

High Willingness to use Injectable Antiretroviral Therapy among Women who have been Lost to Follow-Up from HIV Programmes; A Nested Cross-Sectional Study.

Eva Laker Agnes Odongpiny<sup>1,2</sup>, Fiona Cresswell<sup>1,3,4</sup>, Arnold Arinaitwe<sup>1</sup>, Vivian Nakate<sup>1</sup>, Joshua Kyenkya<sup>1</sup>, Mohammed Lamorde<sup>1</sup>, Catriona Waitt<sup>1,5</sup>, David Meya<sup>1,6</sup>, Agnes Kiragga<sup>1</sup>

Author affiliations

1 Infectious Diseases Institute, Makerere University, Kampala, Uganda,

2. Postgraduate School of Medicine, University of St Andrews, Scotland, United Kingdom

3 Clinical Research Department, London School of Hygiene and Tropical Medicine, London, United Kingdom

4 MRC-UVRI London School of Hygiene and Tropical Medicine Uganda Research Unit, Entebbe, Uganda

5 Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, UK

6 Division of Infectious Diseases and International Medicine, Department of Medicine, University of Minnesota, Minneapolis, Minnesota, USA

Key words

Injectable ART, Loss to follow up, PVT program, pregnant, nursing, HIV/AIDS

Corresponding Author

Eva Laker Agnes Odongpiny

Email; [elaker@idi.co.ug](mailto:elaker@idi.co.ug)

## Abstract

### Objectives

Efforts to achieve zero transmission of HIV to infants born to women living with HIV in sub-Saharan African are undermined by high rates of loss to follow up in Prevention of Vertical Transmission (PVT) programs. The fear of HIV status disclosure by discovering pill bottles at home is a major contributor. Injectable antiretroviral therapy (ART) has proven to be efficacious in clinical trials and is discreet, offering a potential solution. We investigated the knowledge and willingness to use injectable ART among women who were lost to follow up from the PVT programme in Uganda.

### Methods

Women were traced by nurse counselors and knowledge and opinions relating to injectable ART, including willingness to use it when it becomes available, were collected. Generalized linear models were used to determine predictors of willingness to use injectable ART.

### Conclusion

Among 1023 women registered between 2017 – 2019 under the PVT programmes in Kampala and Wakiso districts, Uganda, 385 (38%) were lost to follow up from care and 22% of these (83/385) were successfully traced and interviewed. Only 25% (21/83) had heard of injectable ART. Over half (55%, 46/83) were very willing to use injectable ART, 40% (33/83) were somewhat willing and four (5%) were not willing. Those who associated ART tablets with disclosure risk were more willing to consider injectable ART (adjusted OR 4.21; 95% CI 1.45-12.19; P=0.008).

We report high willingness to use injectable ART associated with fears that ART tablets caused potential for HIV status disclosure. Injectable ART could be a solution for women that have challenges with disclosure.

## Introduction

Despite the rapid expansion of HIV programmes including the prevention of mother-to-child transmission (PMT), in 2019 8% [6–10%] (1) of babies born to women living with HIV (WLHIV) in sub-Saharan Africa HIV positive. Data suggests that one of the main factors for children infected is women discontinuing antiretroviral therapy (ART) (2) (1, 3). Women disengage at different stages after HIV diagnosis but more especially during the postpartum period (up to 53%)(4) .

Several reasons influence women's disengagement from HIV care and these can be broadly categorized as; structural (e.g. transport difficulties, accessibility of healthcare facilities and limited resources), clinical (e.g. clinic delays, negative attitudes/experiences with healthcare personnel and fear of drug side effects) and psychosocial (e.g. HIV stigma, disclosure and poor family support) (5). Several studies have described that for many people living with HIV (PLHIV) who disengage from care and do not reengage the main reasons are psychosocial especially stigma and the fear of disclosure (5-7). Many women discover their HIV status during mandatory HIV testing in antenatal care and need to start antiretroviral therapy (ART) urgently to prevent vertical transmission to their offspring. They might not have time to deal with their new diagnosis and also disclose to partners and household members (8-10). Taking tablets might lead to unsolicited disclosure by medicine pills discovered by household members (11, 12).

