The HIV Care Cascade for Older Adults in Rural South Africa: A Longitudinal Cohort Study (2014–2019)

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Background: As people with HIV grow older, stable engagement in care is essential for healthy aging. We evaluate the HIV care cascade for older adults in rural South Africa at 2 time points cross-sectionally and assess movement in the cascade over time.

Setting: We evaluated the cascade stage at waves 1 (2014–2015) and 2 (2018–2019) of Health and Aging in Africa: A Longitudinal Study of an INDPETH Community in South Africa, a population-based longitudinal cohort study in Mpumalanga Province, South Africa.

Methods: Biomarker screening defined cascade stages [HIV+/no antiretroviral therapy (ART); ART+/unsuppressed viral load; ART+/suppressed viral load]. Between-wave probability of death, cascade progression, regression, cascade transitions, and sociodemographic predictors were assessed with Poisson regression. The impact of death was considered using the Fine and Gray competing risk model.

Results: We observed a higher prevalence of antiretroviral therapy with viral suppression over time (50% in wave 1 vs. 70% in wave 2). Among those alive, the oldest age group (70+ years old) was most likely to have cascade progression [adjusted risk ratio for treatment initiation vs. 40–49 years old: 1.38 (95% confidence interval: 1.02 to 1.86)]. However, there was a significant risk of death and cascade regression. Death between waves reached 40% for 70+-year-olds who were ART+/unsuppressed. In competing risk models, older age was associated with equivalent or less cascade progression.

Conclusion: Older age groups who were unsuppressed on treatment and men had poorer cascade outcomes. Improvements observed in HIV treatment coverage over time for older adults must be interpreted in the context of the high risk of death for older HIV-positive adults, especially among those failing treatment.

Key Words: cohort studies, HIV care continuum, viral suppression, ART, mortality, South Africa

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INTRODUCTION

Populations with HIV are aging globally because of improved life expectancy associated with access to antiretroviral therapy (ART), as well as declines in HIV incidence among younger adults.[1–3] In 2016, there were approximately 5.7 million people living with HIV (PLHIV) aged 50 years and older worldwide, and this number continues to grow.[3,4] The burden of HIV among older populations is especially large in low- and middle-income countries, where 80% of PLHIV aged 50 years or older live.[4] Models predict substantial aging of the HIV-positive population in South Africa, home to the world's largest HIV epidemic, presenting challenges for the healthcare system.[5] Aging populations with HIV face unique concerns and complications from a larger burden of aging-related comorbid chronic conditions.[3,6] Aging-associated declines in cognitive function can impact access to HIV testing and awareness of HIV status,[7] while frailty and severity of HIV infection are risk factors associated with HIV-associated neurocognitive disorders.[8] HIV viral suppression improves healthy aging, including preserved cognitive function and decreased risk of disability.[9] Understanding the gaps in HIV treatment and viral suppression for older adults in South Africa is important for ensuring their successful treatment and well-being.

Population-wide HIV testing and treatment targets are often monitored and evaluated through the HIV care cascade

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framework.[10,11] The Joint United Nations Programme on HIV/AIDS (UNAIDS) has updated the 90-90-90 cascade targets for 2020 to the 95-95-95 targets for 2030, which aim for 95% of the HIV-positive population to know their status, 95% of those diagnosed to be on ART, and 95% of those on ART to be virally suppressed.[12] Previous analyses from South Africa among younger adults have demonstrated that ART coverage targets are not being met, because of critical gaps around initial linkage to care and retention on ART.[13–15] Men have also been shown to have worse outcomes throughout the cascade among younger to middle-aged adults in South Africa.[14–19] How older adults fare in the HIV care cascade is less well understood. Older adult populations have been traditionally understudied in HIV research, and the sex discrepancy in treatment outcomes is not always observed at older ages.[15,20]

Many HIV care cascade studies are based on cross-sectional data that do not account for deaths or changes over time, or from clinical cohorts and medical records that can make estimates of the proportion of the population accessing care difficult to assess.[14–16,18,20] Although often used as a tool to evaluate population treatment coverage, cross-sectional cascades face limitations in their interpretation. Simulation models have demonstrated that analyses based on cross-sectional cascades can lead to incorrect conclusions about healthcare system performance.[21] Longitudinal cascades allow for more realistic and dynamic analyses, accounting for movement across the cascade, mortality, and engagement and disengagement in treatment.[22–24]

