


# Optimising neonatal antiretroviral therapy using raltegravir: a qualitative analysis of healthcare workers' and caregivers' perspectives

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## ABSTRACT

**Background** In 2020, Zimbabwe adopted the WHO's recommendation to use raltegravir (RAL) granule-based regimens for treatment of neonates identified with HIV at the time of birth testing. This study explores the acceptability of RAL granules by caregivers and healthcare workers (HCWs).

**Methods** Interviews were conducted with 15 caregivers and 12 HCWs from 8 health facilities in Zimbabwe participating in the introductory pilot of RAL granules treatment for newborns. Eligible caregivers included those who had administered RAL to their infant and attended either 8th or 28th day of life appointments. Caregivers of neonates recently initiated on RAL were selected through convenience sampling. Eligible HCWs who provided RAL preparation, administration instructions and support to caregivers of neonates on RAL for at least 3 months were recruited from the same facilities as the caregivers. Interview transcripts were coded and thematically analysed.

**Results** Caregivers reported that their babies looked healthier after RAL initiation, with improved skin appearance and weight gain. Some caregivers wanted their child to remain on RAL beyond 28 days instead of switching regimens, as recommended by national guidelines. HCWs observed that RAL granules improved health outcomes compared with other regimens. HCWs reported challenges with caregivers understanding dosing instructions, measuring with a syringe, swirling and not shaking the medicine, discarding unused medication and following the changes in the dosing schedule and amount when RAL was initiated a few days after birth. HCWs stated that adequate counselling and repeat demonstrations were crucial to ensure that caregivers clearly understood RAL dosing and administration instructions. HCWs requested more standardised training targeting nurses with guidance on handling missed doses and clarification on mixing RAL granules with water and not breastmilk.

**Conclusion** While feedback from caregivers and HCWs on RAL implementation was positive, barriers were also noted. Adequate training and sufficient instruction and support for caregivers would help to ensure that RAL granules are prepared, dosed and administered correctly.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ The WHO has recommended raltegravir (RAL)-based regimens for neonatal HIV treatment.
- ⇒ Preparing RAL granules for neonates is a complicated procedure and involves changing dosage and dosage frequency after 7 days of initiating RAL.
- ⇒ While minimal research has been conducted on the acceptability and feasibility of RAL granules for neonates, previous research has found major errors with insufficient mixing time and incorrect suspension volume.

## WHAT THIS STUDY ADDS

- ⇒ Caregivers accepted RAL and reported that their babies looked healthier after RAL initiation, with improved skin appearance and weight gain.
- ⇒ Healthcare workers reported challenges with caregivers understanding dosing instructions, measuring with a syringe, swirling and not shaking the medicine, discarding unused medication and following the changes in the dosing schedule and amount when RAL was initiated a few days after birth.
- ⇒ Recommendations to improve the implementation of RAL include: adequate counselling and repeat demonstrations to ensure that caregivers clearly understand RAL administration instructions and more standardised training for nurses with guidance on handling missed doses and clarification on mixing RAL granules with water and not breastmilk.

## BACKGROUND

Zimbabwe has a generalised HIV epidemic and is among the 22 highest burden countries that account for over 90% of all pregnant women living with HIV worldwide.<sup>1</sup> The Zimbabwe National Statistics Agency reported that 14.3% of pregnant women are HIV-positive<sup>2</sup> and at least 8.7% of their infants become infected with HIV.<sup>3</sup>

Early identification of children living with HIV and linkage to life-saving antiretroviral



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### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

- ⇒ As countries prepare to introduce RAL granules, it is important to ensure standardized training materials, job aids, and sufficient time to successfully train healthcare workers and caregivers on RAL administration.
- ⇒ These study findings may be helpful for countries considering adopting policies to support birth testing and use of RAL granules. The study findings may also influence policies regarding human resources for health to ensure consistent, well-trained staff.
- ⇒ Further research is needed to understand whether the recommended interventions address the current barriers to RAL administration.

