Original article *(formatted for AIDS)*

Advanced HIV Disease in the Botswana Combination Prevention Project: Prevalence, Risk Factors, and Outcomes

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Abstract (250 words)

Objective(s): To determine the proportion of individuals linking to HIV-care with advanced HIV-disease (CD4 ≤200 cells/µL) in the Botswana Combination Prevention Project, describe the characteristics of these individuals, and examine treatment outcomes.

Design: A sub-analysis of a cluster-randomized HIV-prevention trial. HIV status was assessed in 16-64-year-olds through home and mobile testing. All HIV-positive persons not on antiretroviral-therapy (ART) were referred to local Ministry of Health and Wellness clinics for treatment.

Methods: Analysis was restricted to the 15 intervention clusters. The proportion of individuals with advanced HIV disease was determined; associations between advanced HIV disease and sex and age explored; and rates of viral suppression determined at 1-year. Mortality and retention in care were compared between CD4 strata (CD4 ≤200 cells/µL vs. >200 cells/µL).

Results: Overall, 17.2% (430/2,499; 95% confidence interval [CI] 15.7-18.8%) of study participants had advanced HIV disease (CD4 ≤200 cells/µL) at time of clinic linkage. Men were significantly more likely to present with CD4 ≤200 cells/µL than women (23.7% versus 13.4%, adjusted odds ratio [aOR] 1.9, 95% CI 1.5-2.3). The risk of advanced HIV disease increased with increasing age (aOR 2.2, 95% CI 1.4-3.2 >35 years versus <25 years). Patients with CD4 ≤200 cells/µL had significantly higher rates of attrition from care during follow-up (hazards ratio 1.47, 95% CI 1.1-2.1).

Conclusions: Advanced HIV disease due to late presentation to or disengagement from ART care remains common in the Treat All era in Botswana, calling for innovative testing, linkage, and treatment strategies to engage and retain harder-to-reach populations in care.

Introduction

Botswana was one of the first African countries to introduce a national antiretroviral therapy (ART) treatment programme, rolling out free ART to clinically-eligible HIV-positive citizens in 2002. In June 2016, following updated World Health Organization (WHO) guidance[1], universal HIV treatment ("Treat All") was introduced, with population-level data suggesting that Botswana was close to achieving the Joint United Nations Programme on HIV/AIDS 90-90-90 targets[2, 3]. Despite these notable successes, Botswana still has one of the highest HIV-prevalence rates globally with an estimated 20.3% of adults living with HIV in 2018[4], and continues to have high estimated HIV incidence rates of 1% or more[5, 6]. Data also show a considerable ongoing burden of HIV-related morbidity and mortality, including high rates of tuberculosis[7], cryptococcal meningitis[8], and HIV-associated malignancies[9]. Both late initiation of ART and default or disengagement from HIV care are likely to contribute to both the high rates of onward HIV-transmission at a population level[10], and the prevalence of advanced HIV disease (CD4 cell counts ≤200 cells/μL or WHO stage 3 or 4 disease)[11], HIV-related morbidity, and mortality[12]. Botswana, in common with most African countries, has adopted a public health approach to ART provision which has understandably focussed on initiating as many individuals as possible on ART. This has been particularly notable since the switch to universal treatment, with considerable resources allocated to finding and initiating newly eligible individuals, often with high CD4 counts. A potential unintended consequence of this may be a failure to appropriately provide the more intensive management needed to effectively engage and retain vulnerable individuals who may then present with advanced HIV disease. Understanding which patient populations are at risk of developing advanced HIV disease is important to enable implementation of strategies to appropriately identify and engage them in HIV treatment services.

Using data from the Botswana Combination Prevention Project (BCPP)[6], a large community-based HIV prevention trial, we determined the proportion of individuals linking to HIV-treatment services with advanced HIV-disease in Botswana, describe the characteristics of the individuals with advanced HIV-disease, and report treatment outcomes stratified by CD4 cell count.

