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Lack of Virological Suppression among Young HIV-Positive Adults in Botswana

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Abstract

Background: HIV-1 RNA load is the best biological predictor of HIV transmission and treatment response. The rate of virologic suppression among key sub-populations can guide HIV prevention programs.

Methods: The Botswana Combination Prevention Project performed a population-based household survey among adults in 30 communities in Botswana. Data collected included knowledge of HIV-positive status, ART coverage and virologic suppression (HIV-1 RNA ≤400 copies/mL). Individuals aged 16–29 years were considered young adults.

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Results: Among 552 young people living with HIV (PLHIV) enrolled with RNA load data and ART status available, 51% (n=279) had undetectable HIV-1 RNA, including 54% of young women and 32% of young men (gender PR: 0.53; 95% CI: 0.43–0.80; p<0.001). Compared with older adults (30–64 years old), young HIV-infected adults were significantly less likely to have undetectable HIV-1 RNA (PR: 0.65; 95%CI: 0.59–0.70; p<0.0001), including both men (PR: 0.43; 95%CI: 0.34–0.56; p<0.0001) and women (PR: 0.67; 95%CI: 0.62–0.74; p<0.0001). Among a subset of PLHIV receiving ART, young adults also were less likely to have undetectable HIV-1 RNA load than older adults (PR: 0.93; 95%CI: 0.90–0.95; p=<0.0001). Analysis of the care continuum revealed that inferior HIV diagnosis and sub-optimal linkage to care are the primary reasons for low virologic suppression among young adults.

Conclusions: Young adults in Botswana are significantly less likely to have undetectable HIV-1 RNA load compared with older adults. In the era of broad scale-up of ART, interventions able to diagnose young adults living with HIV and link them to effective therapy are urgently needed.

Keywords

HIV-1C epidemic; young adults; HIV suppression; receiving ART; virologically suppressed

Introduction

Increased access to HIV treatment has saved millions of lives and reduced HIV transmissions.[1–3] Southern African countries have adopted the World Health Organization (WHO) recommendations to provide antiretroviral therapy (ART) to all HIV-infected individuals,[4] as an important move toward ending the HIV epidemic. To optimize health and HIV transmission prevention outcomes, the Joint United Nations Program on HIV/AIDS (UNAIDS) has established new targets aimed at ending the AIDS epidemic: by 2020, 90% of all people living with HIV (PLHIV) should know their HIV status, 90% of those diagnosed with HIV infection should receive sustained combination ART, and 90% of all people receiving ART should have viral suppression (“90–90-90”).[5]

Botswana is in the midst of a generalized HIV epidemic with an estimated 24.3% of the adult population (15–49 years) living with HIV.[6] In 2002, experiencing a devastating burden of epidemic HIV infection, Botswana initiated a national ART program (free to all citizens). The successful scale-up of the ART program has resulted in Botswana’s approaching the UNAIDS 90–90-90 goals.[7,8] By the end of 2015, based on a population-based survey, 83% of PLHIV aged 16–64 years old residing in 30 Botswana peri-urban communities knew their HIV status, 87.4% of them were receiving ART, and 96% of people on ART had undetectable HIV-1 RNA.[8] Despite this impressive achievement, new HIV transmissions are still occurring in the same communities, and HIV-1 incidence in adults in Botswana is estimated at 1.0–1.35%.[9,10]

High HIV incidence and prevalence among young women remains a hallmark of the HIV-1C epidemic in sub-Saharan Africa.[11–13] Young women and men in Africa represent the populations most in need of treatment services.[14] Younger age in discordant couples in Kenya and Uganda has been found to be associated with delayed ART initiation, failure to achieve viral suppression, and increased risk of virologic rebound.[15,16] In a study conducted

in Chicago, 46 adolescents and young adults had lower rates of virologic suppression, and higher rates of loss to follow-up compared with 46 older PLHIV.[17] Studies in South Africa demonstrated that rapid ART initiation is acceptable and feasible, and increases uptake, although rapid initiation of ART among men and younger adults is challenging.[18,19] The population level rates of virologic suppression among young adults in Southern Africa remain unknown.

Early and durable suppression of viral replication evident by undetectable levels of HIV-1 RNA should be the ultimate goal of public health interventions. The population level of viral suppression is depicted by the third "90" of the UNAIDS goals[5], an approach that helps to prioritize public health strategies and interventions. However, rates of ART coverage and virologic suppression among some key sub-populations in Africa remain unknown, particularly for young PLHIV.

In this study we focused on PLHIV in 30 communities in Botswana and performed the following analyses: assessed attainment of the "90–90-90" UNAIDS goals[5] among young (aged 16–29 years) and older (aged 30–64 years) adults in Botswana, estimated HIV prevalence stratified by age and gender, evaluated the proportions of individuals currently on ART by age and gender, and estimated the extent of virologic suppression by age and gender.

Methods

Ethical approval

The study was approved by the Botswana Health Research and Development Committee (Institutional Review Board of the Botswana Ministry of Health and Wellness) and the US Centers for Disease Control and Prevention Institutional Review Board. All participants provided written informed consent (or assent with guardian permission, in the case of persons at least 16 but less than 18 years of age).