therapy (ART) are critical steps to reduce HIV-related morbidity and mortality among this population. In Zimbabwe, HIV-exposed infants can be tested at birth using a point-of-care (POC) diagnostic machine. Infants who test positive for HIV are initiated on treatment soon after diagnosis, however, options for neonatal ART are limited. The WHO has recommended raltegravir (RAL)-based regimens for neonatal HIV treatment.<sup>4</sup> RAL is an integrase inhibitor available as a dispersible granule and replaces the non-nucleoside reverse transcriptase inhibitors, nevirapine, for which increasing rates of transmitted HIV drug resistance have been detected among ART-naïve infants living with HIV.<sup>5</sup> The government of Zimbabwe adopted the WHO recommendations on birth HIV testing and the use of RAL granules for treating neonates born with HIV in an addendum to their 2016 guidelines.<sup>4</sup>

The dosing, preparation and administration of RAL granules are quite nuanced. Each dose must be freshly prepared with clean, safe water and the granules must be mixed using a swirling motion (not shaken) until evenly dispersed. The correct amount of this liquid is drawn into a clean syringe and administered to the neonate orally within 30 min of preparation and the unused portion is discarded. Dosing is based on both age and weight. On day 8 of life, the dose must be adjusted for weight, which usually requires the caregiver to bring their baby back to the facility to make this adjustment. At this visit, the dose is doubled and administration changes from once a day to two times a day, to adjust for the rapid changes in RAL metabolism that occur in the first few weeks of life.<sup>6</sup> At 28 days of life, current guidance recommends switching from a RAL granule-based regimen to a dolutegravir (DTG)-based or lopinavir/ritonavir (LPV/r)-based regimen, depending on the country's available paediatric formulations. The additional visits, dosing changes and regimen switch required for the use of neonatal RAL, add significant levels of complexity to service delivery. Ensuring both caregivers and healthcare workers (HCWs) understand appropriate dosing, preparation and administration is critical to prevent toxicities related to overdosing.<sup>7</sup> Correct dosage also helps to prevent the development of resistance from under-dosing, which can impact the future effectiveness of DTG-based regimens.

Treatment success for oral medications taken by younger children also hinges on drug acceptability or palatability.

Zimbabwe was the first country to implement the use of RAL granules programmatically. The Ministry of Health and Child Care worked with the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) to pilot the introduction of RAL granules at 14 sites in Zimbabwe, in collaboration with Catholic Relief Services and the Centers for Disease Control and Prevention. The 14 sites were purposively selected, as they were already implementing POC birth testing and had high volumes of infants exposed to HIV within 72 hours of birth. HCWs were trained by EGPAF on RAL use from June to July 2020 and began prescribing RAL granules to neonates. Within the first year of the RAL pilot implementation at the 14 sites, 3204 (46%) of 6989 HIV-exposed infants had received POC birth testing, 59 (1.9%) tested positive for HIV and 27 were initiated on RAL.<sup>8</sup> A qualitative study was conducted to explore the acceptability of using RAL granules and to identify any challenges and lessons learnt to support its further successful implementation. Interviews were conducted with caregivers of neonates receiving RAL granules and HCWs who provided support to the caregivers of these neonates.

## METHODS

### Study population and recruitment

In-depth interviews (IDIs) were conducted with caregivers of neonates receiving RAL-based ART and HCWs providing care and support to the neonates on RAL and their caregivers. An HCW/nurse in-charge used a standardised script to contact eligible caregivers until 15 participants were enrolled in the study. Eligible caregivers were at least 18 years of age (or emancipated minors), had a newborn that tested HIV-positive and was initiated on RAL granule-based ART, attended either the 8th or 28th day of life appointment and had administered the RAL granules to their neonate themselves.

Eligible HCWs were at least 18 years old, worked in the maternal, newborn and child health or similar department, and counselled caregivers on the use of RAL granules for at least 3 months. HCWs were selected using a convenience sampling approach and recruited by the nurse in-charge of the facility on the same days that the study research assistants (RAs) were scheduled to interview caregivers.

### Site selection

Of the 14 sites that had initiated infants on RAL, data were collected from eight. These eight locations were selected since they had caregivers who completed appointments for the 8th or 28th day of life. The remaining six sites were excluded since they did not have caregivers who had completed these appointments prior to the time of data collection. The participating sites were located in six of Zimbabwe's ten provinces. While the included locations

were in urban areas, they served clients from both urban and rural settings.