In this analysis, we leverage data from the HAALSI study (Health and Aging in Africa: A Longitudinal Study of an INDPETH Community in South Africa) to evaluate progression and regression in the HIV care cascade among HIV-positive older adults from 2014 to 2019.[25] The richness of the data in this cohort study allows us to implement best practices for cascade analyses, including a population-based study sample, longitudinal data collection, full mortality ascertainment, and cascade stages defined through biomarkers. We aim to assess how the HIV care cascade for older adults has changed over time, evaluating treatment coverage among older adults and identifying key predictors of cascade progression and regression in a rural South African setting.

METHODS

Study Population

HAALSI is nested within the Agincourt Health and Socio-Demographic Surveillance System (HDSS), running since 1992 in Mpumalanga Province, South Africa.[26] This ongoing cohort study aims to evaluate biological, social, and economic determinants of healthy aging in South Africa. The wave 1 survey took place in 2014–2015 and wave 2 in 2018–2019. Individuals within the HDSS area aged 40+ years were randomly sampled. Five thousand fifty-nine individuals enrolled in this study, reflecting an 86% response rate. The study population is typical of rural South Africa, with low formal education and high unemployment, and some gaps in access to electricity and water.[25] During each wave of data collection, interviewers visited participants at their homes and conducted face-to-face computer-assisted personal interviews in the local language of Shangaa and collected anthropometric and biomarker measurements. Dried blood spots (DBSs) were collected and assessed for HIV, viral load, and the presence of ART drugs.

We evaluated the care cascade with 2 approaches: (1) the cross-sectional cascade status at each time point and (2) the change between the waves accounting for deaths and bidirectional movement in the cascade. The analytic sample included all individuals who screened HIV positive by DBS in wave 1. During wave 1 data collection, 4707 of the 5059 enrolled (93%) consented to blood collection for DBS and there were 4582 individuals with DBS results available (97% of those who consented). HIV prevalence was 23%, and these 1048 individuals comprised the analytic sample. There were 14 individuals found as newly HIV positive in wave 2, but they were not included.

Participants provided informed consent. Ethical approval for HAALSI was obtained from the University of the Witwatersrand Human Research Ethics Committee (no. M141159), the Harvard T.H. Chan School of Public Health Office of Human Research Administration (no. 13-1608), and the Mpumalanga Provincial Research and Ethics Committee.

Definition of Cascade Stages and Variables

We identified 3 stages of the cascade through biomarkers: HIV positive and not on ART (HIV+/no ART group), on ART but not virally suppressed (ART+/unsuppressed group), and on ART and virally suppressed (ART+/suppressed group). We did not include the first stage of the cascade, HIV diagnosis, because it could not be verified outside of self-report. In wave 1, DBS was screened for emtricitabine (FTC) and lamivudine (3 TC), the second drug of all standard three-drug regimens in first-line and second-line ART in South Africa. The presence of either drug at a concentration as low as 0.02 μg/mL was considered positive for ART. In wave 2, DBS screening was expanded to cover all drugs in standard ART regimens at the time: 3 TC, FTC, abacavir, efavirenz, lopinavir, nevirapine, tenofovir, and zidovudine. The presence of any of these drugs was considered positive for ART in wave 2. Through a comparison of 3 TC and FTC screening only to all 8 drugs screened in wave 2, we observed that 3 TC and FTC screening alone identified 97% of all ART-positive DBS samples. Viral suppression was defined as $<$200 copies/mL. Mortality and date of death were obtained through the Agincourt HDSS census, allowing for complete ascertainment of vital status regardless of whether an individual was located in wave 2.

Predictors of movement within the cascade included the following, defined at wave 1: sex, age group, education level, marital status, household wealth index quintile, cognition score, and depression score. Principal component analysis was used to create the wealth index based on ownership of household items, vehicles, and livestock, and households were grouped into quintiles.[27] Cognition score is a summary score of correct responses to mental status questions,

including counting, number series, date, current president, and word recall, and can range from 0 to 26. Depression score is based on an abbreviated 8-item Center for Epidemiologic Studies—Depression Scale (CES-D) questionnaire and can range from 0 to 8, with a higher score indicating higher depression.[28] A continuous depression score and a cut-off for depression at 4 points were considered in the models.