Methods

Study design and participants. BCPP was a cluster-randomized HIV-prevention trial evaluating the impact of prevention interventions on population-level HIV incidence in 15 rural or peri-urban community clusters, with 15 matched control community clusters[3, 6]. We conducted a cross-sectional analysis using baseline BCPP data to examine the prevalence and correlates of advanced HIV disease, an analysed prospective cohort data to determine clinical outcomes in patients according to advanced HIV-disease status. BCPP study interventions took place between October 2013 and March 2018. HIV status was assessed in all 16-64-year-old community residents identified through BCPP testing activities. All newly-identified and known HIV-positive persons not on ART were referred to their local Ministry of Health and Wellness (MoHW) community clinic for ART initiation. ART was provided free of charge to citizens and their spouses. Prior to the introduction of "Treat All" and rapid ART initiation, from 2013 to June 2016, all HIV-positive individuals not on ART had a point-of-care (POC) CD4 count performed by trained HIV counsellors (PIMA™ CD4, Alere, Inc. Waltham, MA, USA) at the initial community intake contact. During this period ART was initiated (i) at CD4 <350 cells/μL or WHO clinical stage 3 or 4; or (ii) if they met the BCPP expanded ART eligibility criteria of CD4 <500 cells/μL or CD4 $\geq$500 cells/μL and viral load (VL) > 10,000 copies/mL. First-line therapy during this period consisted of tenofovir, emtricitabine, and efavirenz as a single

fixed-dose combination tablet. From June 2016, “Treat All” was implemented and all HIV-positive persons were eligible and referred for ART regardless of CD4 count or disease stage. Baseline VL testing and POC CD4 testing were discontinued in June 2016; routine CD4 testing was still performed at the initial clinic visit using the BD FACSCalibur (Beckton Dickinson, Inc.), although ART was initiated prior to receiving CD4 (or safety lab) results. First-line ART also changed in June 2016 to tenofovir and emtricitabine as a combination tablet, plus dolutegravir. Patients were followed-up according to Botswana national guidelines[13]. Deaths were ascertained from clinic records and the electronic medical records system. Efforts were made to trace individuals lost to follow-up and to encourage them to return to clinic through telephone calls or home visits. Individuals who received ART outside of standard of care (prior to June 2016) provided informed consent, and waiver of consent was obtained for all others.The study was approved by the United States Centers for Disease Control and Prevention (CDC) Institutional Review Board (Protocol #6475) and the Botswana Health Research and Development Committee, and prospectively registered at ClinicalTrials.gov (NCT01965470).

Statistical analysis. The primary objectives of the analysis were to determine the proportion of HIV-positive individuals linking to clinics for HIV care with advanced HIV disease, describe factors associated with advanced HIV disease, and assess clinical outcomes according to baseline CD4 count (defined as the CD4 count closest to time of clinic linkage, no more than 90 days prior to or 30 days post linkage). The proportions of individuals presenting with advanced HIV disease in the pre-Treat All and Treat All periods were compared. This analysis was restricted to study participants in the 15 intervention clusters who linked to care at a MoHW facility in the intervention community. Baseline characteristics of the study participants were described, and the overall proportion of individuals with advanced HIV

