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Determinants of time from HIV infection to linkage-to-care in rural KwaZulu-Natal, South Africa

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Abstract

Objective—To estimate time from HIV infection to linkage-to-care and its determinants.

Linkage-to-care is usually assessed using the date of HIV diagnosis as the starting point for exposure time. However, timing of diagnosis is likely endogenous to linkage, leading to bias in linkage estimation.

Design—We used longitudinal HIV serosurvey data from a large population-based HIV incidence cohort in KwaZulu-Natal (2004–2013) to estimate time of HIV infection. We linked these data to patient records from a public-sector HIV treatment and care program to determine time from infection to linkage (defined using the date of the first CD4⁺ cell count).

Methods—We used Cox proportional hazards models to estimate time from infection to linkage and the effects of the following covariates on this time: sex, age, education, food security, socioeconomic status, area of residence, distance to clinics, knowledge of HIV status, and whether other household members have initiated antiretroviral therapy.

Results—We estimated that it would take an average of 4.9 years for 50% of HIV seroconverters to be linked to care (95% confidence intervals: 4.2–5.7). Among all cohort members who were linked to care, the median CD4⁺ cell count at linkage was 350 cells/μl (95% confidence interval:

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Conflicts of interest

There are no conflicts of interest.

330–380). Men and participants aged less than 30 years were found to have the slowest rates of linkage-to-care. Time to linkage became shorter over calendar time.

Conclusion—Average time from HIV infection to linkage-to-care is long and needs to be reduced to ensure that HIV treatment-as-prevention policies are effective. Targeted interventions for men and young individuals have the largest potential to improve linkage rates.

Keywords

care continuum; CD4⁺ cell count; HIV/AIDS; linkage-to-care; sex; treatment cascade; treatment-as-prevention

Introduction

Antiretroviral therapy (ART) improves patient outcomes, increases life expectancy, and reduces population-level transmission of HIV [1–3]. Timely linkage-to-care among the newly infected is important to maximize such individual-level and population-level benefits. The time from infection to linkage becomes especially relevant as HIV programs move from treatment to treatment-as-prevention. For treatment-as-prevention to achieve maximum success in reducing population-level incidence, linkage-to-care should ideally occur immediately following HIV infection for rapid ART initiation. In practice, however, several studies have found low linkage levels among HIV-infected populations in sub-Saharan Africa [4–7]. A recent trial in rural KwaZulu-Natal (ANRS 12249) showed that low linkage-to-care was likely responsible for the failure to reduce population incidence through a community-based HIV treatment-as-prevention intervention [8, 9].

Although earlier evidence demonstrated substantial losses to follow-up after ART initiation in several settings [4, 10, 11], it has recently become clear that the losses in the early phases of the HIV care continuum are even more severe [6, 7, 12–17]. Most of this research has relied on data from provider-initiated counseling and testing and, to a lesser extent, individuals using voluntary counseling and testing (community-based or home-based) [5]. Few studies have used population-based estimates of engagement in care [6–8]. Further, all the prior studies on linkage-to-care have in common that time to linkage was examined using the date of diagnosis, rather than the date of infection, as the starting point. Despite the urgency to improve early testing and treatment, substantial proportions of HIV-positive populations in sub-Saharan Africa still test late in the course of HIV disease [18]. Testing and treatment-seeking behaviors might be partly driven by perceived health status, and examining the determinants of time to linkage-to-care from the date of infection, instead of date of HIV diagnosis (i.e., receipt of a first HIV-positive test), can substantially advance our understanding of barriers to linkage — because the date of HIV diagnosis is likely endogenous to linkage rates. In other words, those who get diagnosed earlier are on average also more likely to link-to-care rapidly. Previous estimates of determinants of linkage-to-care are therefore potentially biased.

In this study, we aim to estimate the time from HIV infection to linkage, as well as the determinants of this time. We use data from one of the largest population-based HIV incidence cohorts in Africa and link these data to patient records from the local public-sector

HIV treatment and care program. Improving our understanding of the factors influencing time from HIV infection to linkage-to-care can substantially improve our ability to design and target interventions aimed at addressing barriers to early linkage and treatment initiation. Such interventions will be especially important for the success of HIV treatment-and-prevention policies and the attainment of the UNAIDS 90–90–90 targets [19].

Methodology

Study population

Since 2000, the Africa Health Research Institute (AHRI) has operated a longitudinal population health surveillance in rural KwaZulu-Natal (uMkhanyakude district), South Africa [20]. Nested within the population health surveillance is one of Africa's largest population-based HIV incidence cohorts. The surveillance covers an area approximately 440 km² in size, encompassing a population of 87 000 individuals (75 000 residents and 12 000 nonresidents). The surveillance was designed to capture the complex and interwoven health, social, and demographic dynamics of a poor rural Southern African population. In 2011, HIV prevalence in the adult population (15–49 years) living in the surveillance area was 29%, and ART coverage of all HIV-positive adults was 31% [21].