Women who have disengaged from HIV care place themselves at risk of ill health, and their nursing infants and sexual partners at risk of HIV transmission. Ortblad et al described that despite the widespread coverage of ART, the 90-90-90 UNAIDS targets might not be reached because of core marginalized groups that fail to engage with HIV services for several reasons including stigma. Therefore, efforts must be directed at these groups and include novel HIV service delivery models and new technologies such as long-acting ART (LA).

Two monthly injectable ART regimens containing cabotegravir and rilpivirine has recently been approved for use in the USA and Europe (13, 14). Participants in studies who have used injectable ART report high satisfaction and described it as more “discrete” than pills, with less opportunity for stigma or discrimination or non-desired disclosure of HIV status. Given that injectable ART is discreet it is predicted that it may offer a solution for those with adherence challenges due to non-disclosure. (15-17).

We therefore set out to determine the knowledge about injectable ART and willingness to use it among women disengaged from HIV care.

## Method

The LOCATOR study was undertaken to locate WLHIV initiated in HIV care under Option B + who later were lost to follow up from care, to assess their health and wellbeing and that of their infants. Women were considered lost to follow up if they had not visited the HIV clinic within 90 days of the last scheduled appointment and those who were traced successfully and found not to be in HIV care were categorized as disengaged from care. The study also determined the reasons for disengagement and willingness to return into care. Traced women

were supported to reengage in care. The current study was nested in the LOCATOR study. The protocol was approved by the Joint Clinical Research Centre IRB (JC3517) and registered with the National Council of Science and Technology and the office of the President of Uganda (HS175ES).

Community tracing by trained nurse counselors used contact information including phone numbers and physical residence addresses obtained at enrollment in HIV care. Using structured-questionnaires, knowledge about injectable ART, HIV disclosure, experiences with use of oral ART and willingness to use injectable ART when available, were collected. After asking about the knowledge on injectable ART women were provided information on injectable cabotegravir /rilpivirine including the fact that it has not yet been licensed but studies were ongoing, there were likely to be two options available a monthly and two monthly option, there would be a need to come into the hospital to receive these injections and side-effects included those common to other injections like injection-site pain. Opinions on willingness to use injectable ART were measured using a 3-point Likert scale (1= not at all, 2 = somewhat willing, 3 = very willing).

Generalized linear models were used to explore what factors were associated with willingness to use injectable ART. Factors included age, education (categorized as primary level and below and above primary), employment status (employed or not), marital status (living with partner or not), whether they had ever used injectable medicines or implants before (yes or no), whether they felt like having to take tablets caused unwanted disclosure (yes or no), whether they ever heard of injectable ART (yes or no), the outcome of the pregnancy at enrolment into HIV care (infant alive or dead) and whether they have any child (yes or no) and if they had seen anyone for HIV care since their last visit at original clinic (yes or no). Factors that were significant in unadjusted analyses ( $p < 0.2$ ) were included in adjusted analyses with level of significance at 95%.

## Results

Among a total of 1023 women registered between 2017 – 2019 under the PVT programmes in Kampala and Wakiso districts, 385 (38%) had disengaged from care and 22% (83/385) were successfully traced between June 2017 and July 2019 and interviewed in October 2019.

The population had a median age of 26 years (IQR; 23-29). Majority had an education level above primary (49/83, 59%) and were unemployed (49/83, 59%). 88% (73/83) had a live infant and 66% (55/83) were living with their partner. Almost half (40/83, 48.2% of the women were not receiving HIV care since they were lost to follow from their previous HIV clinics. Only 37 women (45%) had disclosed to their sexual partner. A quarter; 25% (21/83) had heard of injectable ART.