Study participants

The Botswana Combination Prevention Project (BCPP; also known as the "Ya Tsie" study) is an ongoing pair-matched, cluster-randomized clinical trial in which 15 community pairs were randomized 1:1 to test whether a combination HIV prevention intervention package is able to reduce cumulative 3-year HIV incidence on a population level, as compared with the enhanced national standard of care. Targeted communities were matched in pairs by size, health services, population age structure, and geographic location. The baseline household survey (BHS) enrolled a random, population-based sample of approximately 20% of 16–64-year-old residents between October 2013 and November 2015. The approach to selecting and enrolling the 20% random sample has been previously described. [8] Survey staff performed HIV testing and counseling (HTC), provided point-of-care (POC) CD4 testing, collected blood from PLHIV for HIV-1 RNA testing and viral genotyping, evaluated uptake of HTC, and assessed ART and male circumcision coverage. Only Botswana citizens were eligible to consent to study participation.

During the household visits, eligible residents were asked to sign a written consent form to participate; to complete an individual questionnaire with socio-demographic and HIV-related information, including history of their HIV testing, ART status, and patterns of sexual behavior; and to donate a blood sample for a rapid HIV test (if no documentation on a previous HIV-positive test was available). Newly diagnosed and ART-naïve PLHIV were offered POC CD4 testing, and were asked to donate about 10 mL of blood for HIV-1 RNA testing and viral genotyping (venous blood was collected by phlebotomy in households). PLHIV in the control communities were referred to the Botswana national ART program (free-of-charge treatment for all adults with CD4 ≤350 cells/μL or WHO Stage III/IV at the time of the initial survey in 2013–2015). PLHIV in the intervention communities were referred to local government clinic to receive a package of interventions according to the study protocol. Services for pregnant women were focused on identification of HIV-infected pregnant women and strengthening their linkage to care, initiation of treatment and retention on ART post-delivery. HIV re-testing during the third trimester was enhanced for pregnant women with a previous HIV-negative test. Participants in the baseline household survey received a BWP 20 (approximately US $2) cellular-telephone prepaid voucher.

HIV testing

Participants who self-reported HIV-positive status and provided documentation, such as, written test results, or ART prescription, were not retested for HIV. All other participants were offered counselling and testing for HIV. HIV testing was performed in the household using Botswana HIV Testing guidelines,[20] which include two rapid tests in parallel: KHB (KHB, Shanghai Kehua Bio-Engineering Co Ltd, China) and Unigold (Trinity Biotech Plc, Wicklow, Ireland). Only concordant results in both tests were considered valid. If results were discordant, confirmatory HIV testing was performed at a reference laboratory using EIA (Murex HIV 1.2.0 test, Murex Biotech Ltd, Dartford, Kent, England; or Biorad Genetic Systems™ HIV-1/HIV-2 PLUS O, BioRad, Redmond, WA; and/or Genetic Systems HIV-1 Western Blot, Bio-Rad Laboratories, Redmond, WA). The results of the EIA and/or Western Blot superseded the discordant or indeterminate results obtained in the field.

HIV-1 RNA testing

Venous blood was collected by phlebotomy in households during the baseline survey and was processed in a mobile clinic within 4 hours from sampling. HIV-1 RNA was quantified in all PLHIV enrolled. The completeness of HIV-1 RNA testing was 99.7%. HIV-1 RNA load was quantified by Abbott m2000sp/Abbott m2000rt (Abbott Laboratories, Wiesbaden, Germany) at the Botswana-Harvard HIV Reference Laboratory, which is accredited by the South African National Accreditation System (SANAS) for HIV-1 viral load testing (ISO 17025) and participates in Rush University's Virology Quality Assurance program. HIV-1 RNA load >400 copies/mL was considered detectable.

Statistical analysis

To assess coverage by the UNAIDS "90–90-90" targets[5] by age and gender, this analysis used existing data from the baseline household survey in Botswana[8]. Women and men 16–29 years old were defined as young adults, while individuals 30–64 years old were defined

as older adults. The numbers of study participants per group are presented in Supplementary Tables 1 and 2.

The first “90” is defined as documented previous knowledge of HIV-positive status. The second and the third 90’s were expressed with two denominators each. For the proportion of participants on ART, we used either all PLHIV, or only previously diagnosed HIV-positive participants (the second UNAIDS target[5]), as denominators. For the proportion of participants with undetectable HIV-1 RNA, ≤400 copies/mL, we used either all PLHIV, or only previously diagnosed HIV-positive participants receiving ART (the third UNAIDS target[5]), as denominators. The analyses that include all PLHIV in the denominator are adjunctive; they are technically not part of the UNAIDS 90–90-90 estimates.

