



Published in final edited form as:

J Acquir Immune Defic Syndr. 2016 March 1; 71(3): 338–344. doi:10.1097/QAI.0000000000000846.

Changing antiretroviral eligibility criteria: impact on the number and proportion of adults requiring treatment in Swaziland

Naomi N Bock, MD, MS¹, Ruth C Emerson, MPH², Jason B Reed, MD, MPH¹, Rejoice Nkambule, MPH³, Deborah J Donnell, PhD², George T Bicego, PhD¹, Velephi Okello, MBChB, MPH³, Neena M Philip, MPH⁴, Peter D Ehrenkrantz, MD, MPH¹, Yen T Duong, PhD¹, Janet S Moore, PhD¹, and Jessica E Justman, MD⁴

¹Centers for Disease Control and Prevention, Atlanta, USA and Mbabane, Swaziland ²Statistical Center for HIV/AIDS Research and Prevention and the Vaccine and Infectious Disease Institute, Fred Hutchinson Cancer Research Center, Seattle, USA ³Ministry of Health - Swaziland, Mbabane, Swaziland ⁴ICAP-Columbia, Mailman School of Public Health, Columbia University, New York, USA

Abstract

Objective—Early initiation of antiretroviral treatment (ART) at CD4+ cell count ≥ 500 cells/ μ L reduces morbidity and mortality in HIV-infected adults. We determined the proportion of HIV-infected people with high viral load (VL) for whom transmission prevention would be an additional benefit of early treatment.

Design—A randomly selected sub-set of a nationally representative sample of HIV-infected adults in Swaziland in 2012.

Methods—Eight to twelve months after a national survey to determine adult HIV prevalence, 1,067 of 5,802 individuals identified as HIV-infected were asked to participate in a follow-up cross-sectional assessment. CD4+ cell enumeration, VL measurements and ART status were obtained to estimate the proportion of currently untreated adults and of the entire HIV-infected population with high VL (≥ 1000 copies/mL) whose treatment under a test-and-treat or VL threshold eligibility strategy would reduce HIV transmission. .

Results—Of the 927 (87% of 1,067) participants enrolled, 466 (50%) reported no ART use. Among them, 424 (91%) had VL ≥ 1000 copies/mL; of these, 148 (35%) were eligible for ART at the then existing CD4+ count threshold of <350 cells/ μ L; an additional 107 (25%) were eligible

Corresponding author and requests for reprints: Naomi N Bock, MD, HIV Prevention Branch, Division of Global HIV/AIDS, Centers for Disease Control and Prevention, 1600 Clifton Road Mail Stop E-04, Atlanta, GA 30033, neb2@cdc.gov, Phone: 404-735-8581, Fax: 404-639-8114.

Conflicts of interest

The authors declare no conflicts of interest.

Disclaimer: The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention.

Previously presented in part as: Naomi Bock, Ruth Emerson, Azih Charles Ikechi, Deborah Donnell, George Bicego, Velephi Okello, Peter Ehrenkrantz, Neena Philip, Rejoice Nkambule, Yen Duong, Jessica Justman. Potential Impact of Viral Load on ART Eligibility Criteria in Swaziland. Abstract 2258. Conference on Retroviruses and Opportunistic Infections, Boston, MA USA February 2014.

with expanded CD4+ criterion of <500 cells/ μ ; and 169 (40%) remained ART-ineligible. Thus 36% of the 466 currently untreated and 18% of the total 927 had high VL yet remained ART-ineligible under a CD4+ criterion of <500 cells/ μ L.

Conclusions—A test-and-treat or VL threshold for treatment eligibility is necessary to maximize the HIV transmission prevention benefits of ART.

Keywords

HIV; antiretroviral therapy; HIV treatment eligibility; CD4+ count; viral load; Swaziland

Introduction

Well into the fourth decade of the global human immunodeficiency virus (HIV) epidemic, an estimated 35 million people are living with HIV. Sub-Saharan Africa accounts for approximately 24.7 million prevalent infections as well as more than two-thirds of new annual HIV infections worldwide (1). Though the numbers remain daunting, the high prevalence partially reflects reduced morbidity and mortality through increasing access to antiretroviral therapy (ART). Recent studies have documented that morbidity and mortality can be further reduced by early initiation of ART in asymptomatic persons with high CD4 counts (2,3). In response, the World Health Organization has announced that new treatment guidelines recommending treatment for all regardless of CD4+ cell count will be forthcoming (4).