The AHRI population health surveillance collects information on all individuals who live in the surveillance area. The surveillance is conducted in two separate data collection approaches. First, every 4 months, a household survey is administered to a key household informant to gather data on attributes and events regarding the household and individual household members [20]. Second, every year, trained field workers collect data through individual interviews, during which confidential HIV testing is offered to each adult. Eligibility criteria for the HIV serosurveys from 2003 to 2007 were all women aged 15–49 years and men aged 15–54 years. After 2007, HIV testing was administered to all individuals aged 15 years and over.

ART became available in the area shortly after the national rollout in 2004 [22]. At that time, HIV-positive individuals could only get access to treatment from the surveillance area's hospital clinic. ART delivery has subsequently been scaled up to 17 public-sector primary-care clinics in the Hlabisa subdistrict of uMkhanyakude district; six of these clinics are located in the AHRI surveillance area [23]. The *Hlabisa HIV Treatment and Care Program* provides free HIV testing and counseling, condoms, and ART. In this study, linkage-to-care was operationalized as having a first CD4⁺ cell count (the required diagnostic criterion to assess ART eligibility during the time of this study) in the local HIV treatment and care program [22]. Further details on both the AHRI population health surveillance, the data collection in the HIV treatment and care program, and the data linkage between these two databases can be found elsewhere [1, 20, 22, 24].

Procedures and variables

Recent HIV seroconverters (aged 15 years or older) were identified as all repeated HIV testers who had at least one positive HIV test and at least one prior negative HIV test in the population-based HIV incidence cohort. Slightly modifying the approach used by

Vandormael *et al.* [25], the date of HIV infection was proxied by estimating the date of HIV seroconversion. Given the time lag between subsequent serosurveys, we could not precisely ascertain the date of HIV seroconversion but it must have occurred in the interval between the last negative HIV test and the first positive HIV test in the HIV incidence cohort. For some individuals, the date of the first CD4⁺ cell count in the HIV treatment and care program preceded the first positive HIV test in the incidence cohort. In those cases, we used the date of the first CD4⁺ cell count to demarcate the HIV seroconversion interval. For our main analysis, we randomly assigned the date of infection between the last HIV-negative test and the first HIV-positive test, or first CD4⁺ cell count test, whichever occurred first. A total of 10 datasets with random imputation of HIV infection dates were constructed in that way. Random imputation allows us to propagate the uncertainty associated with the unobserved HIV infection dates to our results. For presentation of baseline descriptive statistics, we used the midpoint date between the last negative HIV test and first positive HIV test (or between the last negative HIV test and the first CD4⁺ cell count test) for simplicity (hereafter referred to as ‘midpoint imputation’). Summary of the descriptive statistics of the 10 imputed datasets can be found in Supplemental materials (Table S1, <http://links.lww.com/QAD/B53>). Infections occurring before August 2004 were excluded as ART had not been rolled out prior to that date, and the individuals were hence not eligible for the outcome (i.e., linkage-to-care). Seroconverters in the population-based HIV incidence cohort were linked to the HIV treatment and care program database, using the South African identification number (or, if the identification number was missing, full names, sex, and birth date). Linkage-to-care was identified and defined as the first CD4⁺ cell count test performed in the HIV treatment and care program.

We estimated the determinants of time to linkage-to-care using time-varying covariates. The dynamic nature of the AHRI population cohort is captured through exposure episodes. If an individual changes residency or migrates inside or outside of the surveillance area, a new exposure episode is created for that period. Exposure episodes are thus of variable lengths, and seroconverters can only live in one residence at a time (but multiple household memberships are allowed). All individuals who migrated out of the surveillance area, even temporarily, were censored on their emigration day. If an individual’s infection date was estimated to have occurred while outside of the surveillance area, this person was excluded. Hence, the 10 randomly imputed datasets may have slightly different sample sizes and person-time of follow-up. If seroconverters were not found to be linked to HIV care, they were censored on their last day of follow-up, the date they died, or January 2014 — whichever occurred first.

The main outcome of this study is time from HIV infection to linkage-to-care. The only time-invariant variables considered are sex, knowledge of HIV status at baseline (i.e., first positive test), and the calendar year of infection. Time-varying variables are age, area of residence, socioeconomic status (asset-based index categorized into quartiles, among seroconverters, using the first axis of a principal component analysis of 21 household assets), education level, whether one’s household members are receiving ART, and the Euclidian distance to the closest health facility where ART is provided. As some of the exposure episodes are retrospectively constructed (i.e. they are within two survey dates), we assigned them on the basis of the closest survey date (but not more than 1 year after the

beginning of the exposure episode). Household-level variables were attributed on the basis of household residence and closest survey date. For missing education level values, we imputed that value using the previously reported education level, if an individual was aged 19 years or older and had at least one observation with information on education level.

