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# Reported viral non-suppression, missed ART doses and interest in long-acting injectable treatment among people living with HIV in Uganda

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**Short Report**

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## Abstract

# Background

Interest in long-acting injectable antiretroviral therapy (ART) among people reporting viral non-suppression or missed oral doses deserves attention as treatment options expand. We described interest within these clinical subgroups in a Ugandan survey.

# Methods

This exploratory analysis included 116 people living with HIV on ART from the parent study's locked 232-person roster. Interest meant willing or very willing to use injectable treatment. Viral status referred to the previous 12 months and missed doses to the previous 30 days. We calculated subgroup proportions with Wilson 95% confidence intervals (CIs), reporting groups below 10 participants as counts only. Sensitivity analysis included all 131 ART participants in the 251-record export.

# Results

Overall, 104/116 participants expressed interest (89.7%, 95% CI 82.8–94.0). Interest was reported by 24/25 participants reporting non-suppression (96.0%, 80.5–99.3) and 80/90 reporting suppression (88.9%, 80.7–93.9). The difference was 7.1 percentage points (95% CI − 9.2 to 15.9). Interest was reported by 56/62 participants with no missed doses, 41/46 with 1–2 missed doses and seven of eight with three or more missed doses. Twenty-one of 25 participants reporting non-suppression also reported missed doses. Expanded-cohort results were similar: 118/131 expressed interest overall and 26/27 among those reporting non-suppression.

# Conclusions

Interest was high across the clinical subgroups. These data do not establish greater or equivalent interest in any subgroup, clinical eligibility, or treatment benefit. Prospective studies should link preferences to verified clinical measures and observed injectable treatment outcomes.

## Background

Long-acting injectable ART offers an alternative to daily oral treatment for selected people living with HIV. In the FLAIR trial, cabotegravir plus rilpivirine maintained suppression after oral induction, with most recipients preferring the injectable regimen [1]. Such results concern people who received treatment under trial conditions. Interest expressed before treatment is a different measure, especially among people reporting difficulty taking daily medication.

Ugandan research has already documented high acceptability and perceived feasibility of injectable ART among people with viraemia and health workers [2]. The present report adds quantitative descriptions by reported viral status and recent missed doses within a shared survey cohort. It does not seek to establish a new overall acceptance estimate or identify demographic predictors already addressed in related analyses. Our question was whether interest remained common among participants reporting non-suppression or missed oral ART doses.

## Methods

We analysed a cross-sectional survey from a broader mixed-methods study of long-acting injectable HIV options at Mildmay Hospital Uganda in central Uganda during 2026. Research assistants administered an electronic questionnaire using Open Data Kit in English or Luganda after consent. Participants considered hypothetical injectable options and did not receive injectable ART through the survey. This report uses the same participants as the parent acceptance study and related readiness and financial-distress analyses, with a separate focus on clinical subgroups.

The parent analytic roster contained 232 participants, including 116 people living with HIV and 116 participants recruited through prevention services. All 116 people living with HIV reported current ART use and were aged at least 15 years. We retained their exact roster identifiers. The complete export contained 251 unique records, including 131 participants on ART. Fifteen ART participants fell outside the parent roster. The equal-group selection in the parent analysis accounts for the smaller cohort, but the available records do not establish the selection procedure for those 15 participants. We therefore included all 131 ART participants in a sensitivity analysis rather than assuming random selection. The sample was not powered for the clinical subgroup comparisons.

Interest meant a willing or very willing response on the five-level willingness item. We retained the complete scale in supplementary outputs. Participants reported whether their viral status in the previous 12 months was suppressed, not suppressed or not tested. No laboratory value, suppression threshold or resistance result accompanied this item. Missed ART doses in the previous 30 days were recorded as none, 1–2, 3–5 or more than five. We combined the last two categories descriptively as three or more missed doses. Adherence challenges allowed multiple responses.

We reported counts, percentages and Wilson 95% confidence intervals. Subgroups below 10 participants appear as counts only. We estimated absolute differences in interest using Newcombe hybrid-score intervals and reported exploratory Fisher exact tests [3]. A supplementary unadjusted modified Poisson model with HC0 robust standard errors described the association between any missed doses and reported non-suppression among participants reporting a tested result [4]. This model does not measure agreement, validate either report or establish causation. Age remained descriptive because younger and older participants were interviewed in separate sessions. Analyses used R. No multiplicity adjustment was applied.