disease (defined as a baseline CD4 cell count ≤200 cells/μL as staging data were not available for all participants) determined. Associations between advanced HIV disease and sex, age, prior knowledge of HIV status (determined through self-report or evidence of prior HIV-positive diagnosis in the electronic medical records system), and HIV testing location were explored in stratified analyses, and quantified using univariable logistic regression models and adjusted multivariable models including age and sex. The sensitivity and specificity of WHO clinical staging for identification of advanced HIV disease were calculated in those with WHO staging data. Rates of viral suppression (defined as a plasma VL <400 copies/mL) were determined at 1-year post-ART initiation in individuals eligible for ART initiation. The proportions of individuals who had died within one year of linkage and at completion of study follow-up were reported, and overall retention in care presented using Kaplan-Meier curves and compared between CD4 strata (CD4 ≤200 cells/μL vs. >200 cells/μL) using a Cox proportional hazards regression model. All analyses accounted for clustering by community, with hierarchical mixed effects regression models incorporating a random effects term for community, and robust 95% confidence intervals (95%CIs) reported throughout. P-values for comparisons of medians were derived from ranked testing (F-testing) of Somers' D parameter estimates accounting for clustering by site (comparable to a Kruskal-Wallis test). Patients were considered lost to follow-up if they had not attended any HIV-related clinic activity (clinic appointment, blood draw, or ART refill) within 180 days of data censoring on 28th June 2018. Data were analysed using Stata version 14 (StataCorp, College Station, TX, USA). P-values of <0.05 were considered to be statistically significant.

Results

Between October 2013 and March 2018 2,908 HIV-positive community residents who were not taking ART were identified and linked for ART at a BCPP intervention community clinic, of whom 2,499 (85.9%) had a documented baseline CD4 cell count and were included in this analysis (details of the full BCPP cohort are given in supplementary tables 1 and 2). Of the 2,499 baseline CD4 cell counts performed, 1,872 (74.9%) were measured using the PIMA CD4 (Alere, Inc.) and 627 (25.1%) using the BD FACSCalibur (Beckton Dickinson, Inc.). Baseline characteristics of participants are shown in Table 1. Overall, 17.2% (430/2,499; 95%CI 15.7-18.8%) of study participants had advanced HIV disease defined as baseline CD4 count ≤200 cells/μL at the time of clinic linkage (Figure 1a). Men were significantly more likely than women to present with CD4 ≤200 cells/μL (23.7% versus 13.4%, adjusted odds ratio (aOR) 1.9, 95%CI 1.5-2.3). The risk of advanced HIV disease increased with advancing age (9.1% of those <25 years, 15.0% of those aged 25-34 years, and 20.4% of those >35 years; aOR relative to the <25 years category of 1.5 (95%CI 1.0-2.4) and 2.2 (95%CI 1.4-3.2) respectively)(Figure 1b). Other factors found to be significantly associated with higher rates of advanced HIV disease were a new (rather than previously known) HIV diagnosis (aOR 1.3, 95%CI 1.0-1.6); HIV-testing through mobile rather than home-based contact (aOR 1.3, 95%CI 1.0-1.6); and being widowed or divorced (aOR 2.6, 95%CI 1.6-4.3) (Table 1.b). There was no decline in the proportion of individuals linking to care with CD4 ≤200 cells/μL over time; in fact, the proportion increased from 15.5% (315/2,034; 95%CI 13.4-17.9%) prior to introduction of Treat All, to 24.7% (115/465; 95%CI 20.4-29.6%) during Treat All, p<0.001. One hundred and thirty of the 2,499 participants (5.2%, 95% CI 4.3-6.3%) had very advanced HIV disease (CD4 count ≤100 cells/μL); presentation with very advanced disease was significantly associated with male sex and older age (Table 2).

WHO clinical staging were available for 1,787/2,499 study participants. Clinical staging using WHO stage 3 or 4 disease had a sensitivity of 6.0% (95%CI 3.6-9.3%) and specificity of 96.8% (95%CI 95.8-97.7%) for detecting CD4 counts ≤200 cells/μL, giving a 27.7% positive predictive value (95%CI 17.3-40.2%) and 83.6% negative predictive value (81.8%-85.3%). Eighty-two percent (246/300) of individuals with CD4 ≤200 cells/μL and staging data available had WHO stage 1 disease.