Modified Poisson generalized estimating equations (with robust standard errors to account for within-community clustering) were used to estimate prevalence ratios (PR) and 95% confidence intervals (CI) for the following binary outcomes: HIV infection status, prior knowledge of HIV-positive status, documented receipt of antiretroviral therapy, and undetectable HIV-1 RNA load (≤400 copies/mL). Estimated HIV prevalence and 95% CI according to age (16–29 years vs. 30–64 years) and gender were calculated by fitting an intercept-only logistic regression model with generalized estimating equations (GEE) accounting for clustering by community. All analyses were conducted using SAS software version 9.4 (SAS Institute, Cary, NC) and R version 3.3.1.[21]

Results

We recently reported on Botswana’s achievement of high rates of HIV testing, treatment coverage, and virologic suppression overall.[8] However, in the current analysis by age, we found that the proportion of young PLHIV aware of their HIV infection (the first 90 in the UNAIDS targets[5]) was 66%, which is lower than among older adults (87%; Figure 1A; see Supplementary Table 1 for the number of participants in each group). The proportion of young adults diagnosed with HIV infection on ART (second 90) was 75%, which is lower than among older adults (89%; Figure 1A). The proportion of diagnosed young adults on ART with undetectable HIV-1 RNA (third 90) was 90%, which is also lower than among older adults (97%; Figure 1A). Among all PLHIV, the proportion of young adults on ART was 49% vs. 77% in older adults. Similarly, the proportion of virologically suppressed young adults was 44% among all PLHIV vs. 75% in older adults (Figure 1A).

Compared with older men, fewer young men knew about their positive HIV status (45% vs. 81%; 1st 90); they were less likely to be on ART (32% vs. 73%; Proportion of all men living with HIV who are on ART), and were less likely to have undetectable HIV-1 RNA (24% vs. 71%; Proportion of all men living with HIV who are virologically suppressed; Figure 1B). A similar pattern was found among young women (Figure 1C). As compared with older women, a smaller proportion of young women were aware of their HIV infection (70% vs. 89%); young women were less likely to be receiving ART (52% vs. 79% among all women living with HIV), and fewer of them had undetectable HIV-1 RNA (48% vs. 77% among all women living with HIV; Figure 1C).

Compared with older adults (30–64 years old), young HIV-infected adults were significantly less likely to have undetectable HIV-1 RNA (PR: 0.65; 95%CI: 0.59–0.70; p<0.0001), including both men (PR: 0.43; 95%CI: 0.34–0.56; p<0.0001) and women (PR: 0.67; 95%CI: 0.62–0.74; p<0.0001). Among a subset of PLHIV receiving ART, young adults also were less likely to have undetectable HIV-1 RNA load than older adults (PR: 0.93; 95%CI: 0.90–0.95; p=<0.0001).

Reducing the age cut-off from 30 years to 25 years resulted in similar proportions across all comparisons. Compared with older adults (25–64 years old), young HIV-infected adults were significantly less likely to have undetectable HIV-1 RNA (PR: 0.59; 95%CI: 0.52–0.68; p<0.0001), including both men (PR: 0.41; 95%CI: 0.26–0.65; p<0.0001) and women (PR: 0.62; 95%CI: 0.53–0.73; p<0.0001). Among a subset of PLHIV receiving ART, young adults also were less likely to have undetectable HIV-1 RNA load than older adults (PR: 0.87; 95%CI: 0.82–0.92; p=<0.0001).

HIV prevalence

We found a substantial gender gap in HIV prevalence across 30 villages in Botswana. Among men aged 16–64 years, 21% (95% CI: 19%–23%) were HIV-infected. Among women of the same age, 33% (95% CI: 30%–35%) were infected (P<0.0001).

Figure 2A demonstrates HIV prevalence by age group (see Supplementary Table 2 for the number of participants in each group). HIV-1 prevalence among women started to rise during teenage years, and gradually increased with age, exceeding 50% in women aged 35–49 years. HIV prevalence in men remained under 10% until age 30, and then gradually increased to levels close to 50% in men 40–49 years.

Knowledge of HIV-positive status

Knowledge of HIV-positive status by age group (Figure 2B) was similar to the HIV prevalence graph (Figure 2A). In women aged 16 to 24 years, awareness of positive HIV status was approximately 60% and gradually increased with age (Figure 2B). Knowledge of HIV-positive status was particularly low (below 50%) among men 20–29 years old. Young PLHIV were less likely to be aware of their positive HIV status compared with older adults (PR: 0.76; 95% CI: 0.71–0.80; P<0.0001).

PLHIV receiving ART

Stratified by age and gender, the distribution of individuals on ART revealed that younger age was associated with not receiving ART (Figures 3A and 3B; see Supplementary Table 2 for the number of participants in each group). Young HIV-infected men and women were significantly less likely to be on ART, compared with older adults (PR 0.63; 95% CI: 0.57–0.69; p<0.0001).

The proportions of HIV-infected individuals receiving ART gradually increased with age (Figure 3A). Among HIV-positive men over 50 years old, ≥84% were receiving ART. About 50% of young women living with HIV were receiving ART. In contrast, at least 76% of women over 35 years old were on ART.

Figure 3B is restricted to PLHIV who tested HIV-positive in the past and already knew about their positive HIV status at the time of household visit. Young PLHIV were significantly less likely to be on ART, compared with older adults (PR 0.84; 95% CI: 0.79–0.89; p<0.0001). A comparison of Figures 3A andFigures 3B highlights that once diagnosed and initiated ART, there are no gender differences in those who remain on ART.