# Results

The main cohort comprised 116 participants on ART. Median age was 26.5 years (interquartile range 21.8–38.2), 52 (44.8%) were aged 15–24 years and 79 (68.1%) were female. Median ART duration was nine years (interquartile range 6–17). Most participants reported a single-tablet regimen (112/116, 96.6%). Pill fatigue was reported by 66 participants (56.9%), stigma by 33 (28.4%), forgetfulness by 32 (27.6%) and travel by 28 (24.1%). Multiple responses were permitted. Participant characteristics appear in Table 1.

Table 1
Participant characteristics

| Characteristic | Main cohort (n = 116) | All eligible PLHIV (n = 131) |
|---|---|---|
| Age in years, median (IQR) | 26.5 (21.8–38.2) | 25 (21-38.5) |
| Aged 15–24 years, n (%) | 52 (44.8) | 60 (45.8) |
| Female, n (%) | 79 (68.1) | 89 (67.9) |
| Years since HIV diagnosis, median (IQR) | 9 (6-17.2) | 10 (6–18) |
| Years on ART, median (IQR) | 9 (6–17) | 9 (6–17) |
| Regimen: Single-tablet regimen, n (%) | 112 (96.6) | 126 (96.2) |
| Regimen: Multiple pills, n (%) | 4 (3.4) | 5 (3.8) |
| Regimen: Not sure, n (%) | 0 (0.0) | 0 (0.0) |
| Viral status (past 12 months): Reported suppressed, n (%) | 90 (77.6) | 103 (78.6) |
| Viral status (past 12 months): Reported not suppressed, n (%) | 25 (21.6) | 27 (20.6) |
| Viral status (past 12 months): Not tested, n (%) | 1 (0.9) | 1 (0.8) |
| Missed doses (past 30 days): No missed doses, n (%) | 62 (53.4) | 70 (53.4) |
| Missed doses (past 30 days): 1–2 missed doses, n (%) | 46 (39.7) | 51 (38.9) |
| Missed doses (past 30 days): 3 or more missed doses, n (%) | 8 (6.9) | 10 (7.6) |
| Adherence challenge: Pill fatigue, n (%) | 66 (56.9) | 72 (55.0) |
| Adherence challenge: Side effects, n (%) | 13 (11.2) | 14 (10.7) |
| Adherence challenge: Stigma, n (%) | 33 (28.4) | 35 (26.7) |
| Adherence challenge: Travel, n (%) | 28 (24.1) | 32 (24.4) |
| Adherence challenge: Food insecurity, n (%) | 8 (6.9) | 9 (6.9) |
| Adherence challenge: Forgetfulness, n (%) | 32 (27.6) | 34 (26.0) |
| Adherence challenge: Other, n (%) | 26 (22.4) | 30 (22.9) |

*ART, antiretroviral therapy. PLHIV, people living with HIV. Values are n (%) or median (interquartile range), as labelled. Adherence challenges allowed multiple responses.*

Ninety participants reported suppression, 25 reported non-suppression and one reported no test. Fifty-four reported at least one missed dose, including eight reporting three or more. Interest in injectable treatment was reported by 104/116 participants (89.7%, 95% CI 82.8–94.0). Table 2 shows high interest in both tested viral-status groups and each missed-dose category. The participant reporting no test expressed a neutral response.

Table 2
Interest in long-acting injectable treatment by clinical subgroup

| Clinical subgroup | Main cohort n/N; % (95% CI) | All eligible n/N; % (95% CI) |
|---|---|---|
| All PLHIV on ART | 104/116; 89.7 (82.8 to 94.0) | 118/131; 90.1 (83.8 to 94.1) |
| Reported suppressed | 80/90; 88.9 (80.7 to 93.9) | 92/103; 89.3 (81.9 to 93.9) |
| Reported not suppressed | 24/25; 96.0 (80.5 to 99.3) | 26/27; 96.3 (81.7 to 99.3) |
| Not tested | 0/1; count only | 0/1; count only |
| No missed doses | 56/62; 90.3 (80.5 to 95.5) | 64/70; 91.4 (82.5 to 96.0) |
| 1–2 missed doses | 41/46; 89.1 (77.0 to 95.3) | 45/51; 88.2 (76.6 to 94.5) |
| 3 or more missed doses | 7/8; count only | 9/10; 90.0 (59.6 to 98.2) |
| Suppressed, no missed doses | 52/58; 89.7 (79.2 to 95.2) | 60/66; 90.9 (81.6 to 95.8) |
| Suppressed, any missed doses | 28/32; 87.5 (71.9 to 95.0) | 32/37; 86.5 (72.0 to 94.1) |
| Not suppressed, no missed doses | 4/4; count only | 4/4; count only |
| Not suppressed, any missed doses | 20/21; 95.2 (77.3 to 99.2) | 22/23; 95.7 (79.0 to 99.2) |

