

Barriers to Care and 1-Year Mortality Among Newly Diagnosed HIV-Infected People in Durban, South Africa

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Background: Prompt entry into HIV care is often hindered by personal and structural barriers. Our objective was to evaluate the impact of self-perceived barriers to health care on 1-year mortality among newly diagnosed HIV-infected individuals in Durban, South Africa.

Methods: Before HIV testing at 4 outpatient sites, adults (≥18 years) were surveyed regarding perceived barriers to care including (1) service delivery, (2) financial, (3) personal health perception, (4) logistical, and (5) structural. We assessed deaths via phone calls and the South African National Population Register. We used multivariable Cox proportional hazards models

to determine the association between number of perceived barriers and death within 1 year.

Results: One thousand eight hundred ninety-nine HIV-infected participants enrolled. Median age was 33 years (interquartile range: 27–41 years), 49% were females, and median CD4 count was 192/μL (interquartile range: 72–346/μL). One thousand fifty-seven participants (56%) reported no, 370 (20%) reported 1–3, and 460 (24%) reported >3 barriers to care. By 1 year, 250 [13%, 95% confidence interval (CI): 12% to 15%] participants died. Adjusting for age, sex, education, baseline CD4 count, distance to clinic, and tuberculosis status, participants with 1–3 barriers (adjusted hazard ratio: 1.49, 95% CI: 1.06 to 2.08) and >3 barriers (adjusted hazard ratio: 1.81, 95% CI: 1.35 to 2.43) had higher 1-year mortality risk compared with those without barriers.

Conclusions: HIV-infected individuals in South Africa who reported perceived barriers to medical care at diagnosis were more likely to die within 1 year. Targeted structural interventions, such as extended clinic hours, travel vouchers, and streamlined clinic operations, may improve linkage to care and antiretroviral therapy initiation for these people.

Key Words: mortality, barriers to care, HIV/TB coinfection, South Africa

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INTRODUCTION

People living with HIV (PLWH) in sub-Saharan Africa who consistently receive antiretroviral therapy (ART) can achieve a life expectancy similar to that of the general population.^{1,2} South Africa is home to nearly 7 million PLWH, leading to more than 180,000 deaths annually.³ Despite having the largest ART program in the world, 58% of South Africans with HIV are not on treatment.⁴ Those diagnosed with HIV but not yet on ART experience high mortality rates, as do those initiated on ART but who are inconsistently in care.^{4–9}

We and others have documented high rates of loss to follow-up and mortality after HIV or tuberculosis (TB) diagnosis but before treatment initiation.^{5,10–17} Accurate ascertainment of mortality, particularly among those classified as lost to follow-up, is critical for evaluating the success

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of ART programs. Furthermore, studies evaluating risk of mortality in sub-Saharan Africa have only minimal clinical data assessing potential predictors of risk.⁸ However, contextual factors, poor emotional health, lack of social support, and competing needs at the time of diagnosis are likely to have an important effect on linkage to care and survival.^{18,19}

PLWH in sub-Saharan Africa cite barriers to care, including low perceived need (because of not feeling sick enough to require treatment), structural factors (eg, transportation), and health system characteristics (eg, long wait times for care), as reasons for delaying ART initiation.^{18,19} Our objective was to evaluate whether self-identified barriers are independent predictors of mortality among newly diagnosed PLWH in Durban, South Africa. We hypothesized that these issues are integrally related to each other and that reporting self-perceived barriers to care at the time of HIV diagnosis would be an independent predictor of 1-year mortality.