PLHIV with HIV-1 RNA load ≤400 copies/mL

Younger age was associated with having detectable HIV-1 RNA (Figure 4A; see Supplementary Table 2 for the number of participants in each group). Among young men living with HIV, only 35% in the age group 16–19 years old, 26% in the age group 20–24 years old and 36% in the age group 25–29 years old had HIV-1 RNA ≤400 copies/mL. The proportion of men living with HIV having undetectable HIV-1 RNA load gradually increased with age. More than 84% of men over 50 years old had undetectable HIV-1 RNA. The proportion of virologically suppressed women gradually increased across young age groups and plateaued in the range of 81%–86% after 35 years of age (decreasing to 77% in the age group 60–64 years).

Young PLHIV were significantly less likely to have undetectable HIV-1 RNA load (PR: 0.57; 95% CI: 0.52–0.63; p<0.0001). Young men were less likely to have undetectable HIV-1 RNA compared to older men (PR: 0.37; 95% CI: 0.29–0.48; p<0.0001).

Figure 4B shows the proportion of PLHIV with undetectable HIV-1 RNA load among those who were previously diagnosed and receiving ART. Remarkably, all individuals in the oldest age groups had undetectable HIV-1 RNA load. Within the subset of previously diagnosed individuals receiving ART, young adults were less likely to have undetectable HIV-1 RNA load than older adults (PR: 0.93; 95%CI: 0.90–0.95; p<0.0001).

We found a subset of young HIV-infected adults (7 men and 29 women) who reported no use of ART, but had undetectable HIV-1 RNA, and therefore fell out of the care continuium scheme, as they were not included in the second 90. Accounting for these virologically suppressed individuals, effectively increased the proportion of young PLHIV with undetectable HIV-1 RNA to 51%.

Discussion

This study highlights that despite the overall success of the national ART program among the general population in Botswana,[8] coverage by the UNAIDS 90–90-90 targets remains significantly lower among young people aged 16–29 years living with HIV in Botswana. The lowest coverage was found among young men – only 24% of men living with HIV aged 16–29 years had undetectable HIV-1 RNA load. Overall, 55% of young PLHIV surveyed had detectable HIV-1 RNA and were at risk for transmitting the virus to others. Results from this analysis should inform public health policy in Botswana and assist in prioritizing HIV prevention interventions in the country.

Importantly, elevated prevalence of viremia in young adults does not appear to be primarily related to poorer ART adherence or retention. Young adults on ART were 7% less likely to

have achieved virologic suppression than older individuals, suggesting lower adherence or retention. However, the predominant contributor to lack of virologic suppression among young adults was lack of knowledge that they had HIV, and decreased use of ART among those aware that they had HIV infection. Some other factors could also contribute to the elevated levels of HIV-1 RNA in young adults.

The observation of increased viremia prevalence among young adults can likely be attributed in part to ART guidelines at the time of the survey. At the time of the survey, HIV-infected people with CD4 count below 350, or with other indications for treatment, were eligible for ART [22]. As HIV incidence peaks during the third decade of life, [23] young adults are more likely to have recently acquired HIV infection and consequently more likely to have a preserved CD4 cell count than older individuals. Therefore, young adults could be disproportionately affected by prior CD4-driven treatment ineligibility. It is likely that implementation and scale-up of the universal ART policy could improve engagement and access to ART among young PLHIV. However, lack of knowledge of HIV positive status in young adults remains a major barrier, particularly among men, even in the context of universal ART. A strong antenatal HIV testing program [24–29] has minimized undiagnosed HIV infection among young women in Botswana, but new programs effective with men are urgently needed.Targeted interventions, such as clinics focusing on young adults,[30] or dedicated programs aimed at young PLHIV,[31,32] could be critical components of national ART programs in southern Africa.

Additionally, reaching men is crucial for ultimate control of the HIV epidemic in southern Africa. To improve access to diagnosis and linkage to care, men-friendly environments including men peer campaigners and men-targeted HIV services are needed.[33] To target men, comprehensive interventions should be partnered with community mobilization strategies and include a broad range of services, such as community-based testing, workplace testing, self-testing, and men-only facilities or men-only hours.[34] In addition, community models of ART service delivery may be needed in communities where men do not access HIV care and treatment services in the facilities.

It is well known that PLHIV need to take ART in order to reach virologic suppression. However, virologic suppression among ART-naïve PLHIV (e.g., “elite”, or viremic controllers) has been reported previously [35–39]. Some studies reported a high frequency of undetectable HIV-1 RNA among ART-naïve people [40,41]. In this study 36 (7%; 95% CI 5–9%) of young HIV-infected adults reported no use of ARV but had undetectable HIV-1 RNA. It is possible that at least some of these individuals were taking ART. Accounting for young PLHIV who reported being ART-naive but who had undetectable HIV-1 RNA load effectively increased the overall proportion of virologically suppressed young adults to 51%. Although this estimate is not technically the 3rd 90 of the UNAIDS targets,[5] we believe it is an important component of the ‘big picture’ of the HIV epidemic among young adults.

The study has limitations. The study results could be influenced by CD4-driven initiation of ART at the time of the survey, as this approach could disproportionately affect young HIV-infected adults more likely to have shorter duration of HIV infection. Using overall knowledge of HIV-status, we analyzed prevalence of viral suppression. However, if a person

does not know they are HIV-infected or has not been referred for treatment, viral suppression is unlikely. While we highlight that detectable levels of HIV-1 RNA are more prevalent in young adults, merely testing those who are not aware of their HIV status may not be sufficient in achieving community viral suppression. The behaviors and beliefs of young adults in our cohort who were unaware of their HIV status may differ from those young adults aware of their HIV-positive status who pursued treatment. Therefore, programmatic public health strategies must evaluate and monitor the care cascade with a focus on identifying predictors of failure in order to best customize programming efforts for those least likely to achieve viral suppression and most likely to transmit virus.