Analytic Methods

First, the participants' cascade stage at wave 1 and wave 2 was evaluated cross-sectionally at both time points. Next, we assessed dynamic movement through the HIV care cascade similarly to Mauer et al's[29] methods analyzing the hypertension care continuum. We estimated the probability of progression to any subsequent cascade stage, the probability of regression backward to any prior stage, and the probability of death between waves. To determine if social or demographic groups were at increased risk of less cascade progression, we obtained risk ratio estimates using Poisson models with robust standard errors to evaluate predictors of cascade progression and regression.[30] Additional outcomes included important cascade transitions: initiated treatment, among those ART negative at wave 1; stopped treatment, among those on ART at wave 1; and reached the final cascade stage of treated and suppressed, among those not in this stage at wave 1. We evaluated predictor variables in unadjusted and adjusted models and included the wave 1 cascade stage as a covariate to account for the differential baseline distribution of participants.

We conducted additional models for comparison purposes. Owing to the large number of deaths in this aging population, we considered the impact of death as a competing risk. Using the date of death, we calculated time to death from wave 1 for those who died and reassessed models for each outcome using the Fine and Gray[31] competing risk regression model. We estimated the timing of cascade transition among those who progressed or regressed in the cascade using a midpoint between DBS measurements. Second, we used inverse probability weighting to account for nonresponse to biomarker measurements among those alive during the wave 2 survey. Last, in a sensitivity analysis, we used a viral suppression threshold of <1000 copies/mL rather than <200 copies/mL.

TABLE 1. Population Characteristics by Wave 1 (2014–2015) HIV Care Cascade Status

	Wave 1 Cascade Status		
	HIV+/No ART	ART+/ Unsuppressed	ART+/ Suppressed
N	386	143	519
Sex (female)	56.7%	49.7%	53.0%
Age group (yr)			
40–49	35.0%	22.4%	25.2%
50–59	34.2%	42.7%	37.8%
60–69	20.2%	23.8%	26.8%
70+	10.6%	11.2%	10.2%
Education category			
No formal education	40.4%	42.7%	40.9%
Some primary education	32.9%	33.6%	36.4%
Some secondary education or higher	26.4%	22.4%	22.5%
Marital status			
Never married	9.6%	6.3%	6.4%
Separated or divorced	21.5%	24.5%	18.1%
Widowed	31.4%	29.4%	34.1%
Currently married/ cohabitating	37.6%	39.2%	41.4%
Household wealth asset index quintile			
Q1 (poorest)	26.9%	25.2%	22.4%
Q2	20.2%	21.0%	20.6%
Q3	20.7%	20.3%	20.4%
Q4	17.6%	18.9%	20.0%
Q5 (wealthiest)	14.5%	14.7%	16.6%
Cognition score (mean, SD)	14.9 (3.8)	14.2 (4.7)	14.8 (3.7)
Depression score (mean, SD)	1.3 (1.6)	1.4 (1.6)	1.2 (1.4)

Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI), Mpumalanga Province, South Africa.

RESULTS

Baseline Population

Characteristics of the 1048 individuals who comprised the HIV-positive population at wave 1 are displayed in Table 1. Individuals not on ART were more likely to be women, in the youngest age group, and the poorest wealth quintile (Table 1).

Cross-Sectional Cascades

In wave 2, 801 of the 1048 participants in the analytic sample (76%) had an outcome defined, including 690 with a DBS result, and 111 identified as deaths. There were 247 (24%) alive but without an outcome for wave 2 (49 refused the interview or were not located; 198 were interviewed but declined DBS). When comparing wave 1 characteristics (age, sex, education, marital status, wealth index, depression score, cognition score) between those who did and did not provide a DBS sample in wave 2 among the living population, there was no significant difference for any variable, except for sex, where women had 7% higher DBS participation compared with men. Importantly, there was also no significant difference in participation in wave 2 DBS by wave 1 cascade stage (χ^2 P-value = 0.830). Thus, we applied inverse probability weights (IPWs) for nonparticipation in wave 2 DBS for all results that used wave 2 cascade status as an outcome and were not sex adjusted.

