experience in administering rotavirus vaccine, none were interviewed as part of this study.

Methods

PATH worked with investigators in six countries to interview 71 national stakeholders who work in roles that influence vaccine adoption and 64 healthcare providers who administer vaccines to assess their perceptions about existing and hypothetical new rotavirus vaccine options. Through a series of comparisons, interviewees were asked to indicate their preference for different rotavirus vaccine options with varying attributes and explain the reasons for their choice.

National stakeholders were presented with information comparing actual or hypothetical efficacy, cost, presentation, delivery, and storage attributes for different rotavirus vaccine approaches. Five comparisons involved existing LORVs versus hypothetical iNGRVs and two comparisons involved a neonatal oNGRV candidate versus an iNGRV. Healthcare provider interviews included similar comparisons but involved fewer options and focused on delivery issues. All comparisons assumed that iNGRV is given as three injections and that LORVs are given in two or three oral doses in the routine infant schedule.

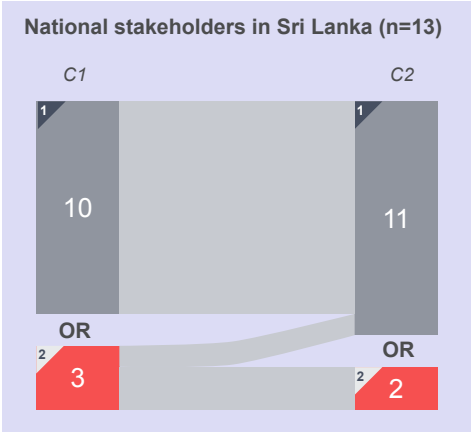
In Sri Lanka, 13 national stakeholders and no healthcare providers were interviewed. Since rotavirus vaccine has not yet been introduced, only one interviewee was a member of a national immunization advisory body to avoid influencing policy decisions. The national stakeholders generally did not perceive rotavirus to be a major public health problem in the country, citing a low number of cases and a strong health system.

Results

Findings from interviews with national stakeholders and healthcare providers provide important insights around three key questions.

Key Question 1: Would a standalone iNGRV be a preferred alternative to LORV if it averted more child deaths and hospitalizations, was less costly to procure, or both?

NGRV attribute assumptions			
National stakeholders	Comparison 1	1 LORV 2 iNGRV	The iNGRV has 50% higher efficacy than LORV. The iNGRV is less costly than LORV but requires more cold chain resources.
	Comparison 2	1 LORV 2 iNGRV	Same as above but assumes iNGRV efficacy is equal to LORV efficacy.



The graphic on the left above shows that 38 of 71 national stakeholders preferred LORV to a higher efficacy iNGRV, and 59 of 71 national stakeholders preferred LORV to an iNGRV with equal efficacy. The gray curves show how individual preferences changed (or did not change) from one comparison to the next.

When asked to choose between an existing LORV and a standalone iNGRV with greater health impact, national stakeholders were evenly split across all six study countries in their preferences. Those who preferred the more efficacious iNGRV cited fewer deaths and hospitalizations as a principal reason followed by its lower cost, though much less frequently. A few explicitly preferred iNGRV’s injectable delivery, seeing it as “more hygienic” and “more effective” by ensuring the full dose is given, avoiding potential loss of an oral vaccine dose from children “vomiting.” When efficacy of iNGRV and LORV were assumed to be equal, preference for iNGRV decreased.