METHODS

Study Setting

This study includes participants from the Sizanani Trial (NCT01188941), a randomized controlled trial that examined the efficacy of health system navigation and short messaging service–based reminders to attend appointments and to retrieve test results on linkage to and retention in HIV/TB care. Because the randomized intervention did not lead to a difference in linkage to HIV care, TB treatment completion, or death between the 2 study arms, we analyzed both groups together as a single cohort in the current study. The trial is described in further detail elsewhere.^{20,21} Briefly, participants were enrolled between August 11, 2010, and January 16, 2013, at 4 sites in the greater Durban area of South Africa: 2 outpatient departments at McCord and St. Mary's Hospitals and 2 primary health clinics. The McCord Hospital had a President's Emergency Plan for AIDS Relief (PEPFAR)–funded ART clinic, Sinikithemba, which closed on June 15, 2012, because of loss of PEPFAR funding; enrollment stopped at McCord's outpatient department on August 6, 2012.²² St. Mary's Hospital served a poorer peri-urban population 20 km west of Durban; it similarly had a PEPFAR–funded ART clinic. Participants were also enrolled at Tshelimnyama and Mariannahill, 2 nurse-driven municipal primary health clinics within the service area of St. Mary's Hospital. At the beginning of this study, these municipal clinics offered HIV testing and referral to St. Mary's Hospital for ART initiation. As a part of South Africa's decentralization of HIV care, starting October 1, 2011, these clinics began to offer ART and ongoing HIV care.

Participants

We enrolled English- or Zulu-speaking adults, 18 years or older, voluntarily presenting for HIV testing and not previously known to be living with HIV. We excluded children and pregnant women from the study because they entered HIV care through a separate system that had more active linkage to care procedures. The current analysis focuses on participants who were found to be HIV infected

at enrollment. The study was approved by the McCord Hospital Medical Research Ethics Committee, St. Mary's Hospital Research Ethics Committee, University of KwaZulu-Natal Biomedical Research Ethics Committee, and Partners Institutional Review Board (Protocol 2011-P-001195, Boston, MA).

A bilingual (Zulu/English) research assistant approached patients awaiting an HIV test to determine interest in and eligibility for the study. Eligible willing participants provided written informed consent in their preferred language. Consent was followed by a 15- to 20-minute baseline questionnaire to obtain detailed demographics and psychosocial information regarding their emotional health, social support, and self-perceived barriers to engaging in medical care, after which HIV testing was completed.

Data Elements

Self-perceived Care Barriers

The questionnaire included 12 questions regarding perceived barriers to care during the previous 6 months.²³ We grouped these perceived care barriers into 5 categories that included (1) concerns about service delivery (eg, waiting too long to see a provider, not being treated with respect by clinic staff), (2) financial considerations (eg, inability to afford medication or transport), (3) personal health perception (eg, not being sick enough or being too sick), (4) logistical (eg, failure to get out of work, having care responsibilities for others), and (5) structural (eg, inability to access clinic because of clinic hours or transport, not knowing where to find care).

Emotional Health and Social Support

To gauge emotional health, we asked questions adapted from the 5-item Mental Health Inventory screening test and calculated a mental health composite (MHC) score.²⁴ The questionnaire also contained 13 questions about availability of social support. These questions incorporated 4 social support scales (emotional/informational, tangible, positive interaction, and affectionate) used to calculate the Social Support Index (SSI) from the Medical Outcomes Study.²⁵ The MHC and SSI scores were each averaged separately and converted into 2 separate scales from 0 to 100, with higher numbers corresponding to better emotional health and social support. Based on the previous literature,²⁶ we determined that an MHC ≤ 52 indicated a positive depression screen and we defined an SSI below the study sample median to be a lack of social support.²⁷

At the end of the questionnaire, participants provided their own contact information and that of a friend or family member for tracking purposes.

Outcome Ascertainment

Nine months post-enrollment, study staff members contacted the participants diagnosed with HIV at enrollment by phone for a brief interview. They also collected HIV test dates and results, CD4 counts, and the first 3 ART dispensing dates from electronic records and paper records at the study sites. We

obtained vital status from clinical records, patients, and friends/family members reached during follow-up phone calls. In addition, we verified mortality data within 12 months of enrollment using South African identification numbers through a crossmatch with the South African National Population Register, which encompasses ~90% of all deaths nationwide.⁸

The primary endpoint was death. The observation time was defined as the time from study enrollment until 12 months following baseline study visit. Events were restricted to the deaths that occurred within 12 months after the participants' baseline study interview. Study participants who did not reach the primary endpoint by 12 months were censored.