In addition to the benefits to individual health, in 2011, a randomized controlled trial found 96% reduction in HIV transmission among discordant heterosexual couples where the HIV-infected partner was started on ART at CD4+ count between 350-550 cells/ μ L compared to deferral of ART until CD4+ cell count fell to below 250cells/ μ L, establishing the efficacy of treatment as prevention (5). Possibilities of and barriers to expanding HIV treatment for prevention, either by treating those with high VL despite high CD4+ cell counts, or by treating all HIV-infected individuals irrespective of CD4+ cell count and VL, have been widely discussed (6-8).

A major barrier to expanding ART coverage is the complex continuum of HIV care, which Gardner et al refer to as the “spectrum of engagement in HIV care” (9). Each of six defined steps along the continuum—HIV diagnosis via testing, linkage to care, retention in care, starting appropriate ART, adherence with ART, and achieving viral suppression—have been demonstrated as programmatic vulnerabilities, where individual patients can and do disengage, ultimately resulting in morbidity and mortality as well as uncontrolled VL and increased transmission risk. Initial cost for treatment expansion, despite the long term cost-savings, is another barrier (10).

Given the risks of overburdening already stretched infrastructures, as well as the additional costs, it is helpful to quantify the degree to which a national ART program would have to expand if it were to include either all HIV-infected adults, or those with high VL who are at the greatest risk of transmitting HIV but not eligible for treatment based on CD4+ cell count. In this study, we use data from the nationally representative Swaziland HIV Incidence

Measurement Survey (SHIMS) to examine the potential prevention impact of current treatment guidelines in Swaziland, a country with one of the highest HIV incidence and prevalence rates in the world (11,12).

Methods

Sampling scheme and eligibility criteria

A detailed description of the SHIMS sampling scheme has been previously described (19). Briefly, a two-stage cluster sample design selected census or enumeration areas (EA) and then households within each EA. Adult household members who agreed to participate underwent HIV testing and those who were HIV-negative were offered enrolment in a sero-incidence cohort. Those who were HIV-infected were counselled about the benefits of HIV care and treatment services, provided a referral to facilitate their linkage to those services, and asked for consent to be contacted for future research. A subset of participants who were identified as HIV-infected at baseline and who gave consent to be contacted for future research was randomly selected to participate in a follow-up household visit eight to twelve months after their initial visit.

Study procedures

The selected HIV-infected individuals who were located underwent verification of their participation in the earlier survey and were asked to participate in a follow-up cross-sectional assessment. Those who agreed provided written informed consent and then underwent an interviewer-administered survey regarding medical care including current ART use. When available, participants' medical booklet records of ART initiation ascertained ART use at baseline and follow-up. When medical booklets were unavailable, this ART information was based on self-report. Counselling about the benefits of HIV care and treatment services and information on how to link to them was provided to all participants. Approximately 10 mL of blood was obtained by venipuncture.

Laboratory methods

Whole blood samples were transported in ethylenediaminetetraacetic acid tubes (Greiner Bio One, Frickenhausen, Germany) in cooler boxes to the National Reference Laboratory in Mbabane within 24 hours of collection.

CD4⁺ enumeration was determined using the Becton Dickinson FACSCalibur automated flow cytometry system according to the manufacturer's instructions. Quality assurance testing was performed on 5% of the whole blood samples. VL quantification was performed using undiluted plasma on the COBAS® AmpliPrep/COBAS® TaqMan® System platform and the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test (Roche Diagnostics, Indianapolis, United States) version 2.0 assay according to the manufacturer's instructions; the limit of detection for the assay was of 20 copies/mL.

Those participants who agreed to receive their CD4⁺ count results received a paper copy of the results within 28 days. The study staff counselled about the benefits of HIV care services and provided information to help those not in care link to these services. They encouraged

participants to share the CD4+ test results with their health care provider, noting it would assist their provider in making decisions about starting treatment. They also counselled participants about the importance of HIV testing of partners.