*ART, antiretroviral therapy. PLHIV, people living with HIV. CI, confidence interval. Wilson 95% CIs. Subgroups below 10 participants appear as counts only. Clinical subgroups overlap. Viral status refers to the previous 12 months and missed doses to the previous 30 days. Interest means willing or very willing.*

The difference in interest between reported non-suppression and suppression was 7.1 percentage points (95% CI − 9.2 to 15.9, Fisher p = 0.452). Comparing any missed doses with none gave a difference of − 1.4 percentage points (− 13.7 to 10.1). These intervals include differences in either direction and do not establish equivalence. Twenty of the 25 participants reporting non-suppression selected very willing, four selected willing and one selected neutral.

The clinical measures overlapped. Twenty-one of 25 participants reporting non-suppression also reported missed doses. Seven of eight participants reporting three or more missed doses reported non-suppression. Among participants reporting a tested result, non-suppression occurred in 21/53 with missed doses and 4/62 without missed doses. The supplementary unadjusted prevalence ratio was 6.14 (95% CI 2.25–16.77). This describes a cross-sectional association between the two reports. Table 3 presents reported viral status by missed ART doses.

Table 3
Reported viral status by missed ART doses

| Reported viral status | No missed doses | 1–2 missed doses | 3 or more missed doses | Total |
|---|---|---|---|---|
| Reported suppressed | 58 | 31 | 1 | 90 |
| Reported not suppressed | 4 | 14 | 7 | 25 |
| Not tested | 0 | 1 | 0 | 1 |

*ART, antiretroviral therapy. PLHIV, people living with HIV. Values are counts in the main cohort (n = 116). Viral status refers to the previous 12 months and missed doses to the previous 30 days.*

Including all 131 ART participants produced similar descriptive findings. Overall interest was 118/131 (90.1%, 95% CI 83.8–94.1), including 26/27 reporting non-suppression (96.3%, 81.7–99.3) and 92/103 reporting suppression (89.3%, 81.9–93.9). The difference was 7.0 percentage points (− 8.3 to 15.0). Interest was reported by 64/70 participants with no missed doses, 45/51 with 1–2 and 9/10 with three or more. Expanded-cohort findings therefore did not depend on restricting analysis to the parent roster.

## Discussion

Interest in long-acting injectable treatment was common among participants reporting non-suppression and among those reporting missed oral ART doses. It was also common among those reporting suppression and no missed doses. The report supports discussing injectable options with people across these clinical circumstances. It does not show stronger interest among people with adherence difficulties, and the small subgroups leave substantial uncertainty about differences.

The findings complement earlier Ugandan work on injectable treatment acceptability among people with viraemia [2]. Our contribution is the distribution of stated interest within reported clinical subgroups, including their overlap and uncertainty. The overall 104/116 estimate repeats the parent study for context. The clinical descriptions are the focus of this secondary report, rather than a claim of a separate study population or a new acceptance outcome.

Treatment evidence has progressed beyond the original maintenance trials. The 2026 LATITUDE trial found less regimen failure with monthly cabotegravir plus rilpivirine than with oral ART among people with adherence challenges who first received adherence support and conditional incentives and reached an HIV RNA level of 200 copies/mL or lower before randomisation [5]. This sequence matters: willingness does not replace clinical assessment or the support needed to reach and maintain treatment goals.

At Ward 86 in San Francisco, a retrospective cohort also documented suppression after injectable initiation with viraemia, alongside cases of virologic failure and emergent resistance [6]. The programme

provided appointment monitoring, reminders and additional outreach for some patients. NIH guidance permits case-by-case cabotegravir/rilpivirine use in selected people with persistent virologic failure despite intensive adherence support, without evidence of resistance to either drug and through shared decision-making [7]. This is US guidance, not evidence of Ugandan product availability or a local eligibility rule. We cannot classify survey participants as eligible or ineligible from their reported suppression category.