Analysis

We used descriptive statistics to characterize the study sample. We built Cox proportional hazards models to examine the association between number of self-perceived barriers to care and time to death. Preliminary unadjusted models were fit independently for each independent variable before adjusted models. Hazard ratios (HR) and 95% confidence intervals (CI) are reported for each model. Preliminary analyses showed that each individual barrier had similar impact on time to death [adjusted HR (aHR): 1.42–1.55]. Also, very few participants reported only a single barrier or a combination of specific barriers. Given the results of preliminary analyses, we built the final model considering a “number of self-perceived barriers to care” predictor (0 barriers, 1–3 barriers, >3 barriers from the “Self-perceived Care Barriers” listed above). The multivariable analysis adjusted for age, sex, CD4 count category, education, distance from clinic, and TB status at enrollment. Because the randomized intervention did not lead to a difference in linkage to HIV care, TB treatment completion, or death between the 2 study arms, we analyzed both groups together as a single cohort.²¹ We tested the proportional hazards assumption on the final adjusted model by creating a time-dependent covariate. An interaction term between number of self-perceived barriers to care and a function of survival time was included in the model. The time-dependent covariate was not significant ($P = 0.54$) supporting the proportionality assumption. We used an alpha of 0.05 to define the threshold for statistical significance. Analyses were performed using SAS software (version 9.3; SAS Institute, Cary, NC).

Role of the Funding Source

The funding source had no impact on the design and implementation of the study or data interpretation. The Data Coordinating Center investigators (S.M.C. and C.E.C.) and lead biostatistician (E.L.) had full data access.

RESULTS

Cohort Characteristics

Among 6536 people screened for the study, 4954 (76%) were eligible for enrollment and 4903 (99%) were

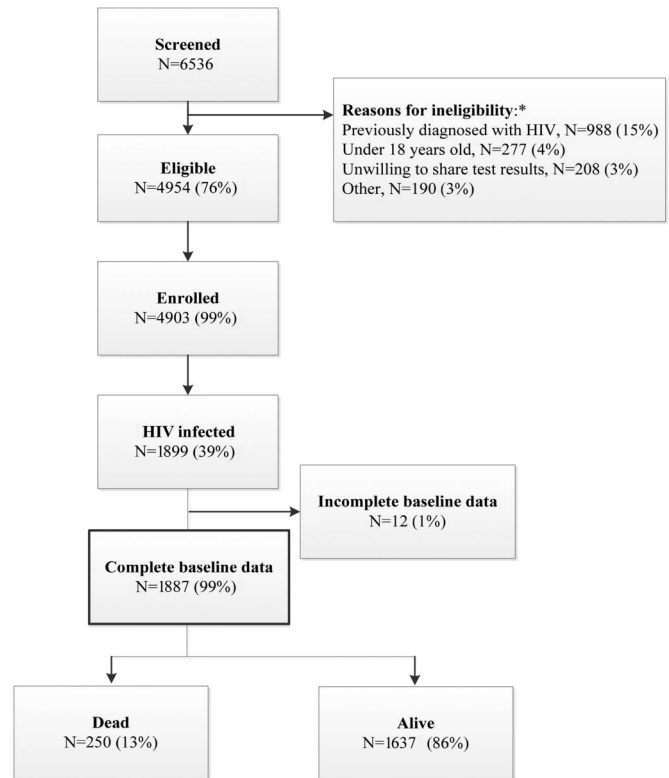


FIGURE 1. Participant flow. *Not mutually exclusive.

enrolled (Fig. 1). After enrollment, 1899 (39%) of the participants were tested and newly diagnosed with HIV. One thousand eight hundred eighty-seven (99%) of these participants had complete baseline survey data and were therefore included in this analysis. The median age was 33 years [interquartile range (IQR): 27–41 years], 928 (49%) were females, and the median CD4 count was 192 cells/ μ L (IQR: 72–346 cells/ μ L) with 848 (45%) presenting with CD4 <200 cells/ μ L (Table 1). Seven hundred seventy-four (41%) of the participants had more than a high school education, 1533 (81%) lived more than 5 km from a clinic, 253 (13%) reported at least one hospital stay in the previous year, and 521 (28%) had positive TB testing on the day of enrollment.