Data analyses

CD4+ cell enumeration, VL measurements and ART treatment status of participants were used to determine the additional number and proportion of untreated adults and of the entire estimated HIV-infected adult population who would be eligible for ART when the then prevailing treatment eligibility criterion of CD4+ cell count < 350 cells/ μ L was expanded to include those between 350 and 499 cells/ μ L. We also calculated the number and proportion of those with high VL (HIV-1 RNA VL >1000 copies/mL) who remained ART-ineligible with the expanded criterion of CD4+ cell count < 500 cells/ μ L (13). Finally we estimated the remaining number and proportion who would be included in a test-and-treat strategy. By estimating the size of the adult HIV-infected population in Swaziland, we converted the proportions to absolute numbers of persons potentially added to treatment programs. We also assessed demographic and health seeking behaviour variables associated with being on ART (for those eligible) and having suppressed VL (for those on ART).

Statistical methods

Survey weights were applied to the data to account for differential probability of selection by the initial cluster sampling procedure as well as non-response rates across sex, age, and geography during both the initial sampling procedure and the follow-up assessment of selected HIV-infected individuals. Weighted estimates were scaled to the size of the SHIMS subset of HIV-infected individuals who underwent the CD4+ assessment. Throughout, reports of number and proportions of participants are based on these scaled weighted estimates, and thus do not always add up to 100%. When available, participants' medical booklet records of ART initiation ascertained ART use at baseline and follow-up. Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated to describe associations from logistic regression models, using binary outcomes for the two dependent variables of interest at follow-up: 1) ART use (yes/no); and, 2) viral suppression (yes/no), defined as <1000 copies/mL. Analyses were performed using Stata (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP).

Size estimation of HIV-infected adult population

The total population of Swaziland is projected to be 1.268 million, with near equal proportion male and female (49.4% versus 50.6%) (14). From the Swaziland 2007 Demographic and Health Survey, the proportion of adult men and women (defined as aged 15 years and older) was 53.8% and 58.4%, respectively, thus 711,348 persons (15). Applying the SHIMS HIV prevalence estimate of 24% of adult males and 39% of adult females (12), yields 226,262 adults estimated to be living with HIV.

Ethical considerations

All study participants provided written informed consent prior to the collection of data and blood samples. Ethical approval was obtained from the Swaziland Scientific and Ethics Committee, Columbia University Institutional Review Board (IRB) and United States Centers for Disease Control and Prevention IRB before initiation of field work.

Results

Participants

Of 5,802 participants identified as HIV-infected at SHIMS baseline eight to twelve months earlier, 1067 (18%) were randomly selected for this follow-up study; 138 of the 1067 (13%) either could not be located or refused to participate and three (0.3%) did not have CD4+ enumeration results available. From February through May 2012, 927 participants (87% of those selected for participation) were enrolled, interviewed, and underwent CD4+ cell enumeration and VL assessment. Of these 927, 65% were women, 69% lived in rural areas, 57% reported being married or partner co-habitation, 50% were on ART, and 69% were aware of their HIV-infected status at the time of the baseline survey eight to twelve months earlier (Table 1).

Distribution of CD4+ cell count and ART eligibility among 466 participants not on ART

Eight to twelve months after the SHIMS baseline survey, about one-third (158 of 466, or 34%) had CD4+ count <350 cells/ μ L and were eligible for ART by national CD4 criteria at the time of the survey; an additional 110 (24%) had CD4+ count between 350 and 499 cells/ μ L and were eligible for ART by new initiation criteria adopted by Swaziland in the summer of 2014 (Table 2). Thus, expanding eligibility criteria from CD4+ count <350 to <500 cells/ μ L added 12% of the adult HIV-infected population (110 of the sampled 927) to those eligible. With the estimate of 226,262 HIV-infected adults nationally, 26,849 more adults became treatment eligible with the higher CD4+ cell count criteria. By 2013 WHO guidelines, 43% of those not on ART (198 of 466) remain ineligible due to a CD4+ cell count of \leq 500 cells/ μ L.

Distribution of VL, CD4+ cell count, and ART eligibility

In terms of VL, 91% (424 of 466) participants not on ART had a VL \leq 1000 copies/mL (Table 2). Among these 40% (169 of 424), had a CD4+ count \leq 500 cells/ μ L and thus would remain ART-ineligible with a CD4+ threshold of <500 cells/ μ L despite having a high VL eight to twelve months after documented HIV-infected status. These 169 individuals represent 18% of the total 927 HIV-positive participants in the population. With the estimated 226,262 HIV-infected adults nationally, 40,727 more adults would become treatment eligible if a VL threshold of \leq 1000 copies/mL were added to CD4+ count criteria of < 500 cells/ μ L. A test-and-treat approach would add the remaining 3% (28 of 927) of persons, those with CD4+ count \leq 500 cells/ μ L and VL < 1000 copies/mL, or 6,788 adults.