Cross-sectional tabulations showed a higher proportion of PLHIV on treatment with viral suppression in wave 2 compared with wave 1. The distribution of the population in each cascade stage was as follows: HIV +/no ART: 37% in wave 1, 18% in wave 2; ART+/unsuppressed: 14% in wave 1, 11% in wave 2; ART+/suppressed: 50% in wave 1, 71% in

wave 2. Applying IPWs to wave 2 prevalence estimates resulted in the following: 19% HIV+/no ART; 11% ART+/unsuppressed; and 70% ART+/suppressed. When stratifying by age group, improvements in treatment coverage were seen across all ages, with the 70+-year-old age group having the highest treatment coverage in wave 2 and exceeding the UNAIDS 90-90-90 treatment targets for 2020 (Fig. 1).

Changes Between Waves

There was significant forward and backward movement in the cascade, and a large proportion of individuals died between waves, especially among those on ART in wave 1 without viral suppression (see Figure, Supplemental Digital Content, http://links.lww.com/QAI/C290; Table 2). Most individuals in the HIV+/no ART and the ART+/unsuppressed group who were alive in wave 2 had forward movement in the cascade (Table 2), yet backward movement also occurred. While discontinuation of ART was not very likely from the ART+/unsuppressed group (5%, 95% confidence interval (CI): 2 to 13), nearly 1 in 7 ART+/suppressed individuals had moved backward in the cascade and were either no longer suppressed or no longer on ART in wave 2 (14%, 95% CI: 11 to 18) (Table 2). Deaths were highest among those on treatment without viral suppression and lowest among those on treatment and virally suppressed (see Figure, Supplemental Digital Content, http://links.lww.com/QAI/C290; Table 2). Death rate over the approximately 4 years between waves among those ART+/unsuppressed approached 25% for the 60–69-year-olds and 40% for 70+-year-olds (Fig. 2).

Models for Predictors of Movement

In the Poisson models predicting cascade progression, regression, and important transitions in care, wealth index, marital status, cognition score, and CES-D score were not predictive in any model. One exception was the unadjusted model for CES-D score, which was marginally significantly associated with cascade regression, with every one-point increase in depression score associated with a 14% higher likelihood of cascade regression (risk ratio [RR] = 1.14 [95% CI: 0.99 to 1.31]). When adjusted for age, sex, and education, this estimate became 1.11 (95% CI: 0.97 to 1.26) and was not included in the final models. Poisson models indicated slightly better cascade progression among women and worse cascade progression among the middle education category, although these results were not always statistically significant (Table 3). Women had similar outcomes to men but some evidence of less regression in the cascade (adjusted risk ratio [aRR] for cascade regression = 0.62 [95% CI: 0.36 to 1.05]).

The age group was predictive of cascade movement. Without adjustment for death, when compared with the 40–49-year-olds, the 70+-year-old age group was more likely to initiate treatment [aRR = 1.38 (95% CI: 1.02 to 1.86)] and appeared to doing the same or better in cascade progression [aRR = 1.20 (95% CI: 0.89 to 1.64)] (Table 3). However, these results were significantly impacted by the death rate, which was especially high for individuals in the ART+/unsuppressed group who were in the oldest age groups (Fig. 2). Thus, in the Fine and Gray models accounting for death as a competing risk, the oldest age group no longer appeared to be doing the best in care and had equivalent or slightly worse outcomes compared with the 40–49-year-olds, though not statistically significant (Table 3). Older age groups were no longer predictive of treatment initiation compared with 40–49-year-olds (Table 3). Unlike for age group, competing risk model estimates for other predictors did not change direction compared with risk ratio estimates (Table 3). The competing risk models yielded stronger evidence for women having better cascade outcomes, for example, the asHR for cascade progression for women vs. men was 1.46 (95% CI: 1.09 to 1.95).