Mortality

By the end of the observation period, 250 (13%, 95% CI: 12% to 15%) participants had died. Participants who died were older (median age 37 years, IQR: 30–46 years) compared with those alive at study conclusion (median age 33 years, IQR: 27–40 years, $P < 0.0001$) (Table 1). Those who had baseline CD4 count <200 cells/ μ L had a higher risk of mortality than those with a baseline CD4 count >350 cells/ μ L (22% versus 3%, $P < 0.0001$). Risk of death was greater among men than women (16% versus 10%, $P = 0.0001$), among those with less than a high school education compared with those with at least some high school education (16% versus 9%, $P < 0.0001$), among those

TABLE 1. Cohort Characteristics of a Study of HIV Linkage to Care and Mortality in Durban, South Africa

	Overall, n = 1887	Dead at Study Conclusion, n = 250	Alive at Study Conclusion, n = 1637	P
Age, yrs				
Median (IQR)	33.0 (27–41)	37.0 (30–46)	33.0 (27–40)	<0.0001
Sex, n (%)				
Male	959 (51)	155 (16)	804 (84)	0.0001
Female	928 (49)	95 (10)	833 (90)	
CD4 count, cells/ μL, n (%)				
0–199	848 (45)	187 (22)	661 (78)	<0.0001
200–350	400 (21)	24 (6)	376 (94)	
>350	404 (21)	11 (3)	393 (97)	
Education, n (%)				
Some high school or greater	774 (41)	72 (9)	702 (91)	<0.0001
Primary school or less	1112 (59)	178 (16)	934 (84)	
Marital status, n (%)				
Never married	1537 (82)	188 (12)	1349 (88)	0.0240
Currently married	265 (14)	47 (18)	218 (82)	
Divorce/separated/widowed	85 (5)	15 (18)	70 (82)	
Distance from clinic, n (%)				
Less than 5 km	354 (19)	30 (8)	324 (92)	0.0033
At least 5 km	1533 (81)	220 (14)	1313 (86)	
Randomization group, n (%)				
Standard of care	927 (49)	119 (13)	808 (87)	0.6044
Intervention	960 (51)	131 (14)	829 (86)	
Hospital stays, n (%)				
1 or more	253 (13)	68 (27)	185 (73)	<0.0001
None	1634 (87)	182 (11)	1452 (89)	
Positive for TB at enrollment, n (%)				
No	1366 (72)	146 (11)	1220 (89)	<0.0001
Yes	521 (28)	104 (20)	417 (80)	

living more than 5 km from the enrollment site compared with those living within 5 km of the site (14% versus 8%, $P = 0.0033$), and among those who had a hospital stay in the previous year compared with those who did not (27% versus 11%, $P < 0.0001$). Twenty percent of participants who had TB at enrollment died compared with 11% of those who did not have TB at enrollment ($P < 0.0001$). We did not find a statistically significant or clinically relevant relationship between emotional health or social support and mortality (Table 2). Those who reported >3 self-perceived barriers to care were twice as likely to die compared with those who

reported 3 or fewer barriers to care (22% versus 11%, $P < 0.0001$).

Self-Reported Barriers to Care, Mental Health, and Social Support at Enrollment

With respect to the 5 self-perceived care barrier categories, 566 (30%) reported service delivery barriers to care, 423 (22%) reported financial barriers to care, 596 (32%) reported personal health barriers to care, 334 (18%) reported logistical barriers to care, and 540 (29%) reported structural barriers to care (Table 2). Three hundred seventy participants (20%) reported 1–3 self-perceived barriers to care and 460 (24%) reported >3 barriers. Four hundred fifty (24%) had a MHI score ≤ 52 , indicative of a positive depression screen, and 924 (49%) had a social support score less than the median (Table 2).