Predictors of being on ART at follow-up eight to twelve months after SHIMS baseline survey among those eligible by CD4+ threshold of <350 cells/ μ L at follow-up

Approximately one-fourth (158 of 619, or 26%) of participants eligible for ART at time of follow-up based on CD4+ count threshold of <350 cells/ μ L reported not being on treatment at the time of the follow-up survey. In multivariate analysis participants on treatment, compared with those eligible but not on treatment, were more likely to be older than 44 years of age (adjusted odds ratio [aOR] 15.28, 95% confidence interval [CI] 3.77, 62.01), and to have already been aware of their HIV-infection prior to the SHIMS baseline survey (aOR 10.62, CI 6.53, 17.25) (Table 3). Sex, urban versus rural residence, marital status, education level, region, and employment status were not associated with ART treatment (data not shown). At follow-up almost half (72/158 or 46%) of those eligible but not on treatment reported never having visited a health facility for HIV-related medical care since diagnosis.

Predictors of viral suppression at follow-up eight to twelve months after SHIMS baseline survey among those reporting ART use at follow-up

Among 461 participants who reported being on ART, VL was <1000 copies/mL in 394 (86%) (Table 4). In multivariate analysis viral suppression among those who reported being on ART was only associated with being older than 24 years of age, but not with having already been aware of their HIV-infection or on ART at the time of the SHIMS baseline survey, nor with other demographic variables, including sex. Those who reported not filling their ART prescription in the previous three months were significantly less likely to have suppressed VL (aOR 0.20, CI 0.04, 0.87).

Discussion

In Swaziland, the country with the most severe national HIV epidemic globally, our analysis determined that eight to twelve months after SHIMS baseline survey had diagnosed or re-confirmed HIV-infected status, almost all participants not on ART had a VL \geq 1000 copies/mL, and 40% of these were ART-ineligible by the 2013 WHO treatment eligibility guidelines (ie, CD4 <500/ μ L). This population of ART-ineligible adults due to high CD4 count represents 18% of the HIV-infected population, or an estimated 40,727 persons with a VL high enough to be a risk factor for HIV transmission.

Swaziland has implemented a strong HIV treatment program, as evidenced by our study finding that 74% of those participants who were ART-eligible based on the prevailing CD4+ count threshold of <350 cells/ μ L reported using ART, and 85% of those who reported using ART had viral suppression. The proportion of those eligible who had started treatment had increased by 22% during the time period between SHIMS baseline and follow-up surveys, and 73% of those starting ART use after SHIMS baseline had achieved viral suppression, further demonstrating the feasibility of effective treatment programs in a low resource setting. Despite these successes, the annual HIV incidence remains high (16), which may be explained in part by the gap in transmission prevention when ART initiation guidelines are based solely on CD4+ cell count.

All participants in the Swaziland analysis had documented HIV-infection eight to twelve months earlier, at SHIMS baseline survey, and most, 71%, reported having already been aware of their infection at that time. Thus, the high VL levels documented in this survey are unlikely to be due to recent infection (17). Our data suggest that for HIV treatment to contribute to prevention in this high incidence setting, eligibility criteria for initiation on ART need to be expanded beyond CD4+ cell count cut-off to include a VL threshold or a test-and-treat approach. Only 3% of the adult HIV-infected population would not be eligible with the combined criteria of CD4 count <500 cells/ μ L and/or VL 1000 copies/mL, and some would be eligible by other criteria already adopted by Swaziland, including pregnancy, tuberculosis, or being in a sero-discordant relationship. Thus test and treat seems the most straightforward strategy, avoiding VL measurement as a potential default point during enrolment in treatment, and in line with recent data from the TEMPRANO and START trials demonstrating individual clinical benefits from starting ART at CD4+ counts higher than 500 cells/ μ L (2,3). Tanser et al have demonstrated in routine programmatic conditions at the community level that increased ART coverage results in population-level reductions in risk (18). In Swaziland it is clear that coverage must extend beyond those eligible based on a CD4+ count threshold.