The study demonstrates low coverage towards UNAIDS goals among young adults in Botswana, which is a health problem for young PLHIV and a challenge for overall HIV epidemic control. Young adults in Botswana may be contributing disproportionately to HIV-transmission networks. The study results suggest that targeted interventions should be tailored to improve HIV testing, linkage to care and treatment coverage among young adults, and young men, in particular. Research on the dynamics of HIV transmission networks among young adults could inform more effective prevention programs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of Interest/Sources of Funding:

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References:

1. UNAIDS. The Gap Report. http://www.unaids.org/en/resources/documents/2014/20140716_UNAIDS_gap_report 2014 Access date: 11/14/2017.
2. UNAIDS. Global Report. UNAIDS Report on the global AIDS epidemic 2013 http://files.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf 2013 Access date: 11/14/2017.
3. UNAIDS. GLOBAL AIDS RESPONSE PROGRESS REPORTING 2015 http://www.unaids.org/sites/default/files/media_asset/JC2702_GARPR2015guidelines_en.pdf 2015. Access date: 11/14/2017.
4. WHO. GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV. 9 2015 http://apps.who.int/iris/bitstream/handle/10665/186275/9789241509565_eng.pdf;jsessionid=3C03F2F9DC44E1EEA402FD8D2F38E096?sequence=1 Geneva, Switzerland: WHO;2015. Access date: 11/14/2017.

5. UNAIDS. UNAIDS. 90–90-90: an ambitious treatment target to help end the AIDS epidemic. http://www.unaids.org/sites/default/files/media_asset/90-90-90_en.pdf Geneva, Switzerland:: UNAIDS; 2014 Access date: 11/14/2017.
6. Statistics Botswana. BOTSWANA AIDS IMPACT SURVEY IV (BAIS IV), 2013. Summary Results. 2013.
7. Gaolathe T , Wirth K , Holme MP , Botswana is Close to Meeting UNAIDS 2020 Goals of 90–90-90 Coverage. Abstract 16–1447 Paper presented at: CROI2016; Boston, MA.
8. Gaolathe T , Wirth KE , Holme MP , Botswana's progress toward achieving the 2020 UNAIDS 90–90-90 antiretroviral therapy and virological suppression goals: a population-based survey. The lancet HIV. 2016;3(5):e221–230.27126489
9. Moyo S , Boleo C , Mohammed T , Cross-sectional HIV incidence at scale-up of ART in 24 rural communities in Botswana. Abstract 16–1126 Paper presented at: CROI2016; Boston, MA.
10. Moyo S , Mohammed T , Kotokwe K , Cross-sectional estimates of HIV incidence remain high in rural communities in Botswana in the era of successful scale-up of ART Abstract TUPDC0103. IAS; 2016.
11. Celum CL , Delany-Moretlwe S , McConnell M , Rethinking HIV prevention to prepare for oral PrEP implementation for young African women. J Int AIDS Soc. 2015;18(4 Suppl 3): 20227.26198350
12. Abdool Karim SS , Abdool Karim Q , Baxter C . Antibodies for HIV prevention in young women. Curr Opin HIV AIDS. 2015;10(3):183–189.25700207
13. Harrison A , Colvin CJ , Kuo C , Swartz A , Lurie M . Sustained High HIV Incidence in Young Women in Southern Africa: Social, Behavioral, and Structural Factors and Emerging Intervention Approaches. *Curr HIV/AIDS Rep*. 2015;12(2):207–215.25855338
14. UNAIDS. 90–90-90 On the right track towards the global target. *URL*https://reliefweb.int/sites/reliefweb.int/files/resources/90_90_90_Progress_ReportFINAL.pdf 2016 Access date: 01/10/2018.
15. Mujugira A , Celum C , Tappero JW , Ronald A , Mugo N , Baeten JM . Younger Age Predicts Failure to Achieve Viral Suppression and Virologic Rebound Among HIV-1-Infected Persons in Serodiscordant Partnerships. AIDS Res Hum Retroviruses. 2016;32(2):148–154.26670218
16. Mujugira A , Celum C , Thomas KK , Delay of antiretroviral therapy initiation is common in East African HIV-infected individuals in serodiscordant partnerships. J Acquir Immune Defic Syndr. 2014;66(4):436–442.24798765
17. Ryscavage P , Anderson EJ , Sutton SH , Reddy S , Taiwo B . Clinical outcomes of adolescents and young adults in adult HIV care. J Acquir Immune Defic Syndr. 2011;58(2):193–197.21826014
18. Rosen S , Maskew M , Fox MP , Rapid ART Initiation Reduces Loss Between HIV Testing and Treatment: The RapIT Trial. Abstract 1091. CROI 2015; 2015.
19. Plazy M , Dray-Spira R , Orne-Gliemann J , Dabis F , Newell ML . Continuum in HIV care from entry to ART initiation in rural KwaZulu-Natal, South Africa. Tropical medicine & international health : TM & IH. 2014;19(6):680–689.24654990
20. Botswana MoH . National Guidelines. HIV Testing and Counseling. https://aidsfree.usaid.gov/sites/default/files/hts_policy_botswana.pdf 2009.
21. R: A language and environment for statistical computing. *URL*https://www.R-project.org/ [computer program]. R Foundation for Statistical Computing, Vienna, Austria ; 2016.
22. Ministry of Health Botswana. Botswana National HIV/AIDS Treatment Guidelines: http://www.med.upenn.edu/botswana/user_documents/BotsNatHIV-AIDSTreatGuideWEB22-05-2012.pdf. In:2012.
23. Mossong J , Grapsa E , Tanser F , Barnighausen T , Newell ML . Modelling HIV incidence and survival from age-specific seroprevalence after antiretroviral treatment scale-up in rural South Africa. AIDS. 2013;27(15):2471–2479.23842131
24. Wynn A , Ramogola-Masire D , Gaolebale P , Acceptability and Feasibility of Sexually Transmitted Infection Testing and Treatment among Pregnant Women in Gaborone, Botswana, 2015. BioMed research international. 2016;2016:1251238.27119076
25. Offorjebe OA , Wynn A , Moshashane N , Partner notification and treatment for sexually transmitted infections among pregnant women in Gaborone, Botswana. Int J STD AIDS. 2017:956462417692455.