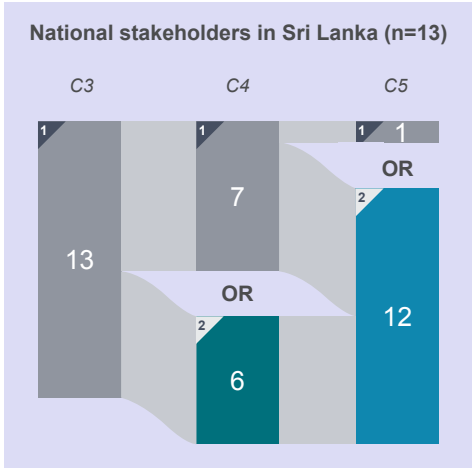
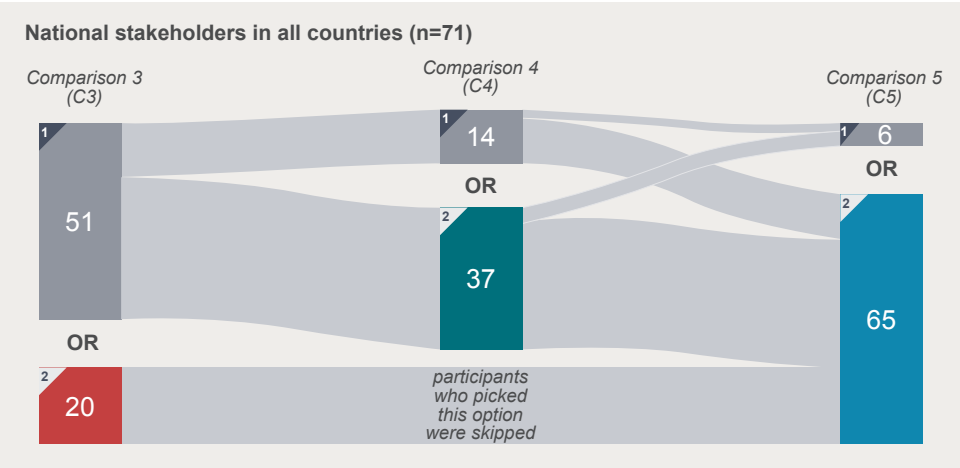
National stakeholders who preferred LORV in either comparison tended to emphasize concerns about adding injections to the schedule, often citing healthcare provider and caregiver reluctance to more injections. Added infrastructure and training requirements to deliver injectables were often mentioned by these stakeholders, in contrast to describing oral vaccines as more “convenient” and “easy to administer.”

Only 6 of the 64 healthcare providers interviewed preferred a standalone iNGRV over LORV. To focus on delivery aspects, these interviews did not include information on comparative vaccine efficacy or cost, so the findings are not strictly comparable to the national stakeholder results. Almost all healthcare providers who preferred LORV cited injection-related delivery challenges and caregiver reluctance as a principal reason.

In Sri Lanka, only three national stakeholders selected the higher efficacy iNGRV over LORV, citing fewer hospitalizations and lower cost. One of these three stakeholders—a policymaker—also preferred the iNGRV with efficacy equal to LORV solely due to cost. Eleven stakeholders preferred LORV over iNGRV overall, citing a mix of programmatic issues, such as concern about caregivers’ acceptance of another injection and the pain it causes for babies. Lower cold chain requirements and a preference for single-dose vials were other factors.

Key Question 2: If an iNGRV is not found to be substantially more efficacious than LORVs, are there formulations in which it would be preferable to LORVs?

NGRV attribute assumptions			
National stakeholders	Comparison 3	<div><div>1</div><div>LORV</div></div>	<div><div>2</div><div>LORV co-administered with iNGRV</div></div> <div>The iNGRV is given alongside LORV, resulting in 50% higher efficacy overall. Compared to LORV alone, this approach is more costly and requires more cold chain and other delivery resources.</div>
	Comparison 4	<div><div>1</div><div>LORV</div></div>	<div><div>2</div><div>LORV co-administered with an iNGRV-DTP-containing combination vaccine</div></div> <div>The iNGRV is given as part of a combination vaccine alongside LORV, resulting in 50% higher efficacy overall. Compared to LORV alone, this approach is slightly more costly, but does not require additional cold chain or other delivery resources.</div>
	Comparison 5	<div><div>1</div><div>LORV</div></div>	<div><div>2</div><div>iNGRV-DTP-containing combination vaccine</div></div> <div>The iNGRV has equal efficacy to LORV and is given as part of a combination vaccine at a greatly reduced cost compared to LORV alone.</div>



The gray curves in the graphics above show how individual preferences changed (or did not change) from one comparison to the next.