Challenges with starting people on ART at higher CD4+ counts, when they are generally healthy, have been poor adherence with associated persistent viremia, and outright refusal to take ART (19-22). However, Jain et al have recently demonstrated high rates of adherence, retention in care, viral suppression and safety when treating patients with high CD4+ counts in Uganda (median 569 cells/ μ L (interquartile range 451-716) (23). They pointed out that patient attitudes may be changing as they learn more about clinical benefits as well as reduced transmission to others when starting ART earlier. Just as knowledge of HIV-infected status has been documented to reduce HIV risk-related behaviour after HIV testing (24,25), it is possible that knowledge of high VL status, and its associated risk for HIV transmission, may change other behaviours like retention in care and adherence with treatment.

To our knowledge this study is the first to assess nationally representative population data to estimate the proportion and number of the HIV-infected adult population with high VL that would remain ineligible for ART with expanding CD4+ count criteria. However, our study has limitations. The association between VL and CD4+ count in untreated adults in a population will vary depending upon the incidence rate in recent years, the age of the epidemic, the predominant viral sub-type, and the viral set point in the population (26,27). Thus, the results from Swaziland, which has a mature generalized epidemic with one of the highest HIV incidence rates in the world, may not apply to all settings. Additionally, we were unable to verify ART treatment status beyond self-report for one-third of the participants, as they did not have their ART clinic record available at the time of interview, and we considered all those reporting being on ART as having been “eligible” per prevailing eligibility requirements at the time of their ART initiation, but did not have clinical verification of their eligibility status at that time. We used data from census and surveys conducted by different methods and with different age ranges for adults to arrive at an estimate of the size of the HIV-infected adult population, then used those estimates to calculate estimated numbers of adults who would be treatment-eligible from the proportions

determined in our sub-study. Finally, the rates of treatment coverage and viral suppression were measured eight to twelve months after home-based HIV testing or re-testing during SHIMS baseline survey and may not reflect the general HIV-infected population in the absence of home-based testing.

Access to VL measurement has been limited in resource-constrained settings because of the cost, and point-of-care quantification technologies, though in development, are not imminent (28,29). Determining eligibility based on VL would require routine VL assessment, which would increase program costs as well as add an additional step along the treatment cascade where patients could be lost to follow-up. Implementing a test-and-treat approach would not require VL measurements for eligibility determination, and in Swaziland would result in an additional 21% of the HIV-infected adult population added to the treatment rolls, the majority of whom, 86%, have VL high enough to be a risk factor for HIV transmission. Treatment for them would provide both an individual and public health benefit. .

Acknowledgments

Source of funding: This publication was supported by Cooperative Agreement #5U2GPS002005 from the U.S. Centers for Disease Control and Prevention.

References

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). The Gap Report. 2014. http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Gap_report_en.pdf. Last accessed 1.14.5
2. The INSIGHT START Study Group. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med*. 2015 DOI: 10.1056/NEJMoa1506816. Epub 2015 Jul 20.
3. The TEMPRANO ANRS 12136 Study Group. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. *N Engl J Med*. 2015 DOI: 10.1056/NEJMoa1507198. Epub 2015 Jul 20.
4. Doherty, M. New directions in the 2015 WHO Consolidated ARV Guidelines; Eighth International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015); Vancouver, Canada. 2015. presentation SUSA0608
5. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. Aug 11; 2011 365(6):493–505. doi: 10.1056/NEJMoa1105243. Epub 2011 Jul 18. [PubMed: 21767103]
6. Proceedings from the 3rd International HIV Treatment as Prevention Workshop. 2013. <http://www.treatmentaspreventionworkshop.org/conference/2013-treatment-as-prevention-workshop>. Last accessed 4.14.14
7. Wilson DP. HIV treatment as prevention: Natural experiments highlight limits of antiretroviral treatment as HIV prevention. *PloS Med*. Jul.2012 9(7):e1001231. [PubMed: 22807656]
8. Novitsky V, Essex M. Using HIV viral load to guide treatment-for-prevention interventions. *Curr Opin HIV AIDS*. 2012; 7:117–124. [PubMed: 22258501]
9. Gardner EM, McLees MP, Steiner JF, et al. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis*. Mar 15; 2011 52(6):793–8001. [PubMed: 21367734]
10. Granich R, Muraguri N, Doyen A, et al. Achieving universal access for human immunodeficiency virus and tuberculosis: potential prevention impact of an integrated multi-disease prevention campaign in Kenya. *AIDS Res Treat*. 2012; 2012:412643. doi: 10.1155/2012/412643. Epub 2012 May 7. [PubMed: 22611485]
11. Joint United Nations Programme on HIV/AIDS (UNAIDS). Global report: UNAIDS report on the global AIDS epidemic 2013. “UNAIDS/JC2502/1E”, revised and reissued, November 2013. <http://>