26. Dryden-Peterson S , Bennett K , Hughes MD , An augmented SMS intervention to improve access to antenatal CD4 testing and ART initiation in HIV-infected pregnant women: a cluster randomized trial. PLoS One. 2015;10(2):e0117181.25693050
27. Creek T , Ntumy R , Mazhani L , Factors associated with low early uptake of a national program to prevent mother to child transmission of HIV (PMTCT): results of a survey of mothers and providers, Botswana, 2003. AIDS Behav. 2009;13(2):356–364.17985228
28. Lockman S , Creek T . Acute maternal HIV infection during pregnancy and breast-feeding: substantial risk to infants. J Infect Dis. 2009;200(5):667–669.19627246
29. Creek TL , Ntumy R , Seipone K , Successful introduction of routine opt-out HIV testing in antenatal care in Botswana. J Acquir Immune Defic Syndr. 2007;45(1):102–107.17460473
30. Zanoni B , Cairns C , Haberer J . High retention and viral suppression rates in a dedicated adolescent-friendly HIV clinic in South Africa. Abstract TUPEB124 AIDS 2016 – 21st International AIDS Conference; 2016; Durban, South Africa.
31. Griffith D , Keruly J , Lee L , Nolan K , Agwu A . Impact of a youth-targeted HIV clinic integrated within a large urban adult clinic. Abstract TUPEB125 AIDS 2016 – 21st International AIDS Conference; 2016; Durban, South Africa.
32. Mark D , Ngombe A , Burford G , Project REACH: a facility-based peer support model across 20 facilities in five sub-Saharan African countries. Abstract TUPEB126 AIDS 2016 – 21st International AIDS Conference; 2016; Durban, South Africa.
33. Matatiyo B , Likongwe D . A study of factors affecting male involvement in HIV-related services in Malawi. Abstract TUPED348 AIDS 2016 – 21st International AIDS Conference; 2016; Durban, South Africa.
34. Pascoe L , Peacock D . Where are the men? Addressing the global blind spot around heterosexual men in the HIV pandemic. Abstract TUPED425 AIDS 2016 – 21st International AIDS Conference; 2016; Durban, South Africa.
35. Crowell TA , Hatano H . Clinical outcomes and antiretroviral therapy in ‘elite’ controllers: a review of the literature. Journal of virus eradication. 2015;1(2):72–77.27123315
36. Walker BD . Elite control of HIV Infection: implications for vaccines and treatment. Top HIV Med. 2007;15(4):134–136.17720999
37. Eyzaguirre LM , Charurat M , Redfield RR , Blattner WA , Carr JK , Sajadi MM . Elevated hypermutation levels in HIV-1 natural viral suppressors. Virology. 2013;443(2):306–312.23791226
38. Miura T , Brockman MA , Brumme CJ , Genetic characterization of human immunodeficiency virus type 1 in elite controllers: lack of gross genetic defects or common amino acid changes. J Virol. 2008;82(17):8422–8430.18562530
39. Miura T , Brumme ZL , Brockman MA , Impaired replication capacity of acute/early viruses in persons who become HIV controllers. J Virol. 2010;84(15):7581–7591.20504921
40. Kahle EM , Kashuba A , Baeten JM , Unreported antiretroviral use by HIV-1-infected participants enrolling in a prospective research study. J Acquir Immune Defic Syndr. 2014;65(2):e90–94.24442233
41. de Oliveira T , Kharsany AB , Graf T , Transmission networks and risk of HIV infection in KwaZulu-Natal, South Africa: a community-wide phylogenetic study. The lancet HIV. 2017;4(1):e41–e50.27914874