Additional outcomes for stopping treatment and newly treated and suppressed are not displayed. Model estimates for

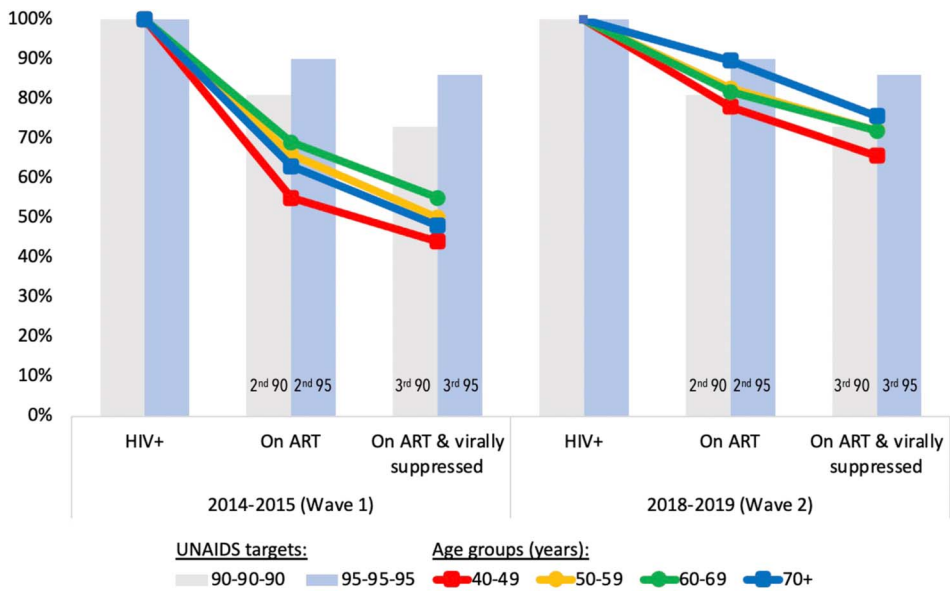

FIGURE 1. Cross-sectional cascade at wave 1 (2014–2015) and wave 2 (2018–2019), stratified by age group. Bars in the background display the UNAIDS 90-90-90 (2020) and 95-95-95 (2030) targets for context. Inverse probability weights are applied to the wave 2 data. Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI), Mpumalanga Province, South Africa.

TABLE 2. Probability (and 95% CIs) of Cascade Progression, Regression, and Death Between Wave 1 (2014–2015) and Wave 2 (2018–2019), by Wave 1 Cascade Status

	Wave 1 Cascade Status		
	HIV+/No ART	ART+/Unsuppressed	ART+/Suppressed
Probability of progression* among those alive in Wave 2	56.7% (50.8–63.2)	72.5% (63.5–82.7)	—
Probability of regression* among those alive in Wave 2	—	4.8% (1.8–12.7)	13.7% (10.5–17.8)
Probability of death	11.4% (8.6–15.1)	16.8% (11.6–24.2)	8.3% (6.2–11.0)

*Inverse probability weights applied for the population who participated in wave 2, to make estimates representative of those alive in wave 2.

stopping treatment yielded no statistically significant results, and the model for newly treated and suppressed showed very similar results to the initiated treatment outcome.

The sensitivity analysis with the higher viral suppression cut-off of <1000 copies/mL showed a relatively higher probability of movement from the ART+/unsuppressed to the ART+/suppressed stage [80% (95% CI: 66 to 95)] and a lower probability of backward movement from the ART+/suppressed stage [8% (95% CI: 6 to 11)]. The proportion of people in the final ART+/suppressed stage in wave 2 increased to 77% (compared with 71% using the <200 copies/mL cut-off). Using this alternate cut-off for viral suppression did not alter the interpretation of the models. Models consistently showed the oldest age group had relatively better cascade progression in the Poisson models and worse outcomes in the competing risk models. Depression score became statistically significantly associated with backward cascade movement in the sensitivity analysis, where every 1-point increase in the CES-D scale was predictive of a 22% higher likelihood of cascade regression [aRR = 1.22 (95% CI: 1.06 to 1.40)]. The direction and significance of other predictors were unchanged.