It remains unknown if iNGRVs will actually be more effective than current LORVs, so this key question explores the perceived value of a less efficacious iNGRV. **National stakeholders** were asked about the above comparisons, whereas **healthcare providers** were only asked open-ended questions about the feasibility of delivering these vaccine options, with no cost or efficacy information provided.

Comparisons 3 and 4 considered co-administration of an iNGRV or an iNGRV and DTP-containing (iNGRV-DTP) combination vaccine, respectively, with LORV in order to achieve higher efficacy overall. Across all countries, **national stakeholders** had moderate interest in co-administering LORV with a standalone iNGRV, citing the complex schedule, high cost, and disadvantages of adding an injectable to the schedule. Interest in a co-administration approach increased considerably when iNGRV was formulated as an iNGRV-DTP combination vaccine, despite its higher cost.

Comparison 5 removed the co-administration aspect, directly comparing an iNGRV-DTP combination vaccine with an LORV with similar efficacy, to explore perceived trade-offs between vaccine efficacy, operational ease, and low cost. All but six of the **national stakeholders** selected the iNGRV-DTP combination option over LORV, and several emphasized the potential to remove LORV from the schedule as a significant advantage. The low cost, reduced cold chain resources, and avoidance of adding new injections were also cited as specific advantages.

Among **healthcare providers**, when presented with the idea that co-administering iNGRV with LORV would increase protection for the child, about half said they could deliver both vaccines, noting the importance of messaging for caregivers about this advantage. The majority of **healthcare providers** had no concerns about the iNGRV-DTP combination vaccine, and even expressed enthusiasm, as it would free up cold chain storage and eliminate LORV in the visit schedule.

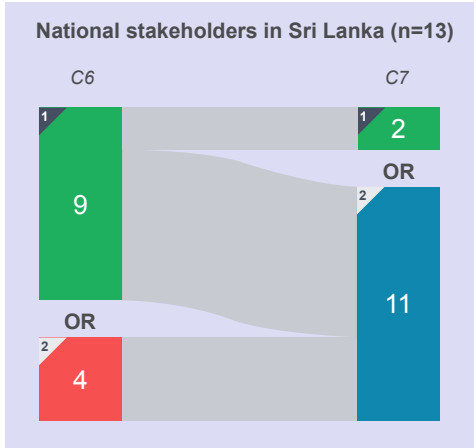
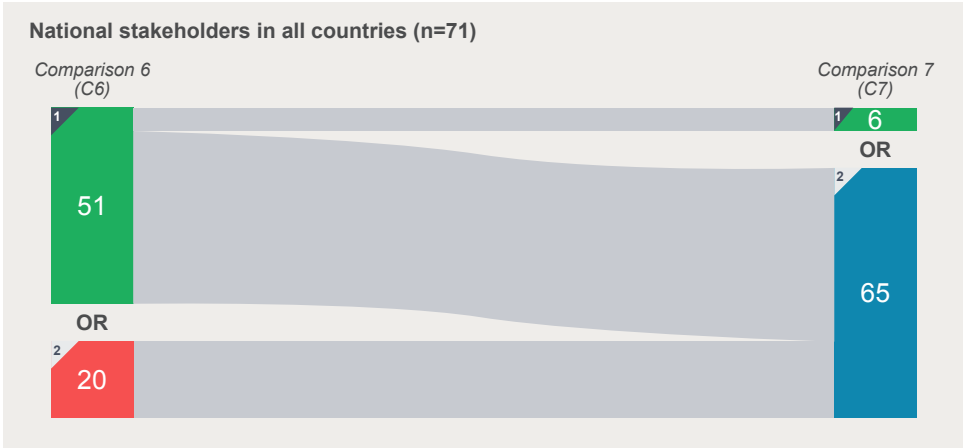
The Expanded Programme on Immunization (EPI) was adopted by Sri Lanka in 1978, with vaccines gradually added in a phased manner to achieve high immunization coverage and disease control.⁸ As of 2019, Sri Lanka’s EPI schedule recommends five different injectable vaccines for infants, with most vaccinations added to the schedule in the last decade.⁹ Given this context, **national stakeholders** felt the option of LORV co-administered with a standalone iNGRV in Comparison 3 “costs too much,” plus the schedule is “complicated” and there are already “too many injectables.” Additionally, there is “not so much” public health impact. The idea of adding an iNGRV to a DTP-containing vaccine and co-administering it with LORV was appealing to stakeholders because it is easier to “catch the child at the time of the [DTP-containing] penta[valent] vaccine while “giving one injection.” Since Sri Lanka is not eligible for Gavi co-financing, some stakeholders believed the cost was too high for “not so much” public health impact in terms of reducing hospitalizations and deaths.