### Data collection

EGPAF hired RAs with previous qualitative experience that were fluent in Shona, Ndebele and English. The RAs were trained by EGPAF on study procedures and human subject ethics during a 1 week, onsite data collection training. All data collection tools were pre-tested at health facilities not participating in the study. Questions were edited and adapted to ensure that the question was correctly conveyed and understood by potential participants.

Between June and July 2021, IDIs were conducted with a total of 15 caregivers and 12 HCWs. Previous literature has indicated that saturation can be reached at 10–12 interviews within a homogenous group.<sup>9</sup> Homogeneity was determined in relation to the participant's use of RAL (ie, being a caregiver providing RAL to a neonate or an HCW prescribing/training caregivers on administering RAL to their neonate). To minimise recall bias, the caregivers of neonates who had most recently completed RAL were included in the qualitative study. All neonates had initiated RAL within 8 months of the interview, with the majority of neonates initiating RAL within 60 days of the interview. Not all of the 14 sites were represented in this study sample, as they may not have had babies who had recently completed a course of RAL granules.

Written informed consent was obtained before each interview, in either English, Shona or Ndebele, depending on the participant's language preference. A trained RA interviewed the participants and all IDIs were audio-recorded with each participant's consent. Participants' demographic data were recorded on a paper-based study form collected separately from the audio-recording.

### Data analysis

Audio-recordings were simultaneously transcribed and translated into English transcripts. Transcripts were imported into the qualitative analysis software programme MAXQDA V.12. A preliminary codebook was developed using a combined inductive and deductive approach. Two coders trained in qualitative analysis coded approximately 20% of the same transcripts, compared the coded text passages and resolved any discrepancies, often through refining or introducing new codes. Once the code list was finalised, the remaining transcripts were coded individually. Thematic analysis was used to identify recurrent patterns and themes in the data. Data matrices were created for the two study population groups of caregivers and HCWs.

### Patient and public involvement

Patients and the public were not involved in the design of the study or recruitment of study participants. Results have been shared with site administrators, Ministry of Health and Child Care and local stakeholders.

## RESULTS

### Demographics

Of the fifteen caregivers, only one was male. Most caregivers (n=9, 60%) were married and living with their partners at the time of interview and the group had a mean age of 28.6 years. All caregivers had at least primary education (primary n=5, 33.3%; secondary n=8, 53.3% and tertiary n=2, 13.3%). The majority of study neonates (n=11) had been on RAL for 4 weeks, three neonates had been on RAL for 3 weeks and one neonate had been on RAL for 2 weeks.

The twelve participating HCWs represented a variety of cadres: six were nurses (50%), three were midwives (25%), two were pharmacists (16.7%) and one was a doctor (8.3%). The majority of the HCWs had been in their current position for 3–6 months (7 HCWs), three HCWs were in their position for 7–12 months and two HCWs had been in their position for more than a year. Seven HCWs had been prescribing RAL for 1–6 months and five HCWs had been prescribing RAL for 7–12 months.

Results were organised into three themes: (1) barriers to RAL initiation and adherence, (2) facilitators to RAL initiation and adherence and (3) recommendations to improve RAL delivery.

### Barriers

Several HCWs reported delays with RAL initiation and attributed them to holdups with HIV birth testing. Leading causes for testing delays included deliveries on weekends or evenings, staff trained on birth testing not being present and stockouts of the cartridges used for the PoC birth testing machines. The delay in diagnosis and RAL initiation led to confusion for a few HCWs and caregivers, who returned to facilities on day 9 or day 10 for the RAL dose adjustment, instead of day 8.

One of the challenges that we encountered when implementing RAL was that children were coming late. So, like the case that we were dealing with now, there is a baby who was initiated on day 4 of life and she was initiated with a double dose 2mls a day (instead of one) so she never returned for day 7 to change frequency and dosage ... Sometimes they were coming after day 7. ... I think we will need more information on dealing with children who present late. (Health-care Worker)

HIV is still a highly stigmatised topic in Zimbabwe, with social and cultural norms presenting challenges to RAL initiation and adherence. Many HCWs reported caregivers were hesitant in getting the consent of their partners and disclosing their baby's HIV status within their social support networks. This could have resulted in lower adherence to RAL, since caregivers may have been unable to administer RAL to their neonates in the company of others.