DISCUSSIONS

We found significant bidirectional movement across the HIV care cascade among this older adult population in rural South Africa over the 4-year study period. There was relatively more cascade progression than regression resulting in a higher proportion with ART coverage and viral suppression among the living HIV-positive population at wave 2. In wave 2, 70% were virally suppressed on ART and thus had achieved the final cascade stage. In the context of the UNAIDS targets, this population is close to the 90-90-90 targets (which indicate 72.9% of PLHIV should be ART+/suppressed) but falls short of the 95-95-95 targets (which indicate 85.7% of PLHIV should be ART+/suppressed).[12] If using the <1000 copies/mL cut-off which resulted in 77% of the population ART+/suppressed at wave 2 in 2019, this population is already in line with the 90-90-90 UNAIDS goals for 2020. Despite this positive metric for the successful ART coverage of the older adult population, there remained a substantial proportion of people at risk of backward movement in the cascade or death. The probability of backward movement in the cascade from the final cascade stage of 13.7% demonstrates the importance of virologic monitoring and adherence support even for those on successful ART.

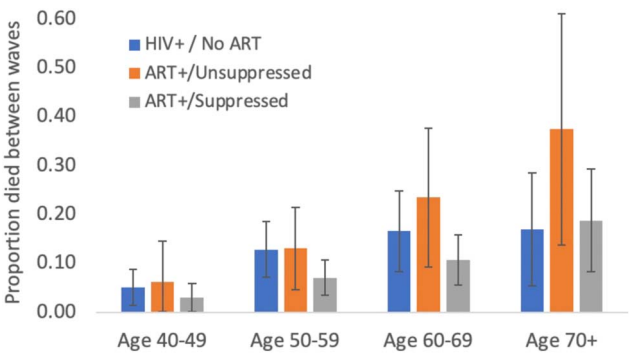

FIGURE 2. Proportion (and 95% confidence intervals) of the HIV+ population who died between wave 1 (2014–2015) and wave 2 (2018–2019). Stratified by age group and wave 1 cascade status. Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI), Mpumalanga Province, South Africa.

The probability of death was highest for those ART+/unsuppressed and among the oldest age groups. We demonstrate the sensitivity of the cascade findings to these mortality patterns among older adults. In the cross-sectional wave 2 cascade, we saw the highest prevalence of ART and viral suppression among those aged 70+, who were meeting or exceeding the 90-90-90 targets. Similarly, when we limited the models to those alive in wave 2, the oldest age group appeared to be doing the best in care. Yet when accounting for deaths, we saw that this positive result was driven by the very high death rate for those not in care or failing ART, especially among older age groups. In the models that accounted for death as a competing risk, positive associations between old age and cascade progression were reversed, and we saw evidence of equal or poorer cascade progression for 60–69- and 70+-year-olds relative to 40–49-year-olds. While the benefits of longitudinal care cascade analyses over cross-sectional analyses have been highlighted elsewhere,[21,32] our results confirm the limitations of cross-sectional cascades and further demonstrate the importance of assessing the impact of death in longitudinal cascade analyses, particularly for populations at high risk of death.

While we observed that older age and those failing treatment were at significant risk of poor outcomes, we did not see differences for most other sociodemographic groups examined. One exception was women, which showed evidence of better cascade progression in the competing risk

TABLE 3. Predictors of HIV Cascade Progression, Regression, and Treatment Initiation Among the HIV-Positive Population From Wave 1 (2014–2015) to Wave 2 (2018–2019)