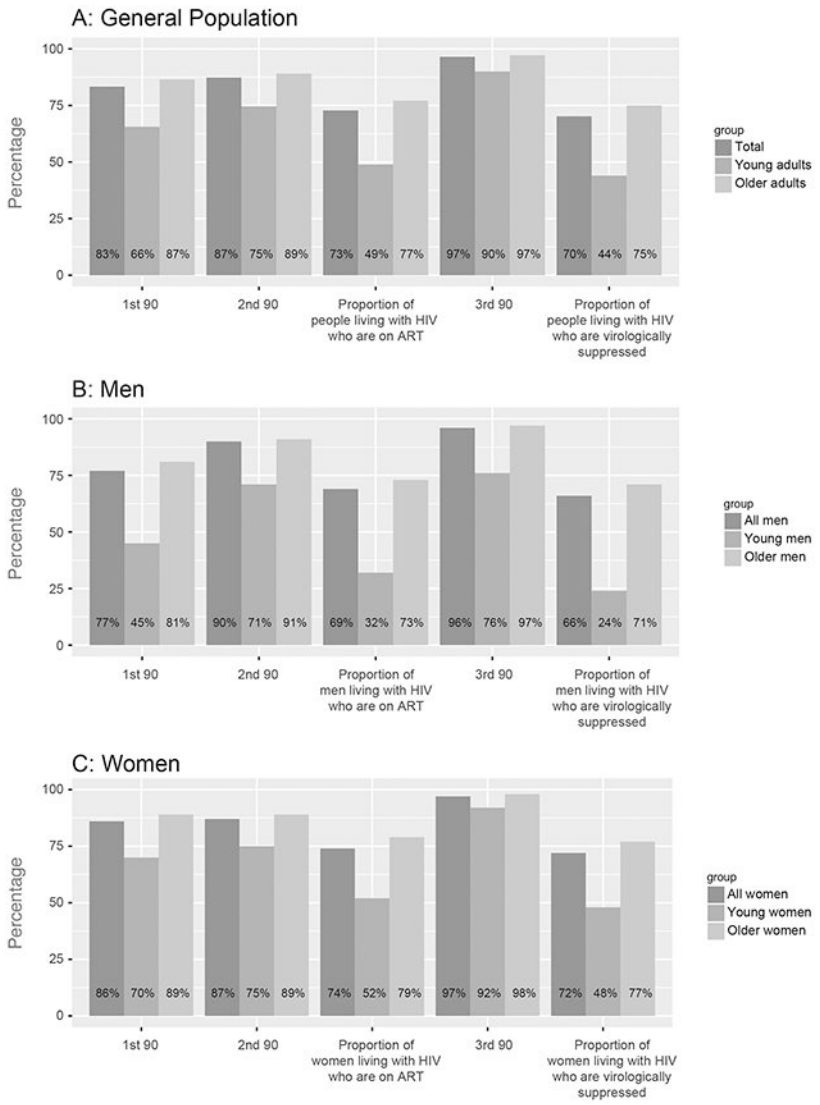

Figure 1.

Proportions of PLHIV meeting the UNAIDS 90–90-90 targets, on ART, and virologically suppressed, overall by age and by gender in Botswana. Study participants were sampled in 20% of households in 30 Botswana communities. See Supplementary Table 1 for the number of participants in each group. **A:** General population (total, both genders) is shown as the darkest gray bar. Young adults (16–29 years old) are shown as medium tone graybar. Older adults (30–64 years old) are presented as the lightest graybar. **B:** Men. The darkest gray bars indicate men of any age (16–64 years old). Medium tone gray bars show young men (16–29 years old). The lightest gray bars delineate older men (30–64 years old). **C:** Women. The darkest gray bars indicate women of any age (16–64 years old). Medium tone gray bars show young women (16–29 years old). The lightest gray bars delineate older women (30–64 years old).

Figure 2.

A: HIV prevalence among adults tested in 30 Botswana communities stratified by age and gender. **B:** Proportion of individuals aware of their positive HIV status stratified by age and gender. Women are represented by circles; men are represented by triangles. Dashed line in **B** denotes the first 90 in the UNAIDS targets.[5] See Supplementary Table 2 for the number of participants in each group.