www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf. Last accessed 4.14.14

12. Bicego GT, Nkambule R, Peterson I, et al. Recent patterns in population-based HIV prevalence in Swaziland. *PLoS One*. Oct 15.2013 8(10):e77101. doi: 10.1371/journal.pone.0077101. eCollection 2013. [PubMed: 24143205]
13. Lingappa JR, Hughes JP, Wang RS, et al. Estimating the impact of plasma HIV-1 RNA reductions on heterosexual HIV-1 transmission risk. *PLoS One*. Sep 13.2010 5(9):e12598. doi: 10.1371/journal.pone.0012598. [PubMed: 20856886]
14. World Population Review. <http://worldpopulationreview.com/countries/swaziland-population/>. Last accessed 12.22.14
15. Central Statistical Office (CSO) [Swaziland], and Macro International Inc. Swaziland Demographic and Health Survey 2006-07. Central Statistical Office and Macro International Inc; Mbabane, Swaziland: 2008.
16. Reed, JB.; Justman, J.; Bicego, G., et al. Estimating national HIV incidence from directly observed seroconversions in the Swaziland HIV Incidence Measurement Survey (SHIMS) longitudinal cohort; Presented at XIX International AIDS Conference; Washington DC. Jul. 2012
17. Cohen MS, Shaw GM, McMichael AJ, et al. Acute HIV-1 infection. *NEJM*. 2011; 364:1943–54. [PubMed: 21591946]
18. Tanser F, Barnighausen T, Grapsa E, et al. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science*. Feb 22.2013 6122 339:966–71. doi: 10.1126/science.1228160.
19. Adakun S, Siedner M, Muzoora C, et al. Higher baseline CD4 cell count predicts treatment interruptions and persistent viremia in patients initiating ARVs in rural Uganda. *J Acquir Immune Defic Syndr*. 2013; 62:317–321. [PubMed: 23242160]
20. Katz I, Essien T, Marinda E, et al. Antiretroviral therapy refusal among newly diagnosed HIV-infected adults. *AIDS*. 2011; 25:2177–2181. [PubMed: 21832935]
21. Geng EH, Bwana MB, Muyindike W, et al. Failure to initiate antiretroviral therapy, loss to follow-up and mortality among HIV-infected patients during the pre-ART period in Uganda. *J Acquir Immune Defic Syndr*. 2013; 63:e64–e71. [PubMed: 23429504]
22. Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. *PLoS Med*. 2011; 8:e1001056. [PubMed: 21811403]
23. Jain V, Byonanebye D, Amanyire G, et al. Successful antiretroviral therapy delivery and retention in care among asymptomatic individuals with high CD4+ T-cell counts above 350 cells/mL in rural Uganda. *AIDS*. 2014; 28:2241–2249. [PubMed: 25022596]
24. Fonner VA, Denison J, Kennedy CE, et al. Voluntary counseling and testing (VCT) for changing HIV-related risk behavior in developing countries. *Cochrane Database Syst Rev*. 2012; 9:CD001224. doi: 10.1002/14651858.CD001224. [PubMed: 22972050]
25. Rosenberg NE, Pettifor AE, De Bruyn G, et al. HIV testing and counseling leads to immediate consistent condom use among South African stable HIV-discordant couples. *JAIDS*. 2013; 62(2): 226–33. [PubMed: 23117500]
26. Santoro MM, Perno CF. HIV-1 genetic variability and clinical implications. *Microbiol*. 2013 published online 2013 June 17. doi:10.1155/2013/481314.
27. Mackelprang RD, Carrington M, Thomas KK, et al. Host genetic and viral determinants of HIV-1 RNA set-point among HIV-1 seroconverters from sub-Saharan Africa. *J Virol*. 2014; pii:JV101573–14.
28. Murtagh, M. Viral Load: Current Technologies and the Pipeline, including Point-of-Care Assays. Consultation on Viral Load Monitoring for African HIV Treatment Programmes. Cape Town, South Africa 18 – 20 April 2013. <http://www.aslm.org/?wpdmdl=95>. Last accessed 11.2.2014
29. Sollis K, Smit P, Fiscus S, et al. Systematic Review of the Performance of HIV Viral Load Technologies on Plasma Samples. *PLoS One*. 2014:0085869.