A high proportion of women (60/83; 72%) had experience with using other injectable drugs/implants, mainly injectable contraceptives (70%; 42/60). The majority of women (69%; 57/83) felt that using ART tablets increased HIV disclosure risk. Women responded to willingness to use injectable ART as follows: 55% (46/83) were very willing to use injectable ART, 40% (33/83) were somewhat willing and four (5%) were not willing. Opinions on willingness to use injectable ART did not differ among those engaged and those not engaged in care (Have you seen anyone for HIV care since your last visit at original clinic,  $p=0.078$ , Table

1). We combined the outcome willing and somewhat willing to create an outcome willing with a resultant binary outcome for willingness to use injectable ART (willing and not willing).

Before adjustment, factors that were significantly associated with willingness to use injectable ART ( $p < 0.2$ ) included employment status, whether they had ever used injectable medication or implant drugs before, whether they had seen anyone for HIV care since their last visit at original clinic and whether they felt like having to take tablets caused unwanted disclosure (Table 1). After adjustment for these factors, those who associated ART tablets with disclosure risk were more willing to consider injectable ART (adjusted Prevalence Ratio [PR] 3.49; 95% confidence interval (CI) 1.45-12.19;  $P = 0.008$ ).

## Discussion

There was a poor knowledge of injectable ART in the population. While previous stories in the Uganda media had publicized incoming clinical trials to be conducted on injectable ART in the country, it is possible that this information has not been accessible to our study population (18).

We found that age was not associated with a willingness to use injectable ART after adjusting for other factors unlike the study by Derrick *et al.* where those of younger age were more willing to switch to injectable ART from oral ART. This could be because our study population were all relatively young (IQR; 23-29 years) and thus not our study was not adequately powered to determine this difference. Social-economic factors like education and employment status also did not affect willingness to use injectable ART. Other factors such as whether they had any living child or the outcome of pregnancy at enrolment in care also did not affect willingness to use injectable ART. Differences could also be due to the different sociocultural settings.

Contrary to our hypothesis, experience with use of injectable medication such as three-monthly contraceptives or longer-term implants did not affect the willingness to use injectables. During qualitative interviews with female sex workers in Tanzania and the Dominican Republic to obtain perspectives on use of injectable ART, women drew analogies between LA ART and the ease and popularity of injectable contraception (19).

Those who felt that using oral tablets caused unwanted disclosure were more willing to use injectable ART. In this population where less than half had not disclosed to their partners and were also not in care, we provide evidence that provision of injectable ART might influence willingness to use ART and potentially return to care. Amongst non-trial participants in the USA, women similarly expressed interest in LA injectable ART because it was discreet and prevented unwanted disclosure reducing stigma (17).

In the study by Kerrigan and colleagues, which was one of the first to collect perspectives on injectable ART that included a sub-Saharan African population, there were low rates of viral suppression (72.64% of sex workers in Dominican Republic and 48.53% of women in Tanzania were virologically suppressed). Women felt that injectable ART would reduce stigma and discrimination. Additionally, many participants expressed the need to hide their pills from their clients and other people in their work, households, and communities to avoid stigma,

discrimination, and potential violence. LA ART was viewed as helping to avoid those negative situations and outcomes, since no one could discover their HIV and could improve adherence.

Women's interests in LA ART has also been described to be related to perspectives that are unique from men including that injectable ART allowed them carry out different gender-related responsibilities and tasks (20). We were not able to explore these in the current study

Limitations include the small sample size which was limited by the number of women that were traceable within the LOCATOR study and this could be the reason why we were not able to determine any other association with willingness to use injectable ART. Larger and more in-depth studies including in-depth interview and focus group discussions are needed in order to understand what could potentially drive the use of injectable and other forms of long acting (LA) as they become available.