At the time of linkage 2,193/2,499 individuals were eligible for ART initiation according to study eligibility criteria. ART was initiated in 97.2% (418/430) of individuals with CD4 ≤200 cells/μL, and 96.4% (1,699/1,763) of eligible individuals with CD4 >200 cells/μL, p=0.40. Retention in care following ART initiation, stratified by CD4 count (≤200 vs. >200), is shown in Figure 1c. Patients with CD4 ≤200 cells/μL had significantly higher rates of attrition from care during study follow-up (hazards ratio 1.47, 95%CI 1.1-2.1). Rates of attrition from care in patients with CD4 ≤200 cells/μL were similar in individuals with new and previously-known HIV diagnosis (hazards ratio 1.1, 95%CI 0.6-2.0; Figure 2). Documented mortality was 2.1% (9/430) in the CD4 ≤200 cells/μL group compared to 0.7% (13/1763) in those with CD4 >200 cells/μL within one year of clinic linkage, and 4.9% (21/430) versus 1.7% (30/1763) at the end of study follow-up (p<0.001). Overall 86.6% (95%CI 81.8-90.2%) of all individuals linking to care with a CD4 ≤200 cells/μL were in care, on ART, and had a suppressed VL after one year, compared to 92.1% (95%CI 89.5-94.0%) of those with baseline CD4 >200 cells/μL, p<0.001.

Discussion

Advanced HIV disease was common among adults presenting for HIV care in rural and peri-urban Botswana between 2013 and 2018. Despite a well-established ART programme with high levels of population coverage[3], almost one in seven women, and one in four men had

CD4 cell counts ≤200 cells/μL at the time of clinic linkage. The proportion of individuals linking to care with advanced HIV disease increased with age in both men and women, with the highest rates in those ≥35 years of age. In keeping with prior studies[12, 14], treatment outcomes were worse in individuals initiating ART with advanced HIV disease compared to those initiating at higher CD4 counts, although our data show that relatively high levels of retention in care and viral suppression can be achieved in this patient group with appropriate management.

The ongoing burden of advanced HIV disease seen in Botswana in the Treat All era is consistent with data from South Africa[15-18], where a nationwide laboratory cohort estimated that 32.9% adults had advanced HIV disease at presentation, and 16.8% had very advanced HIV disease (CD4 <100 cells/μL) in 2016[15]. Subsequent data suggest that these figures have remained stable in 2017-2018 following the introduction of Treat All[17]. Notably, the proportion of advanced HIV disease in our cohort may underestimate the true burden of advanced HIV disease in Botswana as our study was limited to rural and peri-urban areas, and the population under study were exposed to widespread HIV testing interventions in the community and intensive efforts to improve linkage to care, perhaps leading to a higher proportion of patients being identified and initiated on ART while still in early stages of disease. This is supported by recent data from Gaborone (Botswana's capital city) showing that 24.8% of 14,423 individuals undergoing baseline CD4 testing between 2015-2017 had CD4 counts <200 cells/μL[19].

Our findings that men were almost twice as likely as women to enter care with advanced HIV disease, and that the prevalence of advanced HIV disease increases with age, add to extensive regional data demonstrating the failure of HIV services to adequately engage men and those

of working age[15, 18, 20, 21]. Developing strategies to find and engage these groups is therefore essential for successful implementation of Treat All programmes. In our cohort only 33% (612/1,843) of individuals identified through home-based testing were men, compared to 48% (510/1,065) identified through mobile testing, odds ratio 1.8 (95% CI 1.6-2-2; data not shown), suggesting that alternative testing models could facilitate engagement of hard-to-reach populations in care. Importantly, almost half of individuals presenting with advanced HIV disease were already known to be HIV-positive prior to contact with the study team, and 22% of these had previously been on ART. This highlights the important and substantial contribution of patients who have previously tested HIV-positive, have often started ART, and who re-present with low CD4 counts following a period without effective ART, to the overall burden of advanced HIV disease, and the need to adapt HIV treatment services to effectively retain such patients.