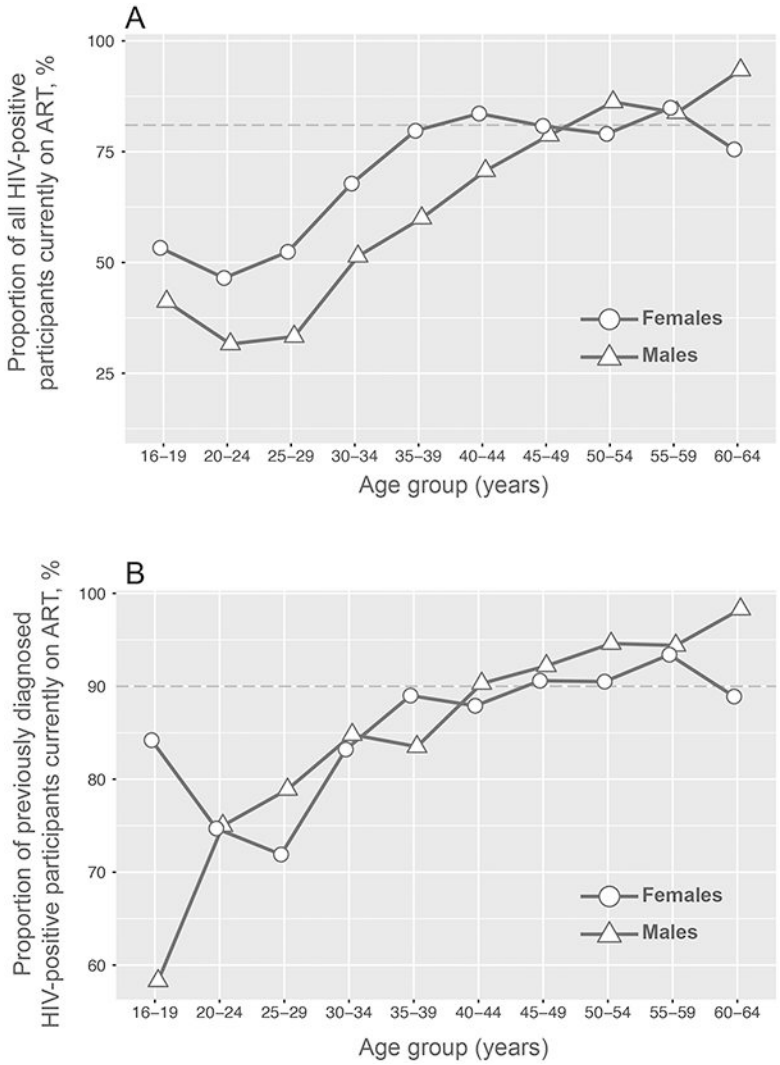

Figure 3.

A: Proportion of all PLHIV receiving ART in 30 Botswana communities, stratified by age and gender. Dashed line denotes the 81% target (0.90 × 0.90) among PLHIV. **B:** Proportion of previously diagnosed participants living with HIV currently on ART. Women are represented by circles; men are represented by triangles. Dashed line denotes the second 90 in the UNAIDS targets.[5] See Supplementary Table 2 for the number of participants in each group.

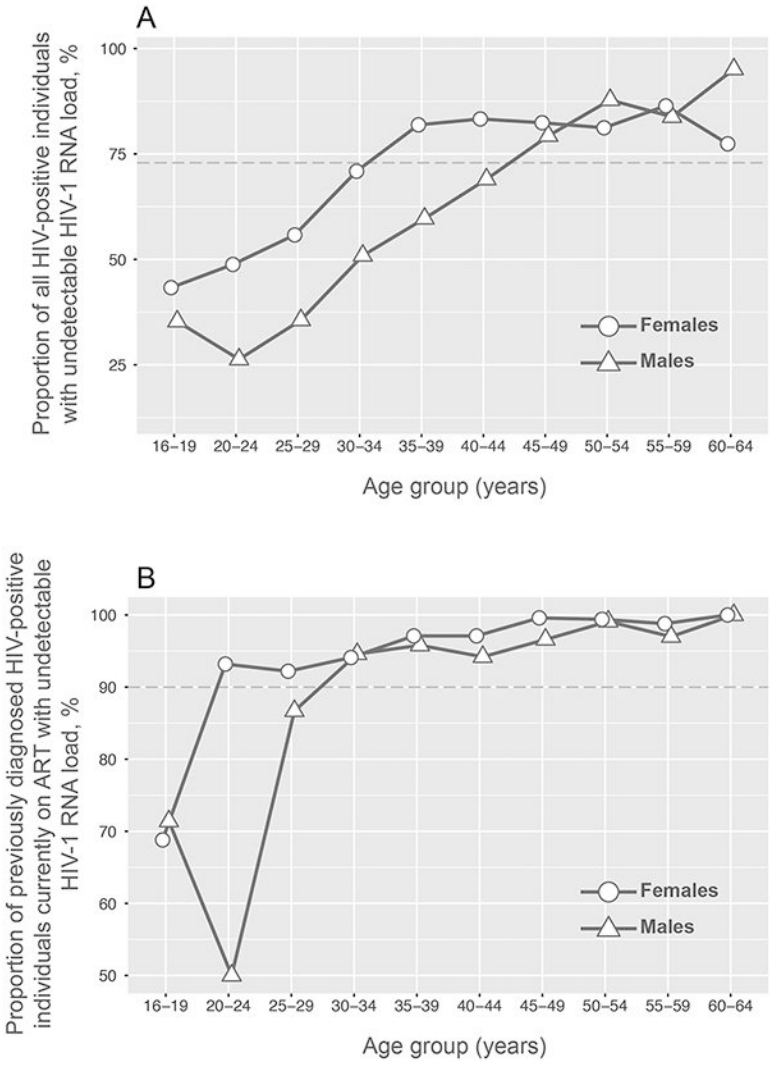

Figure 4.

A: Proportion of all PLHIV with undetectable HIV-1 RNA load (≤400 copies/mL) in 30 Botswana communities, stratified by age and gender. Dashed line denotes the 73% target (0.90 × 0.90 × 0.90) among PLHIV. **B:** Proportion of PLHIV with undetectable HIV-1 RNA load among participants who were diagnosed previously and were receiving ART at the time of household visit. Women are represented by circles; men are represented by triangles. Dashed line denotes the third 90 in the UNAIDS targets.[5] See Supplementary Table 2 for the number of participants in each group.