TABLE 2. Emotional Health, Social Support, and Perceived Care Barriers at Baseline Among a Cohort of Newly Diagnosed HIV-Infected Participants in Durban, South Africa

	Overall, n = 1887	Dead at Study Conclusion, n = 250	Alive at Study Conclusion, n = 1637	P
MHI ≤ 52 , n (%)				
No	1437 (76)	181 (13)	1256 (87)	0.1349
Yes	450 (24)	69 (15)	381 (85)	
SSI <Median (67), n (%)				
No	963 (51)	126 (13)	837 (87)	0.8297
Yes	924 (49)	124 (13)	800 (87)	
Service delivery barriers, n (%)				
No	1321 (70)	139 (11)	1182 (89)	<0.0001
Yes	566 (30)	111 (20)	455 (80)	
Financial barriers, n (%)				
No	1464 (78)	159 (11)	1305 (89)	<0.0001
Yes	423 (22)	91 (22)	332 (78)	
Personal health barriers, n (%)				
No	1291 (68)	136 (11)	1155 (89)	<0.0001
Yes	596 (32)	114 (19)	482 (81)	
Logistical barriers, n (%)				
No	1553 (82)	184 (12)	1369 (88)	0.0001
Yes	334 (18)	66 (20)	268 (80)	
Structural barriers, n (%)				
No	1347 (71)	143 (11)	1204 (89)	<0.0001
Yes	540 (29)	107 (20)	433 (80)	
No. perceived barriers, n (%)				
No barriers	1057 (56)	97 (9)	960 (91)	<0.0001
1–3 barriers	370 (20)	54 (15)	316 (85)	
More than 3 barriers	460 (24)	99 (22)	361 (78)	

MHI, Mental Health Inventory; SSI, Social Support Index.

TABLE 3. Socioeconomic Predictors of Mortality Among HIV- or TB-Infected Patients in Durban, South Africa

	Unadjusted HR (95% CI)	P	aHR (95% CI)	P
No. perceived barriers				
No barriers	1.00		1.00	
1–3 barriers	1.68 (1.20 to 2.34)	0.003	1.49 (1.06 to 2.08)	0.020
More than 3 barriers	2.54 (1.92 to 3.37)	<0.001	1.81 (1.35 to 2.43)	<0.001
Age at enrollment			1.02 (1.01 to 1.04)	<0.001
Male sex			1.34 (1.03 to 1.73)	0.030
CD4 count				
>350 cells/ μ L			1.00	
200–350 cells/ μ L			1.99 (0.97 to 4.11)	0.060
0–199 cells/ μ L			7.13 (3.85 to 13.19)	<0.001
<High school education			1.31 (0.98 to 1.76)	0.070
\geq 5 km from clinic			1.37 (0.92 to 2.04)	0.130
TB at enrollment			1.21 (0.93 to 1.58)	0.160

Predictors of Mortality: Results From Multivariable Analyses

We found that participants who identified 1–3 self-perceived barriers to care (aHR: 1.49, 95% CI: 1.06 to 2.08) and >3 barriers (aHR: 1.81, 95% CI: 1.35 to 2.43) had higher risk of 1-year mortality compared with those with no self-identified barriers (Table 3).

DISCUSSION

Among 1887 PLWH enrolled in outpatient departments in Durban, South Africa, 250 (13%) died within 1 year of enrollment. Self-reported barriers to health care were common, with 44% of the participants reporting at least one barrier to care and 24% reporting more than 3 barriers to care. These self-reported barriers were strong independent predictors of mortality, with a higher number of reported barriers correlating with a greater risk of mortality. After adjusting for demographic factors (ie, age, sex, and education) and clinical factors (ie, CD4 count and TB status at enrollment) known to be associated with mortality in PLWH,^{28,29} participants who reported more than 3 barriers were nearly twice as likely to die within 1 year of diagnosis compared with those who reported no barriers. Screening for barriers is a distinctive and novel method for identifying mortality risk when combined with additional clinical tests, such as CD4 count and concomitant TB screening.

Personal health barriers, service delivery barriers, and structural barriers were the most commonly perceived barriers to care. Many patients presented to HIV testing with incongruent perceptions of their health status, believing that they were too well or not well enough to receive care. Our results show that these incongruent perceptions can contribute to an increased risk of mortality. Other research has revealed that some patients, specifically those who feel healthy, perceive that ART initiation is linked with side effects and an overall decline in physical and mental health.³⁰ As such, adequate counseling at the time of HIV testing and after diagnosis may improve linkage to care and ART initiation for these patients; for example, psychological counseling and adherence education were successful in improving TB treatment adherence.³¹ Furthermore, participants who felt

that they were not treated with respect by clinic staff or that they had to wait too long to receive care were also at increased risk of death. Streamlined clinic operations and improvements in staff training and workload may help improve clinic operations and engagement in HIV care.^{32,33} Many participants found it difficult to seek out care, as they found clinic operating hours and transportation to be inconvenient. Travel vouchers and extended clinic operating hours could help link these patients to care.^{34,35} Although less frequently reported, a substantial number of participants reported financial barriers and logistical barriers (eg, inability to get days off from work or care responsibilities for others) to care. Travel vouchers and extended clinic operating hours may improve engagement in care for these participants.