Clinical staging was of no utility in detecting individuals presenting with CD4 cell counts ≤ 200 cells/µL, with a sensitivity of 6%. Eighty-two percent of individuals with CD4 ≤200 cells/µL and staging data available had WHO stage 1 disease. Baseline CD4 testing therefore remains essential to identify individuals with advanced HIV disease and enable implementation of differentiated models of care as advocated in WHO guidelines[11]. It is of some concern that data from several African countries have shown a marked reduction in the proportion of patients undergoing baseline CD4 testing following the introduction of Treat All strategies[22]. HIV treatment programmes must ensure retention of CD4 testing capacity to identify and appropraiatly manage the population with advanced HIV disease, who continue to make up a sizeable proportion of individuals initiating ART. Our data confirm the higher mortality in this advanced HIV patient population[12, 14], which may have been underestimated given

limitations in our ability to track individuals lost to follow-up, even in a study setting where baseline CD4 count was known and enhanced care could be given.

In conclusion, advanced HIV disease due to late initiation of ART and default or disengagement from ART care remains common in the Treat All era in Botswana in the context of very high levels of HIV testing and free treatment in a mature HIV program, highlighting the need for baseline CD4 testing to identify these at-risk individuals and calling for innovative testing, linkage, and treatment strategies to engage and retain harder-to-reach populations in care.

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Tables

(Overleaf)

Table 1. Patient Characteristics and Associations with Advanced HIV Disease

(i) Baseline characteristics stratified by baseline CD4 count*				
variable	*Overall*	*CD4≤200 cells/μL*	*CD4>200 cells/μL*	*p-value†*
Sex (% male)	37.1% (926/2499)	50.9% (219/430)	34.2% (707/2069)	*<0.001*
Age (median, IQR)	36 (29-44) years	38 (32-46) years	35 (28-44) years	*<0.001*
New or known HIV (% new diagnosis)	48.5% (1212/2499)	54.2% (233/430)	47.3% (979/2069)	*0.010*
WHO stage§ (% stage 1 disease)	88.8% (1586/1787)	82.0% (246/300)	90.1% 1340/1487)	*<0.001*
Education level§ (% secondary)	62.1% (1551/2497)	60.7% (261/430)	62.4% (1290/2067)	*0.516*
Employment§ (% employed)	41.8% (1037/2483)	46.0% (198/430)	40.9% (839/2053)	*0.084*
Marital status§ (% married)	23.8% (594/2498)	21.6% (93/430)	24.2% (501/2069)	*0.002*
(ii) Associations with Advanced HIV-disease (CD4 ≤ 200 cells/μL)				
Variable	*Category*	*%CD4≤200 (95%CI)*	*OR (95%CI)*	*aOR (95%CI ‡*
Sex	Female	13.4% (12.3-14.7)	base	base
	Male	23.7% (20.5-27.2)	2.0 (1.6-2.5)	1.9 (1.5-2.3)
Age	<25 years	9.1% (8.8-9.3)	base	base
	25-34 years	15.0% (12.7-17.7)	1.7 (1.1-2.6)	1.5 (1.0-2.4)
	>35 years**	20.4% (18.1-22.8)	2.5 (1.7-3.7)	2.2 (1.4-3.2)
HIV status	Known HIV	15.3% (12.8-18.2)	base	base
	New HIV	19.2% (16.9-21.7)	1.3 (1.1-1.6)	1.3 (1.0-1.6)
Testing site	Home	16.0% (13.9-18.3)	base	base
	Mobile	19.7% (17.7-21.8)	1.3 (1.0-1.6)	1.3 (1.0-1.6)
Education level	Primary	17.9% (14.8-21.4)	base	base
	Secondary	16.8% (15.6-18.1)	0.9 (0.8-1.2)	1.2 (1.0-1.6)
Employment	Unemployed	16.0% (13.9-18.4)	base	base
	Employed	19.1% (17.1-21.2)	1.2 (1.0-1.5)	1.0 (0.8-1.3)
Marital status	Married	15.7% (12.9-18.9)	base	base
	Divorced/widowed	30.5% (24.4-37.4)	2.4 (1.5-3.9)	2.6 (1.6-4.3)
	Single	17.0% (15.7-18.5)	1.1 (0.9-1.4)	1.3 (1.0-1.8)
(iii) Outcomes stratified by baseline CD4 count				
variable	*Overall*	*CD4≤200 cells/μL*	*CD4>200 cells/μL*	*p-value†*
In care at 1 year†† (% 95%CI)	97.1% (96.4-97.8)	95.4% (92.9-97.1)	97.6% (96.7-98.2)	*0.024*
Viral suppression§§ at 1 year (% 95%CI)	91.0% (88.3-93.0)	86.6% (81.8-90.2)	92.1% (89.5-94.0)	*<0.001*
Mortality - 1 year (% 95%CI)§§	1.0% (0.6-1.6)	2.1% (1.1-4.1)	0.7% (0.4-1.2)	*0.016*
Mortality - overall (% 95%CI)‡‡	2.3% (1.5-3.5)	4.9% (3.0-7.8)	1.7% (1.0-2.9)	*<0.001*