The oral and injectable both is too many and the cost is too much. I don’t like it.

— Sri Lanka national stakeholder

Key Question 3: What are stakeholder preferences for and views about an LORV with an initial neonatal dose (oNGRV) compared to equally efficacious iNGRV options?

				NGRV attribute assumptions
National stakeholders	Comparison 6	1 oNGRV	2 iNGRV	The oNGRV's first dose is given at birth followed by two additional doses in the routine infant schedule. The iNGRV and oNGRV have the same efficacy . The oNGRV is more costly than the iNGRV but requires less cold chain resources .
	Comparison 7	1 oNGRV	2 iNGRV-DTP-containing combination vaccine	Same as above but iNGRV is given as part of a combination vaccine with a reduced cost and cold chain burden .



The gray curves in the graphics above show how individual preferences changed (or did not change) from one comparison to the next.

Despite its higher cost, 51 **national stakeholders** preferred oNGRV over a standalone iNGRV with equal efficacy, citing similar reasons to those who preferred LORVs in the earlier comparisons. Nine noted that early protection and/or anticipated improved coverage made oNGRV more attractive. Those who preferred iNGRV cited its lower cost, its compatibility with the routine immunization schedule, and the perceived effectiveness of injections. Most **healthcare providers** preferred oNGRV, citing a strong preference for an oral vaccine over an injectable. However, a few preferred iNGRV due to vomiting/spitting up issues associated with oral vaccines.

When the iNGRV option was changed to an iNGRV-DTP combination vaccine, **national stakeholders** overwhelmingly preferred this option over an oNGRV. Reasons for this closely resemble those cited in the earlier comparison with an iNGRV-DTP combination. Despite the higher cost, six preferred oNGRV, citing early protection of the child and the possibility of improving coverage because it is given after birth when the mothers are “easy to catch.” **Healthcare providers** were not asked about this comparison.

Conclusions and next steps

This study provides critical, and sometimes surprising, insights into country-level preferences for different types of rotavirus vaccine options and increases understanding of how these stakeholders prioritize different attributes when making vaccine decisions. Sri Lankan **national stakeholders** were the least enthusiastic about a standalone iNGRV across all study countries, consistent with their perception that rotavirus is not a serious problem there. However, they did express some interest in an iNGRV-DTP combination vaccine. An important caveat: the preferences voiced in this study may not translate into real-world preferences when countries face new rotavirus vaccine options.

These findings may help guide investment decisions by donors and vaccine developers to better meet low- and middle-income country needs, influence clinical trial designs, accelerate development of an iNGRV-DTP combination vaccine, or help inform global policy guidance and national vaccine introduction decision-making in the future. Vaccine manufacturers may also want to ensure iNGRV efficacy trials are powered to demonstrate non-inferiority, not just superiority, to LORVs. Lastly, this study demonstrates that countries are likely to welcome these additional tools in the fight against rotavirus.

So, neonate might spit [the vaccine] up. I’m not sure if I’ll be able to give all of the oral to a neonate. Injectable will be better.

— Sri Lanka national stakeholder

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