

Rapidly starting antiretroviral therapy to improve outcomes among disadvantaged groups

Nathan Ford^{a,b}, Keith W. Crawford^c and Wole Ameyan^a

See related paper on page 2201

AIDS 2021, **35**:2217–2219

Keywords: antiretroviral therapy, HIV, men, West Africa

Fifteen years ago, a review of HIV programmes across southern Africa concluded that fewer men were receiving antiretroviral therapy (ART) compared with women [1]. Recognition of this delayed engagement with care, which persists today [2], has grown in recent years, with several recent studies showing that, compared with women, men present with more advanced HIV disease and associated higher mortality risk, are less likely to start ART and are less likely to be retained in care [3,4].

In this issue of *AIDS*, a prospective cohort study [5] provides outcomes of rapid ART initiation among MSM from four countries in West Africa (Burkina Faso, Côte d'Ivoire, Mali, and Togo) between 2015 and 2019. This study is important as it reflects several key challenges in the HIV response. In addition to the challenge of increasing access to ART among men in general, there is a need for more evidence to guide interventions to improve uptake and outcomes of ART for MSM in low-income and middle-income settings [6]. ART coverage and viral suppression among MSM in Africa remain much lower than required to achieve global targets [7]. In addition, as highlighted by an Médecins Sans Frontières report in 2016 [8], and echoed by UNAIDS [9], improvements in access to HIV treatment and care has been slower in West Africa compared with other regions. HIV-positive MSM in West Africa, therefore, represent a distinctly disadvantaged group.

Rapid initiation of ART is one way to increase the number of people starting treatment by reducing losses between testing and treatment. Since 2017, the World Health Organization (WHO) recommends starting ART within 7 days of an HIV diagnosis, and suggests the possibility of starting treatment on the same day of diagnosis [10]. In 2021, WHO also recommended that ART can be started outside of a health facility [11], opening the way for same day ART start as part of community-testing approaches [12]. These guidelines also put forward a good practice statement aimed at promoting uptake of same day ART start, promoting approaches to improve uptake, treatment adherence and retention such as tailored patient education, counselling and support.

The study from West Africa clearly demonstrated the benefits of this approach for MSM. Two-thirds of men (65%) who were offered treatment started within 7 days, and a quarter (24%) on the same day, reflecting a high level of acceptability among a relatively healthy population (96% were WHO Clinical Stage I and median CD4⁺ cell count was 398 cells/ μ l). In multivariate analysis, rapid initiation improved viral suppression [adjusted odds ratio (aOR) 6.96, 95% confidence interval (CI) 1.98–24.46], and there was a tendency towards improved viral suppression associated with same-day ART start in univariate analysis (OR 3.33, 95% CI 0.90–12.31) [13]. Reassuringly, rapid ART initiation and same day

^aGlobal HIV, Hepatitis and Sexually Transmitted Infections Programme, World Health Organization, Geneva, Switzerland,

^bCentre for Infectious Disease Epidemiology and Research, School of Public Health and Family Medicine, University of Cape Town, South Africa, and ^cTherapeutic Research Program, Division of AIDS, National Institute of Allergy and Infectious Disease, National Institutes of Health, Rockville, MD, USA.

Correspondence to Nathan Ford, Global HIV, Hepatitis and Sexually Transmitted Infections Programme, World Health Organization, 20 Ave Appia, 1211 Geneva, Switzerland.

E-mail: ford@who.int

Received: 7 August 2021; accepted: 10 August 2021.

DOI:10.1097/QAD.0000000000003052

ISSN 0269-9370 Copyright © 2021 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

ART start were not associated with increased disengagement from care, a concern that has been reported by several observational studies [14].

Overall, however, a third of those starting treatment were not retained in care after 3 years of follow-up, with the majority of people disengaging within the first 12 months after start of treatment. This effect of reduced retention-in-care must be well understood to determine the value of this intervention among African MSM. Is it a negative consequence of rapid ART initiation or is it a feature of this particular demographic? Some studies have observed an increased risk of loss to care among pregnant women following rapid ART initiation, underscoring the importance of providing postinitiation follow-up and support for populations at risk of disengagement from care [14]. Other studies have reported that African MSM have worse outcomes across a number of important indicators, including increased loss to follow-up [14]. A study among HIV-positive MSM in Kenya found that, in spite of employing evidence-based supportive measures, they experienced lower virologic suppression rates compared with adults in other ART programs in Africa (including the general adult population in Kenya) [15]. Men who acquired coping self-efficacy skills, in this environment of intensive structural stigma, had better outcomes, including engagement in the health system. In a study of rapid ART initiation among men in the United States, there were no differences in loss to care comparing those receiving the intervention and those receiving standard care [16].

In addition to recommending support for retention in care, the latest WHO guidelines recommends that HIV programmes include activities to trace people who have disengaged from care and provide support for re-engagement [12]. Individuals who have simply relocated and continued care at another facility may be misclassified as being lost to care [16]. The benefits of rapid ART initiation will only be realized if people who start treatment are provided with appropriate support to remain in care over the long-term, and nonjudgementally supported to reengage in care if they need to interrupt care for whatever reason.

The impact of the additional burden of the stigma of being a gay male in sub-Saharan Africa must not be underestimated. Homosexuality is criminalized in many countries in sub-Saharan Africa with penalties as severe as imprisonment and death. Beyond the extreme violation of human rights brought on by these laws, they have an adverse effect on access to care and well being of HIV-positive MSM. A recent systematic review found that African countries with the most severe antigay legislation had substantially reduced rates of HIV testing among MSM compared with countries with less severe legislation (e.g. testing in the last 12 months, 35.5 vs. 49.3%, $P=0.01$) [7].