TABLE 1

Demographics and characteristics of 927 adults sampled for CD4+ cell count and viral load stratified by use of antiretroviral therapy (ART)*

	Not on ART at follow-up**:		On ART at follow-up**:		Total: N
	N	%	N	%	
TOTAL	466	50%	461	50%	927
Sex					
Female	303	50%	301	50%	604
Male	163	51%	160	50%	323
Age					
18-24	122	72%	47	28%	169
25-29	122	61%	78	39%	200
30-34	90	47%	102	53%	192
35-39	69	41%	98	59%	168
40-44	42	36%	73	64%	115
45-49	21	25%	63	75%	84
HIV Status Awareness at Baseline					
Unaware	231	85%	40	15%	271
Aware	235	36%	421	64%	656
Marital/Co-habitation Status					
Married or co-habiting	246	47%	280	53%	526
Not married or co-habiting	217	55%	176	45%	393
Missing Response	3	39%	5	61%	8
Education					
Did not attend	43	50%	43	50%	86
Primary	160	46%	187	54%	347
Secondary	220	53%	197	47%	416
Tertiary	40	57%	30	43%	71
Employment					
Employed (any form)	202	50%	201	50%	403
Unemployed (including retired/disabled)	259	50%	257	50%	516
Residence					
Rural	310	48%	330	52%	640
Urban	156	54%	131	46%	287
Region					
Hhohho	133	55%	111	45%	244
Lubombo	79	49%	82	51%	161
Manzini	185	55%	150	45%	335
Shiselweni	69	37%	119	63%	188

* Survey weighted by age, sex and residence; numbers may not add up to 100% due to rounding

** Follow-up occurred 8-12 months after baseline survey

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

TABLE 2

Distribution of viral loads (VL) by CD4+ cell count strata among 466 HIV-positive individuals not on ART*

VL copies/mL	CD4+ count category				Total
	0-199	200-349	350-499	>=500	
0-999	4	6	4	28	42 (9%)
1000-9999	2	7	21	61	91 (20%)
10000-99999	33	40	66	90	229 (49%)
100000+	28	38	20	18	104 (22%)
Total	66 (14%)	92 (20%)	110 (24%)	198 (42%)	466 (100%)

* Survey weighted by age, sex, and residence; numbers may not add up to 100% due to rounding

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

TABLE 3

Predictors of taking antiretroviral treatment (ART) among 619 adults eligible* by CD4+ cell count <350 cells/ml³**

	Not on ART at follow-up***: N (%)		On ART at follow-up***: N (%)		Total N	Un-adjusted odds ratio	95% confidence interval	Adjusted odds ratio	95% confidence interval
TOTAL	158	26%	461	75%	619	--			
Sex									
Female	90	23%	301	77%	391	Ref		Ref	
Male	68	30%	160	70%	228	0.70	(0.48, 1.03)	0.76	(0.46, 1.26)
Age									
18-24	34	42%	47	58%	81	Ref		Ref	
25-29	40	34%	78	66%	118	1.43	(0.77, 2.62)	1.17	(0.56, 2.45)
30-34	29	22%	102	78%	131	2.60	(1.37, 4.94)	1.88	(0.86, 4.09)
35-39	34	26%	98	75%	132	2.14	(1.19, 3.82)	1.72	(0.8, 3.67)
40-44	19	20%	73	80%	92	2.89	(1.47, 5.65)	2.10	(0.84, 5.25)
45-49	3	4%	63	96%	65	17.20	(4.85, 61.01)	15.28	(3.77, 62.01)
HIV-Aware at Baseline									
Unaware	85	68%	40	32%	125	Ref		Ref	
Aware	73	15%	421	85%	494	12.37	(7.81, 19.58)	10.62	(6.53, 17.25)
Visit Health Facility since Diagnosis									
No visit	72	100%	0	0%	72	--			
Have visited health facility	86	16%	461	84%	547	--			
Ever Told by Doctor to take ART									
No	108	96%	0	0%	113	--			
Yes	50	10%	461	91%	506				

* All those reporting being "on ART" were considered as having been "eligible" (CD4<350 or WHO Stage 3 or 4) per prevailing eligibility requirements at the time of their ART initiation