Injectable ART will add to the options of treatments available for HIV in sub-Saharan Africa. There was high willingness to use injectable ART in this population which may relate to fears that ART tablets caused potential for HIV status disclosure. Injectable ART could be a solution for women that have challenges with disclosure; it may potentially increase retention in care and warrants further investigation in this setting. Making injectable ART available to women of childbearing potential could enable them remain in care reducing risk of mother to child transmission so conducting trials of safety and efficacy in women is a key priority.

### Acknowledgements

We acknowledge the LOCATOR study staff who contributed to the collection of data to inform this project. We also acknowledge the participants who were enrolled in this study. This program has been supported by the EDCTP grant number TMA2017CDF – 1036.

Eva Laker Agnes Odongpiny is a research fellow being funded by the Northern Pacific Global Health Fellows Program (grant D43TW009345) and PhD scholar funded by the Scottish Funding Council Official Development Assistance GCRF 2020-21

Catriona Waitt is a Wellcome Clinical Research Career Development Fellow,  
*222075/Z/20/Z*

### Author Contributions

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

### Funding

Funding for this work was has been supported by the EDCTP grant number TMA2017CDF - 1036.

## Contribution to Science

There has been a widespread roll out of antiretroviral therapy include in programs that aim to prevent vertical transmission of HIV. However, many women living with HIV discontinue HIV care putting their babies and sexual partners at risk. The reasons for this are varied but include fear of unsolicited disclosure of their HIV status. Injectable antiretroviral therapy has been described to be discreet and could potentially offer a solution for women who fear that antiretroviral tablets increase stigma. Even as injectable antiretroviral therapy containing long-acting cabotegravir and rilpivirine has been recently approved for use by regulatory authorities, there is need to understand which populations would best benefit from its use. We interviewed women who were lost to follow up from HIV care and determined their knowledge and willingness to use injectable antiretroviral therapy when it becomes available. Many women showed an interest in using injectable antiretroviral therapy and this was highly associated with a fear that oral antiretroviral tablets increased HIV disclosure. This population should therefore be further studied but also prioritized as a group that could benefit from injectable antiretroviral therapy.