The types of co-infections that may be present at the time of ART initiation can determine which antiretrovirals are used, the dosage, as well as the timing for starting ART. Currently, most people are started on a dolutegravir-based first-line regimen; if rifampicin is also being administered for tuberculosis (TB) treatment, the dosage should be raised to 50 mg twice daily [12]. Unlike efavirenz, dolutegravir is active against HIV-2, which is common in West Africa. The key contra-indication for rapid ART start is when cryptococcal meningitis is diagnosed; in such individuals, ART initiation should be deferred 4–6 weeks from the initiation of antifungal treatment [17]. People with advanced HIV disease should be given priority for initiating ART as they are at higher risk of death. They should be evaluated for the risk or presence of TB and cryptococcal meningitis for which point-of-care diagnostic tests exist [12].

Individuals with pretreatment drug resistance, which may occur in greater than 10% of individuals starting ART in some countries in sub-Saharan Africa [18], are more likely to experience virologic failure. This again favours initiating with dolutegravir-containing regimens in resource-limited settings where baseline drug resistance testing is currently not recommended prior to starting ART. Point-of-care genotypic resistance tests may make resistance testing more widely available but the role of such tests in a public health approach to ART delivery remains to be determined [19].

In conclusion, rapid ART initiation is operationally feasible in African MSM and may have an important role in controlling the epidemic. Additional resources are needed to ensure sustainable benefit for this vulnerable group.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1. Muula AS, Ngulube TJ, Siziya S, Makupe CM, Umar E, Prozesky HW, *et al.* **Gender distribution of adult patients on highly active antiretroviral therapy (HAART) in Southern Africa: a systematic review.** *BMC Public Health* 2007; 7:63.
2. Cornell M, Cox V, Wilkinson L. **Public health blindness towards men in HIV programmes in Africa.** *Trop Med Int Health* 2015; 20:1634–1635.
3. Osler M, Cornell M, Ford N, Hilderbrand K, Goemaere E, Boulle A. **Population-wide differentials in HIV service access and outcomes in the Western Cape for men as compared to women, South Africa: 2008 to 2018: a cohort analysis.** *J Int AIDS Soc* 2020; 23 (Suppl 2):e25530.
4. Lurie MN, Kirwa K, Callaway J, Cornell M, Boulle A, Bengtson AM, *et al.* **Quantifying the HIV treatment cascade in a South African health sub-district by gender: retrospective cohort study.** *Trop Med Int Health* 2020; 25:186–192.

5. Dah TTE, Yaya I, Mensah E, Coulibaly A, Kouame J-BM, Traore I, *et al.* **Rapid antiretroviral therapy initiation and its effect on treatment response in MSM in West Africa.** *AIDS* 2021; **35**:2201–2210.
6. Rebe K, Hoosen N, McIntyre JA. **Strategies to improve access for MSM in low-income and middle-income countries.** *Curr Opin HIV AIDS* 2019; **14**:387–392.
7. Stannah J, Dale E, Elmes J, Staunton R, Beyrer C, Mitchell KM, Boily MC. **HIV testing and engagement with the HIV treatment cascade among men who have sex with men in Africa: a systematic review and meta-analysis.** *Lancet HIV* 2019; **6**:e769–e787.
8. Médecins Sans Frontières. Out of focus: How millions of people in West and Central Africa are being left out of the global HIV response. Geneva. 2016.
9. UNAIDS. Communities at the centre: the response to HIV in Western and Central Africa. Geneva. 2019.
10. WHO. Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. Geneva, 2017.
11. Eshun-Wilson I, Awotiwon AA, Germann A, Amankwaa SA, Ford N, Schwartz S, *et al.* **Effects of community-based antiretroviral therapy initiation models on HIV treatment outcomes: a systematic review and meta-analysis.** *PLoS Med* 2021; **18**:e1003646.
12. World Health Organization. *Consolidated guidelines on HIV prevention, testing, treatment, service delivery, and monitoring. Recommendations for a public health approach.* Geneva: World Health Organization; 2021.
13. Hackshaw A, Kirkwood A. **Interpreting and reporting clinical trials with results of borderline significance.** *BMJ* 2011; **343**:d3340.
14. Ford N, Migone C, Calmy A, Kerschberger B, Kanters S, Nsan-zimana S, *et al.* **Benefits and risks of rapid initiation of antiretroviral therapy.** *AIDS* 2018; **32**:17–23.
15. Kunzweiler CP, Bailey RC, Mehta SD, Okall DO, Obondi E, Djomand G, *et al.* **Factors associated with viral suppression among HIV-positive Kenyan gay and bisexual men who have sex with men.** *AIDS Care* 2018; **30** (Suppl 5):S76–S88.
16. Wilkinson LS, Skordis-Worrall J, Ajose O, Ford N. **Self-transfer and mortality amongst adults lost to follow-up in ART programmes in low- and middle-income countries: systematic review and meta-analysis.** *Trop Med Int Health* 2015; **20**:365–379.
17. Eshun-Wilson I, Okwen MP, Richardson M, Bicanic T. **Early versus delayed antiretroviral treatment in HIV-positive people with cryptococcal meningitis.** *Cochrane Database Syst Rev* 2018; **7**:CD009012.
18. Preventing and responding to HIV drug resistance in the African Region: regional action plan 2019-2023, WHO Regional Office for Africa, 2019.
19. Ford N, Ball A, Baggaley R, Vitoria M, Low-Beer D, Penazzato M, *et al.* **The WHO public-health approach to HIV treatment and care: looking back and looking ahead.** *Lancet Infect Dis* 2018; **18**:e76–e86.