And then she also didn't want the maid [house helper] to know that the baby was taking this medication. So, we had to work around with her to see the times that she can give when she goes to work or before going to work, she will give it at this time, trying to come back to work earlier so that if she doesn't want other people to know. (Healthcare Worker)

HCWs cited the cultural belief that young infants should not leave home as a potential reason for why fewer caregivers returned for the day 28 medication change to LPV/r or DTG, compared with the day 8 visit. Both caregivers and HCWs also discussed the challenges caregivers faced with administering RAL granules. Some caregivers struggled with using syringes, including holding the syringe upright to get an accurate measurement, reading the small numbers on the syringes, eliminating air bubbles while drawing medicine and measuring the correct amount without HCWs explicitly marking the syringe. HCWs discussed challenges with teaching caregivers to swirl the medication instead of shaking it and instructing them on how to look for bubbles. HCWs tried to ensure that caregivers understood that they could not use or save the remaining medication, but that it must be discarded.

It might be a challenge for other people to read the ml on the syringe so if for an example you want to give 0.8ml, it was good to have a 0.8ml container and you just fill it, because it can be confusing because the way you hold the syringe can result in it having different readings. ... I had a problem with my husband where we disagreed over the measurements and how to hold the syringe to get the correct measurements. (Caregiver)

Caregivers also mentioned issues with timing of RAL, time-intensive preparation and disruptions with normal cooking and sleeping routines sometimes resulted in delayed and missed doses. Another challenge with the dosing was that some caregivers used breast milk instead of water to mix the medication, after being incorrectly advised by the HCWs.

They said I should squeeze my breast milk and use it to dissolve the medication and give the baby. That one I was given health education by the nurse who prescribed the medication to me. (Caregiver)

HCWs reported some caregivers were hesitant and suspicious about switching medications at day 28 to LPV/r or DTG due to the positive health benefits they had seen in their baby while on RAL. HCWs noted that caregivers may require more information about the justification behind the medication switch. HCWs cited that caregivers also preferred the RAL granule formulation to other paediatric ARTs, such as liquid LPV/r, since the RAL granules were noted to be less bitter.

They had a few concerns because others would see change in their babies who were taking the [RAL] medication well, that they were growing up healthy, others were afraid that it might go the other way [if they switched to LPV/r]. (Healthcare Worker)

Many nurses were unsatisfied with the cascaded training approach and requested direct training from trainers. The challenge of ensuring all appropriate staff were trained was further exacerbated by high staff attrition and staff rotations. HCWs also reported inadequate materials for practicing demonstrations (extra RAL granule sachets and syringes, etc), lack of information on missed RAL doses and if/when another dose should be administered, and other topics.

Yes, there is not enough training. Those who were working for this department went for the training but with the issues of changing departments here at the hospital, those who were trained might have joined other departments and those remaining would not have received any training. (Healthcare Worker)

COVID-19 significantly impacted the rollout of RAL granules in Zimbabwe. During periods of RAL granule stockout, some HCWs resorted to using the remaining paediatric formulations of nevirapine and one health facility gave out weekly supplies of RAL to caregivers, requiring them to return frequently for additional supplies. Additionally, COVID-19 resulted in travel restrictions, so when caregivers could not attend their day 8 appointment the HCWs shared information over the phone and advised caregivers to visit their local, village-level nurses for further help.

The day that the baby was supposed to be given the medicine, the medicine was out of stock and the baby was given the medicine on another day. (Caregiver)

### Facilitators

Caregivers were generally accepting of RAL, citing good improvements with weight gain and skin appearance and a generally healthy-looking child. Discreet packaging that looked similar to other mainstream medications also increased acceptability of RAL granules. As noted above, caregivers preferred RAL to other paediatric ART formulations because it was less bitter, making it easier for the baby to swallow and it decreased issues with partial/missed dosing.