** Survey weighted by age, sex, and residence; number may not add up to 100% due to rounding

*** Follow-up including CD4+ cell enumeration indicating ART eligibility (<350 cells/ml³) occurred 8-12 months after baseline survey

TABLE 4

Predictors of viral load suppression (<1000 copies/mL) among 461 adults who report taking antiretroviral treatment (ART) at follow-up^{*f}

Characteristics	Unsuppressed viral load:		Suppressed viral load:		Total: N	Un-adjusted odds ratio	95% confidence interval	Adjusted odds ratio	95% confidence interval
	N	%	N	%					
TOTAL	67	15%	394	86%	461	--	--	--	--
Sex									
Female	45	15%	256	85%	301	Ref		Ref	
Male	22	14%	138	87%	160	1.13	(0.64, 2.01)	0.82	(0.43, 1.56)
Age									
18-24	22	46%	25	54%	47	Ref		Ref	
25-29	10	13%	68	87%	78	5.74	(2.43, 13.53)	6.16	(2.26, 16.78)
30-34	8	8%	94	92%	102	10.1	(3.68, 27.7)	9.99	(3.11, 32.07)
35-39	12	13%	86	87%	98	5.89	(2.45, 14.18)	5.81	(2.04, 16.55)
40-44	11	15%	62	85%	73	4.83	(1.79, 13)	4.79	(1.43, 16.09)
45-49	4	6%	59	94%	63	14.43	(3.63, 57.35)	14.09	(3.14, 63.3)
HIV-Aware at Baseline									
Unaware	14	34%	26	66%	40	Ref		Ref	
Aware	53	13%	368	87%	421	3.54	(1.69, 7.39)	1.20	(0.32, 4.48)
On ART at Baseline									
Not on ART	27	27%	73	73%	100	Ref		Ref	
On ART	40	11%	321	89%	361	2.96	(1.71, 5.12)	1.98	(0.87, 4.5)
Marital/Co-habitation Status									
Married or co-habiting	41	15%	238	85%	280	Ref		Ref	
Not married or co-habiting	23	13%	153	87%	176	1.13	(0.63, 2.04)	1.41	(0.71, 2.82)
Missing Response	2	35%	3	65%	5	0.32	(0.05, 2.12)	0.16	(0.02, 1.44)
Education									
Did not attend	6	14%	37	86%	43	Ref		Ref	
Primary	28	15%	160	85%	187	0.93	(0.37, 2.33)	1.09	(0.35, 3.38)
Secondary	27	14%	169	86%	197	1.01	(0.41, 2.48)	1.30	(0.39, 4.29)
Tertiary	6	18%	25	82%	30	0.73	(0.22, 2.44)	0.97	(0.27, 3.47)
Missing Response	0	0%	3	100%	3	omitted		omitted	
Employment									
Employed (any form)	24	12%	176	88%	201	Ref		Ref	
Unemployed (incl. retired/disabled)	41	16%	216	84%	257	0.72	(0.43, 1.22)	0.86	(0.45, 1.67)

Characteristics	Unsuppressed viral load:		Suppressed viral load:		Total: N	Un-adjusted odds ratio	95% confidence interval	Adjusted odds ratio	95% confidence interval
	N	%	N	%					
Missing Response	1	36%	2	64%	3	0.24	(0.02, 2.81)	1.33	(0.08, 21.33)
Residence									
Urban	49	15%	281	85%	330	Ref		Ref	
Rural	18	14%	113	86%	131	1.07	(0.62, 1.85)	1.23	(0.56, 2.69)
Region									
Hhohho	12	11%	98	89%	111	Ref		Ref	
Lubombo	16	20%	65	80%	82	0.50	(0.26, 0.98)	0.39	(0.19, 0.82)
Manzini	23	15%	127	85%	150	0.69	(0.35, 1.35)	0.49	(0.21, 1.14)
Shiselweni	15	13%	104	88%	119	0.88	(0.43, 1.77)	0.84	(0.38, 1.84)
Last Refill of ART prescription									
< 3 months ago	62	14%	384	86%	446	Ref		Ref	
> = 3 months ago	4	53%	3	47%	7	0.14	(0.033, 0.61)	0.20	(0.04, 0.87)
Missing Response	1	12%	7	88%	8	1.17	(0.13, 10.17)	2.57	(0.08, 81.47)

* Survey weighted by age, sex and residence; number may not add up to 100% due to rounding

^f Follow-up including viral load measurement occurred 8-12 months after baseline