IQR: interquartile range; HIV: human immunodeficiency virus; ALT: alanine transaminase; IU: international units; CI: confidence interval; OR: odds ratio; aOR: adjusted odds ratio.

Data are restricted to the 2499 HIV-positive community residents identified who were not taking ART, linked for ART at a BCPP intervention community clinic, and had a documented baseline CD4 cell count. During the pre-universal treatment period when point of care CD4 testing was taking place in the community, 92% (1843/2000) individuals with CD4 cell counts >200 cells/μL and 92% (317/343) with CD4 counts ≤200 cells/μL linked to care at an intervention community clinic (p=0.86).

*Of the 2499 baseline CD4 cell counts performed, 1,872 (74.9%) were measured using the PIMA CD4 (Alere, Inc.) and 627 (25.1%) using the BD FACSCalibur (Beckton Dickinson, Inc.).

†All p-values are adjusted to account for clustering by community. P-values for comparisons of proportions were derived from a hierarchical mixed effects regression model incorporating a random effects term for community. P-values for comparisons of medians were derived from ranked testing (F-testing) of Somers' D parameter estimates accounting for clustering by site (comparable to a Kruskall-Wallis test).

§Data were incomplete for WHO stage (missing in 712/2499), education (missing in 2/2499), employment (missing in 16/2499), and marital status (missing in 1/2499).

‡ All odds-ratios were adjusted for clustering by community using a hierarchical mixed effects regression model incorporating a random effects term for community. Adjusted odds-ratios were derived from multivariable models including age and sex (plus the additional exposure variable of interest). The decision to include age and sex in the models was made a priori.

**There was no significant difference in the prevalence of advanced HIV disease in those aged 35-49 years (21%) and those aged >50 years (19%). Separate categories for older age groups were not included due to relatively small numbers of elderly indivuduals in the study population.

††Analysis is restricted to the 2,117/2,193 antiretroviral therapy (ART) eligible individuals who initiated ART. P-value derived from a Cox Proportional Hazards model adjusted for clustering by community.

§§All individuals linking more than one year prior to data censoring.

‡‡Mortality is reported at one year from linkage, and at end of study follow-up in June 2018.

Table 2. Patient Characteristics and Associations with Very Advanced HIV Disease (CD4 count ≤100 cells/μL)