The way that the medication is packaged is also good, because it is not everyone who is free to disclose to parents or relatives ... with the way the sachet is packaged, no one except for the health practitioners can detect which medication is being given to the child. (Caregiver)

Most HCWs were accepting of RAL and felt comfortable initiating neonates on RAL granules. The main reasons HCWs accepted RAL granules included, the effectiveness and their knowledge of RAL, its ability to reduce mortality in HIV-positive neonates, and RAL's capability of rapidly achieving viral suppression. Additionally, HCWs thought RAL was easier to administer since it came in granules instead of tablets, like previous ART regimens (nevirapine).

... other regimens are difficult to administer for example the dispersible tablets. It's actually difficult as compared to the granules which dissolves aah with ease. So, I think it's a good move for our babies. I think it will actually reduce mortality since raltegravir has been shown to actually work well in the first few weeks of life. (Healthcare Worker)

The most frequently cited facilitators to RAL dosing comprehension and ability were having sufficient time for HCWs to counsel/educate caregivers, HCWs providing demonstrations, and HCWs observing caregivers practice the dosing process. To address issues of literacy among caregivers, HCWs reported that providing written instructions in the local languages of Shona/Ndebele and/or giving marked syringes helped caregivers understand how much medication to draw up for each dose.

I was then asked to also do a demonstration while they watch and make corrections. So that I am able to do on my own when I get home. (Caregiver)

### Participant recommendations

HCWs understood the value of RAL and recommended that RAL be implemented at the national level. HCWs had several recommendations regarding changes needed at the facility and improvements to the training for caregivers on administering RAL to their neonates.

Many HCWs cited how critical it was to ensure timely delivery of RAL to babies. To prevent delays in the birth testing process, HCWs recommended ensuring adequate supplies of the cartridges for the POC machines and training more staff on how to use the machines. Some HCWs also called for clear communication between the maternity ward, outpatient ward and pharmacy to optimise the flow of RAL services.

We need to improve our systems, the issue of testing at birth, it has to improve, so that from day one if possible, babies who are positive are identified and referred, then initiated, so, there is need ... for the staff to work together ... and maybe partners to ensure that those machines for testing the babies are working all the time. (Healthcare Worker)

A general recommendation reported by the HCWs was ensuring adequate time for RAL counselling at the

health facility to allow for demonstrations and observations of the caregivers practicing the process. This would require extra supplies of the RAL granules and syringes for training and practicing, along with enough staff to meet the demand of the increased patient interaction time.

Give them room to ask questions on whichever topics they might not have understood and to appreciate that our understanding and comprehension of information is different. You can even repeat four times and one does not understand so let us give them room to ask as many questions as they want no matter the number of questions so that they go home satisfied. (Healthcare Worker)

HCWs recommended that more staff be trained on RAL to build a stronger process of supporting caregivers on initiating HIV-positive neonates on RAL granules. HCWs recommended the standardisation of the training content and duration. This was especially pertinent in cases where training on RAL granules was part of the comprehensive training on several ART formulations. HCWs also requested additional training materials to be distributed and available in English, Shona and Ndebele, including large wall charts to be placed throughout the facility.

If we get a chart which we just maybe stick on the wall then actually refer to a chart I think ... it will be better than the book ... put [charts] on all maybe the stations, the nurse stations, the doctor's room ... A chart, just like in the job aide containing diagrams of how you are going to open the sachet, how you are going to dissolve. (Healthcare Worker)

Many HCWs recommended providing caregivers with educational communication materials featuring large visuals and diagrams to take home and refer to if there were issues with RAL preparation or administration.

IEC materials with step by-step-instructions accompanied by diagrams and pictures—something caregivers can refer to while they are preparing medication at home. We can give them pamphlets and booklets with information. In case they forget how to prepare the medication, they can refer to the booklet. The booklets might come in English or Shona. (Healthcare Worker)

### DISCUSSION

RAL was generally accepted among caregivers. Caregivers made positive statements about RAL, such as reporting a healthier looking child since initiating RAL and noting physical improvements. Previous qualitative research on the use of RAL granules in South Africa reported that



participants found the preparation of RAL for neonates to be acceptable and feasible.<sup>7</sup> Caregivers in our study reported a preference for granule formulations compared with other available ART formulations for infants. This aligns with another study from Zimbabwe that found caregivers generally preferred LPV/r in the form of granules over liquid,<sup>10</sup> most likely due to granules masking the unpleasant medication taste. Previous research has stated that palatability is one of the main challenges with paediatric medications, leaving caregivers struggling to administer bitter-tasting medications.<sup>11</sup>