A strength of our study was the ability to confirm vital status with the South African National Population Register. This allowed a comprehensive assessment of mortality, especially of those lost to follow-up during the study period. In sub-Saharan Africa, a substantial proportion of patients living with HIV are lost to follow-up during the process of linking to care and after ART initiation.^{36,37} Furthermore, patients who become lost to follow-up are at high risk of mortality compared with patients who remain in care.^{38,39} Therefore, studies with significant attrition in their patient population may be underestimating mortality; using the South African National Population Register, which accounts for ~90% of deaths nationally,⁸ can mitigate this issue.

A potential explanation of higher mortality in patients who report barriers may be related to adherence to HIV care (ie, ART and follow-up appointments). Previous studies have established associations between suboptimal adherence and perceived poor service delivery, a lack of financial means for transport, patient perception that he or she is feeling well, responsibilities to care for dependents, and inconvenient clinic hours.^{30,40–45} Suboptimal adherence to HIV care is directly linked to poor virologic outcomes and mortality.^{46,47} Thus, it is possible that participants who reported barriers did not adhere to HIV care, as a mechanism leading to increased risk of death. Although we had previously found poor emotional health to be associated with late presentation with HIV and failure to obtain a CD4 count after diagnosis,^{27,48} we

did not find an association between emotional health or social support and mortality in the current study. Although social support has been associated with reduced distress in PLWH,⁴⁹ its impact on ART adherence has been mixed^{50–53}; poor emotional health has more frequently been associated with nonadherence and accelerated disease progression, although not uniformly.^{54–56} Because barriers were identified before knowledge of HIV status, it is unclear how the new HIV diagnosis itself would affect specific self-identified barriers or whether the number of barriers is a proxy for another factor associated with higher mortality.

These findings should be taken in light of several limitations of the study. First, we did not have data related to opportunistic infections (other than TB) or noninfectious comorbidities that could be associated with mortality. It is possible that a higher prevalence of these comorbidities could have been present in participants who reported barriers to care. Second, we were unable to determine the cause of death for participants. Therefore, characterizing all these deaths as HIV related may lead to an overestimate of HIV-related death. However, regardless of the cause of death, it is likely that the barriers characterized in this study are barriers to obtaining any health care. As such, receiving clinical care and/or health monitoring would likely be beneficial in reducing mortality. Third, women comprised 49% of the cohort, less than in typical South African HIV cohorts. This may reflect that pregnant women were excluded from the study and that we enrolled participants before HIV testing. Fourth, we were unable to determine the proportion of those “in care” before death. Because outcomes were ascertained at study sites only, the proportion on ART in the parent study may have been an underestimate if participants sought care elsewhere. Finally, the instruments used to predict mortality in this study may not be readily transferable to routine clinical care. An important next step in this work will be to develop a short clinically practical screening instrument that can be used to stratify risk before HIV testing, as has been done with alcoholism (CAGE) and depression (PHQ-9, HADS, WBI-5, WHO-5, etc.).^{57–59}

In conclusion, we found that newly diagnosed HIV patients’ perceived barriers to care predict mortality risk within 1 year. Those reporting multiple perceived barriers to medical care at the time of diagnosis are nearly twice as likely to die within 1 year compared with those without barriers. Screening for barriers to care at HIV diagnosis can help identify patients for targeted interventions that may help link them to care and ART initiation, subsequently reducing their likelihood of death. Targeted structural interventions, such as extended clinic hours, travel vouchers, and more streamlined clinic operations, may improve outcomes for high-risk patients. The high prevalence of patients who report multiple barriers to care underlines the urgency for developing interventions that will alleviate these barriers and attenuate mortality.

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