Malawi 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 Malawi.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.

Malawi experiences a rotavirus mortality rate of 22 per 100,000 children younger than five years of age,7 which is considered in the medium range globally. With support from Gavi, the Vaccine Alliance, the country introduced rotavirus vaccine into their national immunization program in October 2012.4 In Malawi, a two-dose rotavirus vaccine is given at the ages of 6 and 10 weeks, along with oral polio vaccine, DTP-containing vaccine, and pneumococcal conjugate vaccine. In 2019, Malawi’s rotavirus vaccine coverage rate was 92 percent.8
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.

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?

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<tr>
<th>National stakeholders</th>
<th>Comparison 1</th>
<th>LORV</th>
<th>iNGRV</th>
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NGRV attribute assumptions

- The iNGRV has 50% higher efficacy than LORV. The iNGRV is less costly than LORV but requires more cold chain resources.
- Same as above but assumes iNGRV efficacy is equal to LORV efficacy.

In Malawi, 13 national stakeholders and 14 healthcare providers were interviewed. Ten of the national stakeholders were members of country-level immunization decision-making bodies. All national stakeholders and all but two healthcare providers perceived rotavirus to be a “moderately” or “very serious” public health problem in the country, and while they felt that LORVs have had an impact on diarrheal disease, more needs to be done.

In Malawi, 9 national stakeholders preferred the higher efficacy iNGRV due to significant reductions in hospitalizations and deaths. None of the stakeholders selected the lower efficacy iNGRV, seeing no advantage over LORV.

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 Malawi, nine national stakeholders preferred the higher efficacy iNGRV due to significant reductions in hospitalizations and deaths. None of the stakeholders selected the lower efficacy iNGRV, seeing no advantage over LORV. In contrast, 11 of the 14 healthcare providers preferred LORV most frequently citing “too many injections” or “too much pain for the child,” though they did not have efficacy information. All three providers who preferred iNGRV were explicit that injectables are “safer” and “the child will not spit [up].”
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?

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<tr>
<th>National stakeholders</th>
<th>Comparison 3</th>
<th>LORV co-administered with iNGRV</th>
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<td></td>
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<td>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.</td>
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<th>National stakeholders</th>
<th>Comparison 4</th>
<th>LORV co-administered with an iNGRV-DTP-containing combination vaccine</th>
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<td></td>
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<td>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.</td>
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<th>National stakeholders</th>
<th>Comparison 5</th>
<th>iNGRV-DTP-containing combination vaccine</th>
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<td>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.</td>
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National stakeholders in all countries (n=71)

Comparison 3 (C3)

Comparison 4 (C4)

Comparison 5 (C5)

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 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.

As my concern has mainly been the route of administration, this one [iNGRV-DTP combination] coming in through [DTP-containing] penta, I would say it wouldn’t be like we’re introducing a new injection.

— Malawi national stakeholder
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. Reflecting the country’s high rotavirus rate, Malawian national stakeholders expressed strong interest in a higher efficacy iNGRV, despite a reluctance to add injections. Healthcare providers in Malawi were also more open to a higher-efficacy iNGRV compared to other study countries. 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.

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?

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<tr>
<th>National stakeholders</th>
<th>Comparison 6</th>
<th>Comparison 7</th>
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<td>oNGRV</td>
<td>iNGRV-DTP-containing combination vaccine</td>
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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."

I go for the new neonatal vaccine because, one, the presentation is in a tube which reduces physical damage. Also, the oral route of administration.

— Malawi national stakeholder

References