Delayed birth testing often resulted in the delayed initiation of RAL and some caregivers returning late for dosage changes. Birth testing was reported to be delayed due to cartridge stockouts and a lack of HCWs trained on PoC testing during evenings and weekends. This resulted in caregivers having to return at a later date to have their child tested. Previous research has also documented the challenges that insufficient staffing and expertise can cause with birth testing uptake.<sup>12</sup> Addressing gaps in supply chain and human resources to ensure timely birth testing is critical for the successful uptake of RAL granules.

Stigma is an important consideration for the use of RAL granules, as the preparation takes time and dosing is two times a day, starting on day 8. Caregivers may be less likely to dose their child in front of others that are not aware of the child's HIV status, resulting in missed or delayed doses. The study of RAL granules in South Africa mentioned challenges with the volume of medication being large and difficult to hide.<sup>7</sup> There may have been differences between the packaging provided in South Africa and in Zimbabwe as our study participants did not mention this challenge and stated that medication packaging looked like other common medications, making it less noticeable.

One of the most critical findings highlighted is the need to ensure adequate training of both caregivers and HCWs. The RAL study in South Africa found that caregivers experienced challenges using the syringes, measuring the correct amount and mixing the medication for a long enough period of time.<sup>7</sup> This study reported that the majority of caregivers found the preparation of RAL difficult at first, but became more comfortable doing it over time. The Zimbabwe LPV/r study also recommended appropriate counselling to ensure caregivers can confidently administer granules.<sup>10</sup> Ensuring appropriate preparation, administration and dosing of RAL granules in neonates is essential for preventing the development of HIV drug resistance to RAL, which may impact the effectiveness of the DTG-based regimens that are currently the recommended first-line regimens for infants and children  $\geq 4$  weeks of age.<sup>4</sup>

HCWs requested that the trainings are standardised and that they are trained directly by trainers, as opposed to having previously trained HCWs teaching them how to use RAL. It is important to note that Zimbabwe's system of rotating staff among different departments

every 6 months results in more staff needing to be trained and, due to the cost of training, staff often train each other. Participating HCWs discussed the challenges of these staff rotations and issues of many staff leaving the facilities. Zimbabwe has previously faced significant HCW shortages, but the situation has been further exacerbated by COVID-19. In March 2020, HCWs in Zimbabwe went on strike due to low pay and insufficient provision of personal protective equipment.<sup>13</sup> More favourable pay and work conditions elsewhere also resulted in many HCWs leaving Zimbabwe.<sup>14</sup> Strategies to ensure appropriate HCW training during periods of high staff turnover are needed, including refresher trainings and consistent mentorship on paediatric treatment regimens.

Another challenge identified by HCWs was that training on RAL granules was included as part of a larger training on ARTs. During the pilot phase of RAL granules, several other new paediatric ART formulations were introduced in Zimbabwe, including LPV/r granules and a dispersible formulation of DTG. The introduction of these formulations required training and, for efficiency, may have been combined with the RAL training. The instructions for preparation and administration of RAL granules and LPV/r granules are different, which must be emphasised to both HCWs and caregivers during trainings. With HCW trainings covering multiple drugs, HCWs may have become confused about the ability to mix RAL with breastmilk instead of water. The RAL granules do not dissolve as well in breastmilk or other liquids, which could potentially impact the administration of the solution and absorption of the medication. As a result of this study, HCW training materials have been updated to include information about avoiding mixing RAL with breastmilk.

While HCWs reported inadequate training materials, it is important to note that small informational booklets were provided to the facilities, but were likely removed at some point. Adopting HCWs' recommendations for job aides in the form of posters may help ensure that appropriate educational materials remain present at the facility and are available during counselling sessions with caregivers. These considerations may benefit Zimbabwe as they plan for further RAL granule scaleup, as well as for other countries that are preparing to introduce birth testing and RAL granules.