	Risk Ratio (95% CI)	Subhazard Ratio (95% CI)
Cascade progression		
Female (ref: male)	1.08 (0.9, 1.29)	1.46 (1.09, 1.95)
Age group (ref: 40–49 yr)		
50–59	1.01 (0.81, 1.25)	0.83 (0.58, 1.17)
60–69	0.94 (0.73, 1.23)	0.70 (0.46, 1.06)
70+	1.20 (0.89, 1.64)	0.69 (0.4, 1.19)
Education cat (ref: none)		
Some primary (1–7 yr)	0.81 (0.66, 1)	0.86 (0.62, 1.2)
Some secondary (8–11 yr)	0.98 (0.78, 1.23)	1.00 (0.67, 1.48)
Wave 1 stage (ref: HIV+/no ART)		
ART+/unsuppressed	1.29 (1.09, 1.54)	1.39 (1.03, 1.88)
Cascade regression		
Female (ref: male)	0.62 (0.36, 1.05)	0.78 (0.42, 1.44)
Age group (ref: 40–49 yr)		
50–59	0.96 (0.52, 1.77)	0.93 (0.46, 1.87)
60–69	0.80 (0.39, 1.62)	0.84 (0.38, 1.86)
70+	0.69 (0.21, 2.26)	0.40 (0.11, 1.42)
Education cat (ref: none)		
Some primary (1–7 yr)	1.92 (1.07, 3.45)	1.60 (0.84, 3.03)
Some secondary (8–11 yr)	1.12 (0.52, 2.4)	1.02 (0.43, 2.44)
Wave 1 stage (ref: ART+/ unsuppressed)		
ART+/suppressed	2.99 (1.13, 7.93)	1.87 (0.66, 5.31)
Initiated treatment		
Female (ref: male)	1.00 (0.8, 1.25)	1.30 (0.92, 1.84)
Age group (ref: 40–49 yr)		
50–59	1.05 (0.79, 1.39)	0.79 (0.51, 1.21)
60–69	0.88 (0.62, 1.25)	0.69 (0.42, 1.15)
70+	1.38 (1.02, 1.86)	1.01 (0.56, 1.82)
Education cat (ref: None)		
Some primary (1–7 yr)	0.72 (0.55, 0.95)	0.8 (0.53, 1.2)
Some secondary (8–11 yr)	0.87 (0.65, 1.16)	0.97 (0.61, 1.54)

The first column displays adjusted risk ratios estimated from Poisson regression models for each cascade outcome among the population who was alive in wave 2. The second column displays the adjusted subhazard ratios from the Fine–Gray competing risk model accounting for death between waves as a competing risk.

analysis and some evidence of less cascade regression though not statistically significant. These results are consistent with what is often observed among younger adults in South Africa.[17] The predictive value of depression score on cascade regression in the sensitivity analysis is notable as a potential screening item to identify individuals in care but at risk of developing poor ART adherence. There was no discernible predictive value for cascade movement for education, wealth quintile, marital status, or cognitive score. Although the middle education group was associated with worse cascade outcomes in several models, there was no pattern of different outcomes between the highest and lowest education groups. These other predictors appeared to be of secondary importance in the context of the high-risk groups of older age, men, and those failing treatment, who should be targeted for HIV treatment and adherence programs. Our results can be interpreted partly as a success story of the HIV treatment program in South Africa reaching the rural adult population across socioeconomic groups.

Strengths of this study include the high participation in DBS in wave 1 and the population-based study population, which provided us with an analytic sample representative of the HIV-positive population in the area, regardless of whether an individual knew their HIV status. We avoided complications in the interpretation of self-reported responses about HIV status and treatment through the use of biomarkers. Full assessment of mortality regardless of wave 2 participation allowed us to form a complete picture of the risk of death in the population.

This study had several limitations, including a smaller sample size when examining groups stratified by age group and cascade stage, leading to wide confidence intervals in some stratified analyses. Second, the response rate to wave 2 DBS was lower than wave 1, but we were reassured that wave 2 DBS participation did not differ by wave 1 cascade stage or any sociodemographic characteristic other than sex. Adjusting for DBS participation through inverse probability weighting had minimal impact on results. Last, there are limitations in the use of the Fine and Gray competing risk model for this data, where a semicompeting risk model accounting for interval censoring would be more appropriate. However, these models would not converge given that there were only 2 time points of HIV cascade stage status observed per person in the currently available data. We believe the Fine and Gray model still demonstrates well the substantial impact that death can have on model results and interpretation of who is progressing in the cascade. Future analyses that incorporate additional rounds of data collection will allow us to perform more finely tuned statistical models.

Our results demonstrate the serious risk of poor cascade progression and death for the oldest HIV-positive adults, especially those aged 60 years and older who are not suppressed on treatment. The ongoing risk of cascade regression emphasizes the importance of sustained treatment monitoring even for those on successful ART in this population. We show how cross-sectional cascades that demonstrate the success of older adults in HIV treatment in South Africa can be deceptive when the context of a high death rate is not considered.

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