The frequent coexistence of missed doses and reported non-suppression strengthens the case for obtaining a complete clinical history when discussing preferences. It does not verify either response. The measures concern different recall periods, and a single cross-sectional interview cannot establish whether recent missed doses preceded the reported viral result. Similarly, interest in fewer daily doses gives no information about later injection attendance, retention or suppression.

The study has several limitations. Willingness concerned a hypothetical product and was already high in the parent cohort, leaving few neutral or unwilling responses. The group reporting three or more missed doses contained only eight participants. Self-reported viral status lacks a laboratory threshold and verification, while missed doses are subject to recall and reporting error. Parent-roster selection introduces uncertainty, although full-export estimates were similar. Recruitment sessions were entangled with age, preventing an interpretable age-effect analysis. The clinic-based sample does not represent all people living with HIV in Uganda.

Prospective research should connect stated interest with verified viral-load and resistance information, the support needed for scheduled injections, actual initiation and subsequent outcomes. The present findings indicate a receptive group for such research, including people reporting non-suppression. They do not demonstrate injectable efficacy, clinical suitability or equal preferences between groups.

## Limitations

Several limitations exist with this study. Willingness involved a hypothetical product and had been fairly high for the parent cohort, resulting in few neutral or unwilling responses. The number of participants who reported missing three or more doses was only eight. Self-reports about the virus have no lab cutoffs or confirmations. Missing doses involve the possibility of recall bias. Parent roster sampling introduces some uncertainty, though full-export estimates were comparable. Age was confounded with recruitment session making any meaningful analysis of an age effect impossible. Participants are not representative of all Ugandans with HIV.

## Declarations

Human ethics and consent to participate

The parent study received approval from the Mildmay Uganda Research Ethics Committee, reference MUREC-2026-1828. The study was conducted in accordance with the Declaration of Helsinki. Adults

provided written informed consent. Participants aged 15–17 years provided written assent with written consent from a parent or legal guardian. This report presents aggregate findings.

Clinical trial number

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Data availability

The aggregate analysis outputs accompany this report. Participant-level data contain sensitive HIV-related information and are not publicly shared. Access requests should be directed to solet@musph.ac.ug and remain subject to the study custodian’s permissions and applicable ethical and data-governance requirements.

Author Contributions

Stephen Charles Olet led data management and statistical analysis, interpreted the findings and drafted the manuscript. Wandera Uthmaan Muluga and Drake Musoki conceived the parent study, secured funding and supervised implementation. They also contributed to developing the research question for this report, interpreting the findings and critically revising the manuscript. Suzanne N Kiwanuka and David Musoke contributed to interpretation and critical manuscript revision. Chad D. Stecher provided methodological input, contributed to interpretation and critically revised the manuscript.

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# References

1. Orkin C, Arasteh K, Górgolas Hernández-Mora M, et al. Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection. N Engl J Med. 2020;382:1124–35. 10.1056/NEJMoa1909512.

2. Kennedy CE, Zhao T, Van Vo A, Nakubulwa R, Nabakka P, Jackson J, et al. High Acceptability and Perceived Feasibility of Long-Acting Injectable Antiretroviral Treatment Among People Living with HIV Who Are Viremic and Health Workers in Uganda. AIDS Patient Care STDS. 2023;37:316–22. 10.1089/apc.2023.0017.
3. Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. Stat Med. 1998;17:873–90. 10.1002/. (SICI)1097-0258(19980430)17:8<873::AID-SIM779>3.0.CO;2-I.
4. Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004;159:702–6. 10.1093/aje/kwh090.
5. Rana AI, Zheng L, Castillo-Mancilla J, et al. Cabotegravir plus Rilpivirine for Persons with HIV and Adherence Challenges. N Engl J Med. 2026;394:858–71. 10.1056/NEJMoa2508228.
6. Hickey MD, Gistand N, Grochowski J, et al. Viral Suppression Rates at 48 Weeks in People With HIV Starting Long-Acting Cabotegravir/Rilpivirine With Initial Viremia. Clin Infect Dis. 2025;80:864–70. 10.1093/cid/ciae500.
7. Panel on Antiretroviral Guidelines for Adults and Adolescents. Virologic Failure. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Updated 12 September 2024. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/virologic-failure. Accessed 7 October 2026.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 01participantflow.docx
- 04TableS1perceivedadherencebenefitbysubgroup.docx
- 07TableS3descriptivedifferences.docx
- 09TableS5agebysubgroupdescriptive.docx
- 05TableS2fullwillingnessdistribution.docx
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