There were several limitations to this study. All caregivers offered RAL accepted it, so there was not an opportunity to interview any caregivers who rejected or discontinued RAL and the non-participating population may have provided different experiences and/or perspectives. Additionally, while the majority of interviews occurred within 60 days of initiating RAL, some IDIs were conducted up to 8 months after RAL initiation. The study enrolled caregivers and HCWs who had most recently administered RAL granules in order to minimise recall bias. This may have caused the results do not reflect the experiences of all caregivers and HCWs, particularly



those with neonates who started on RAL granules at the beginning of the pilot.

## CONCLUSIONS

This study provided insight into the acceptability of RAL among caregivers and HCWs and highlighted the challenges affecting successful uptake and utilisation of RAL in Zimbabwe. While RAL granules were well accepted by both caregivers and HCWs, additional steps are needed to ensure adequate training of HCWs, sufficient caregiver instruction and support to ensure proper RAL preparation and administration, and timely diagnosis of HIV-positive neonates. The conduct of this study during the COVID-19 pandemic provided additional insight to the local challenges of an overstretched health system, including staffing issues and stockouts of critical resources. While some of these challenges are more easily addressed, others will require substantially more resources, especially in addressing staffing shortages and transitions. These results can provide insight for other countries preparing to implement RAL granules for neonates.

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## REFERENCES

- 1 World Health Organization (WHO). Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV and syphilis, second edition, 2017. Available: <https://www.paho.org/en/node/21360> [Accessed 8 Jan 2022].
- 2 Zimbabwe Ministry of Health and Child Care (MOHCC). Report on HIV antenatal clinic surveillance using PMTCT program data with additional quality monitoring and strengthening in Zimbabwe. Harare, Zimbabwe Ministry of Health and Child Care; 2017 [Accessed 11 Jan 2022].
- 3 Zimbabwe MOHCC. National and sub-national HIV estimates report. Harare, Zimbabwe AIDS & TB Programme, Ministry of Health and Child Care; 2021 [Accessed 11 Jan 2022].
- 4 WHO. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: supplement to the 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Available: <https://www.who.int/publications/i/item/WHO-CDS-HIV-18.51> [Accessed 27 Jan 2022].
- 5 WHO. HIV drug resistance report 2021, 2021. Available: <https://www.who.int/publications/i/item/9789240038608> [Accessed 27 Jan 2022].
- 6 Clarke DF, Acosta EP, Cababasy M, *et al*. Raltegravir (RAL) in neonates: dosing, pharmacokinetics (PK), and safety in HIV-1-Exposed neonates at risk of infection (IMPAACT P1110). *J Acquir Immune Defic Syndr* 2020;84:70–7.
- 7 Archary M, Zandoni B, Lallemand M, *et al*. Acceptability and feasibility of using raltegravir oral granules for the treatment of neonates in a low-resource setting. *Pediatr Infect Dis J* 2020;39:57–60.
- 8 Elizabeth Glaser Pediatric AIDS Foundation. Assessing the feasibility, acceptability and effects of use of raltegravir-based regimens in HIV-positive neonates identified through birth testing in maternity settings in Zimbabwe: quantitative study scientific report; 2022.
- 9 Guest G, Bunce A, Johnson L. How many interviews are enough?: An experiment with data saturation and variability. *Field Methods* 2006;18:59–82.
- 10 Pasipanodya B, Kuwengwa R, Prust ML, *et al*. Assessing the adoption of lopinavir/ritonavir oral pellets for HIV-positive children in Zimbabwe. *J Int AIDS Soc* 2018;21:e25214.
- 11 Schlatter AF, Deathe AR, Vreeman RC. The need for pediatric formulations to treat children with HIV. *AIDS Res Treat* 2016;2016:1–8.
- 12 Wexler C, Maloba M, Brown M, *et al*. Factors affecting acceptance of at-birth point of care HIV testing among providers and parents in Kenya: a qualitative study. *PLoS One* 2019;14:e0225642.
- 13 Truscott R. Covid-19: health worker strikes, limited testing, and clinic closures hamper Zimbabwe's response. *BMJ* 2020;370:m3267.
- 14 Dzinamarira T, Musuka G. Brain drain: an ever-present; significant challenge to the Zimbabwean public health sector. *Public Health Pract* 2021;2:100086.