## References

1. UNAIDS. UNAIDS Data 2020. [https://www.unaids.org/sites/default/files/media\\_asset/2020\\_aids-data-book\\_en.pdf](https://www.unaids.org/sites/default/files/media_asset/2020_aids-data-book_en.pdf). Accessed 15May2021. 2020.
2. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. *AIDS (London, England)*. 2012;26(16):2039-52.
3. Okawa S, Chirwa M, Ishikawa N, Kapyata H, Msiska CY, Syakantu G, et al. Longitudinal adherence to antiretroviral drugs for preventing mother-to-child transmission of HIV in Zambia. *BMC Pregnancy and Childbirth*. 2015;15(1):258.
4. UNAIDS. UNAIDS data 2019. [https://www.unaids.org/sites/default/files/media\\_asset/2019-UNAIDS-data\\_en.pdf](https://www.unaids.org/sites/default/files/media_asset/2019-UNAIDS-data_en.pdf). 2019.
5. Geng EH, Odeny TA, Lyamuya R, Nakiwogga-Muwanga A, Diero L, Bwana M, et al. Retention in Care and Patient-Reported Reasons for Undocumented Transfer or Stopping Care Among HIV-Infected Patients on Antiretroviral Therapy in Eastern Africa: Application of a Sampling-Based Approach. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2016;62(7):935-44.
6. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. *Journal of the International AIDS Society*. 2013;16(1):18588.
7. Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: a systematic review. *AIDS (London, England)*. 2012;26(16).
8. Yourkavitch J, Hassmiller Lich K, Flax VL, Okello ES, Kadzandira J, Katahoire AR, et al. Interactions among poverty, gender, and health systems affect women's participation in services to prevent HIV transmission from mother to child: A causal loop analysis. *PLOS ONE*. 2018;13(5):e0197239.
9. Zhou A. The uncertainty of treatment: Women's use of HIV treatment as prevention in Malawi. *Social Science & Medicine*. 2016;158:52-60.
10. Suryavanshi N, Mave V, Kadam A, Kanade S, Sivalenka S, Kumar VS, et al. Challenges and opportunities for outreach workers in the Prevention of Mother to Child Transmission of HIV (PMTCT) program in India. *PLOS ONE*. 2018;13(9):e0203425.
11. Philbin MM, Parish C, Bergen S, Kerrigan D, Kinnard EN, Reed SE, et al. A Qualitative Exploration of Women's Interest in Long-Acting Injectable Antiretroviral Therapy Across Six Cities in the Women's Interagency HIV Study: Intersections with Current and Past Injectable Medication and Substance Use. *AIDS patient care and STDs*. 2021;35(1):23-30.
12. Dlamini-Simelane TT, Moyer E. 'Lost to follow up': rethinking delayed and interrupted HIV treatment among married Swazi women. *Health policy and planning*. 2017;32(2):248-56.
13. ViiVHealthcare. ViiV Healthcare announces FDA approval of Cabenuva (cabotegravir, rilpivirine), the first and only complete long-acting regimen for HIV treatment London2021 [cited 2021 February 5]. Available from: <https://viivhealthcare.com/en-gb/media/press-releases/2021/january/viiv-healthcare-announces-fda-approval-of-cabenuva/>. [
14. EuropeanPharmaceuticalReview. First long-acting HIV treatment approved in Europe 2021 [Available from: <https://www.europeanpharmaceuticalreview.com/news/138281/first-long-acting-hiv-treatment-approved-in-europe/#:~:text=The%20European%20Commission%20approval%20of,injectable%20HIV%20treatment%20in%20Europe.> [



15. Philbin MM, Parish CL, Kinnard EN, Reed SE, Kerrigan D, Alcaide ML, et al. Multisite Study of Women Living With HIV's Perceived Barriers to, and Interest in, Long-Acting Injectable Antiretroviral Therapy. *Journal of acquired immune deficiency syndromes (1999)*. 2020;84(3):263-70.
16. Cindy Garris SH, Erin Arthurs, Frank Spinelli, Katelyn Cutts, Erik Lowman, Howard L Rice, Bertrand Lebouche, Hannah Collacott, Gin Nie Chua, Heather Gelhorn. Perceptions of and Preferences for Oral or Long-Acting Injectable Antiretroviral Treatment Regimens in the United States and Canada. *Open Forum Infect Dis*. 2019 Oct; 6(Suppl 2): S866–S867. Published online 2019 Oct 23. doi: 10.1093/ofid/ofz360.2177. 2019.
17. Philbin MM, Parish CL, Kinnard EN, Reed SE, Kerrigan D, Alcaide ML, et al. Multisite Study of Women Living With HIV's Perceived Barriers to, and Interest in, Long-Acting Injectable Antiretroviral Therapy. *Journal of acquired immune deficiency syndromes (1999)*. 2020;84(3):263-70.
18. DailyMonitor. Uganda seeks to start injectable HIV drugs. <https://www.monitor.co.ug/uganda/news/national/uganda-seeks-to-start-injectable-hiv-drugs-1709928>. 2017.
19. Kerrigan D, Sanchez Karver T, Muraleetharan O, Savage V, Mbwambo J, Donastorg Y, et al. "A dream come true": Perspectives on long-acting injectable antiretroviral therapy among female sex workers living with HIV from the Dominican Republic and Tanzania. *PLOS ONE*. 2020;15(6):e0234666.
20. Mantsios A, Murray M, Karver TS, Davis W, Margolis D, Kumar P, et al. "I feel empowered": women's perspectives on and experiences with long-acting injectable antiretroviral therapy in the USA and Spain. *Culture, health & sexuality*. 2020:1-13.