(i) Associations with Very Advanced HIV-disease (CD4 ≤ 100 cells/μL)				
Variable	*Category*	*%CD4≤100 (95%CI)*	*OR (95%CI)*	*aOR (95%CI* **§**
Sex	Female	3.8% (3.0-4.8)	base	base
	Male	7.6% (5.7-10.0)	2.1 (1.4-2.9)	1.9 (1.3-2.7)
Age	<25 years	1.5% (0.6-3.7)	base	base
	25-34 years	4.2% (3.2-5.6)	2.9 (1.2-7.5)	2.6 (1.0-6.8)
	>35 years	6.7% (5.2-8.6)	4.7 (1.9-11.7)	4.1 (1.6-10.1)
HIV status	Known HIV	5.0% (3.6-6.8)	base	base
	New HIV	5.4% (4.0-7.5)	1.1 (0.8-1.6)	1.1 (0.7-1.5)
(ii) Outcomes stratified by baseline CD4 count				
variable	*Overall*	*CD4≤100 cells/μL*	*CD4>100 cells/μL*	*p-value*[*]
In care at 1 year[‡] (% 95%CI)	97.1% (96.4-97.8)	95.2% (88.2-98.0)	98.2% (97.4-98.9)	*0.020*
Viral suppression[**] **at 1 year** (% 95%CI)	91.0% (88.3-93.0)	87.4% (79.0-92.8)	91.2% (88.3-93.4)	*0.115*
Mortality - 1 year (% 95%CI) **††**	1.0% (0.6-1.6)	4.6% (2.0-10.2)	0.8% (0.4-1.4)	*<0.001*
Mortality - overall (% 95%CI) **††**	2.3% (1.5-3.5)	8.5% (4.3-16.0)	1.9% (1.2-3.1)	*<0.001*

HIV: human immunodeficiency virus; CI: confidence interval; OR: odds ratio; aOR: adjusted odds ratio.

*All p-values are adjusted to account for clustering by community. P-values for comparisons of proportions were derived from a hierarchical mixed effects regression model incorporating a random effects term for community.

§ All odds-ratios were adjusted for clustering by community using a hierarchical mixed effects regression model incorporating a random effects term for community. Adjusted odds-ratios were derived from a multivariable model including age and sex.

‡Analysis is restricted to the 2,117/2,193 antiretroviral therapy (ART) eligible individuals who initiated ART. P-value derived from a Cox Proportional Hazards model adjusted for clustering by community. 96.6% and 95.4% of individuals with CD4 counts >100 cells/μL and ≤100 cells/μL respectively initiated ART.

**All individuals linking more than one year prior to data censoring.

††Mortality is reported at one year from linkage, and at end of study follow-up in June 2018.

Figures

Figure 1 Legend. Advanced HIV disease (baseline CD4 cell count ≤200 cells/μL) in the Botswana Combination Prevention Project (BCPP). Panel (A) shows the overall proportion of individuals linking to BCPP intervention community clinics with advanced HIV disease; 430/2499 (17.2%, 95% confidence interval 15.7-18.8%) had a baseline CD4 count ≤200 cells/μL; 130/2499 (5.2%, 95% confidence interval 4.3-6.3%) had very advanced HIV disease (CD4 count ≤100 cells/μL) – see Table 2. Panel (B) shows the proportion of individuals presenting with advanced HIV-disease stratified by age and sex. Men were significantly more likely than women to present with CD4 cell counts ≤200 cells/μL, $p<0.001$ in univariable analysis and after adjustment for age. Older age was significantly associated with increasing odds of presenting with advanced HIV-disease in both men and women, $p<0.001$ in univariable analysis and after adjustment for sex. Panel (C) presents Kaplan Meier curves showing retention in HIV-care following linkage to BCPP intervention community clinics, stratified by baseline CD4 count, restricted to individuals initiating ART. Patients with baseline CD4 cell counts ≤200 cells/μL had significantly higher rates of attrition from care during study follow-up (hazards ratio 1.47, 95% confidence interval 1.1-2.1, adjusted for clustering by community).

Figure 2 Legend. Retention in HIV-care among patients presenting with CD4 cell counts ≤200 cells/μL stratified by prior knowledge of HIV status (new or known diagnosis). Kaplan Meier curves showing retention in HIV-care following linkage to BCPP intervention community clinics, stratified by knowledge of HIV status at study presentation, restricted to individuals initiating ART. There was no significant difference between groups (hazards ratio 1.12, 95% confidence interval 0.6-2.0, adjusted for clustering by community).