Statistical analyses

Time from HIV infection to linkage-to-care was first explored using Kaplan-Meier estimates of the survival curve. CD4⁺ cell counts at linkage, stratified by time to linkage-to-care, were also examined. Cox proportional hazards models were then used to estimate the effect of the different variables on time to linkage-to-care. Covariates with missing observations were retained in the analysis using the missing indicator method [26]. We present results for univariable and multivariable models. Because the question about knowledge of HIV status was not part of the questionnaire in 2004 and 2005, the multivariable model only included observations from individuals who seroconverted from 2006 onward. The method of Grambsch and Therneau [27], based on the scaled Schoenfeld residuals, was used to test that all variables met the proportional hazards assumption. Because some covariates failed that test, we stratified the survival analyses using the calendar year of HIV infection. All analyses were performed individually on the 10 imputed datasets, and results were combined with Rubin's rule [28] using the R statistical software (R Core Team, Vienna, Austria) [29]. The R 'survival' package [30] was used to fit the Cox proportional hazards models.

Ethics

All respondents provided informed consent. The *Biomedical Research Ethics Committee* of the University of KwaZulu-Natal granted ethical approval for data collection.

Results

Among individuals who seroconverted between August 2004 and December 2013, 10 were found to have been linked to care before their last negative HIV test and were therefore excluded from our analyses. As they were potentially outside of the *Hlabisa Treatment and Care Program's* catchment area, individuals not recorded to be in the surveillance area at their estimated time of HIV infection were also excluded. Hence, and depending on the randomly imputed seroconversion dates, between 1713 and 1779 recent seroconverters contributed between 4582 and 4818 person-years of follow-up to our inferences. Results from the midpoint imputation and the randomly imputed datasets differed principally with regard to the uncertainty around the different estimates but not regarding the effect size estimates (refer to Supplemental material Tables S2–S4 and Figs. S1 and S2, <http://links.lww.com/QAD/B53>).

Baseline characteristics of the recent HIV seroconverters are presented in Table 1. The great majority (77%) of recent seroconverters were women, and over 70% had some or completed secondary education. Mean age at HIV infection was 27 years. Most recent seroconverters did not have members of their household who had initiated ART. A total of 63% of seroconverters responded that they were aware of their HIV status at the time of their first

positive HIV test. The median time between last the negative test and the first positive HIV test was 2.0 years [interquartile range (IQR): 1.1–3.2 years; with a maximum of 10 years].

Averaging over the imputed datasets, the median follow-up time was 2.2 years (IQR: 1.1–3.9), and only 14% of those who were followed up for a minimum of 12 months had a CD4⁺ cell count test performed within that time period (this percentage rises to 29% 2 years after HIV infection). At linkage, the median CD4⁺ cell count was 350 cells/μl [95% confidence interval (CI): 330–380] (Table 2). HIV seroconverters that were linked to care in less than 1 year had a higher median CD4⁺ cell count (370 cells/μl; 95% CI: 320–410) than those that linked more than 5 years after infection (290 cells/μl; 95% CI: 160–430). A total of 40 of the recent HIV seroconverters died before being linked to care after a median follow-up time of 3.0 years (IQR: 1.9–4.7) after infection. The pooled Kaplan-Meier estimates of time from HIV infection to linkage-to-care are presented in Fig. 1. From these estimates we calculate that it would have taken an average of 4.9 years (95% CI: 4.2–5.7) for 50% of seroconverters to be linked to care (Table 3). Time to linkage-to-care differed by sex: it took about 1.7 years (95% CI: 1.5–2.0) for 25% of women to link to care versus 3.4 years (95% CI: 2.4–4.4) for men. Time to linkage-to-care also decreased with calendar time with 25% of seroconverters linking in 3.7 years (95% CI: 2.4–5.0) for those who acquired their infection in 2004 to 1.4 years (95% CI: 0.6–2.2) for those who did so in 2010.

In univariable analyses, the main determinants of time to linkage-to-care were sex, age, education level, and knowledge of HIV status from previous testing (Table 4). As compared with women, men had roughly half the hazard rate of being linked to care [adjusted hazard ratio (aHR) = 0.49; 95% CI: 0.37–0.64]. Seroconverters in the 40–49 years of age category had a hazard rate of being linked to care that was 54% higher (95% CI: 14–108%) compared with seroconverters aged 15–29 years old. Individuals with some or completed secondary education had a lower hazard rate of being linked to care than those with a year or less of education (aHR = 0.63; 95% CI: 0.39–1.00). Household comemberships with individuals who had previously initiated ART increased the hazard rate of being linked to care by 23% (95% CI: –2 to 55%), but the CIs of this estimate crossed the null. Finally, the hazard rate of being linked to care for individuals who were aware of their HIV status from previous testing was 35% (95% CI: 9–68%) higher than those who were unaware of their status or who refused to answer the survey question.

Discussion

We estimated that it has taken an average of 4.9 years for 50% of seroconverters to be linked to care during 2004–2013. Comparisons with other empirical data is difficult because time to linkage-to-care has been defined in the past using HIV diagnosis as the starting point. To the best of our knowledge, this study is the first to measure time to linkage-to-care using a direct estimate of the HIV infection date as a starting point. Our empirical estimate of time from HIV infection to linkage is highly policy-relevant because it is a minimum bound on the length of time during which HIV-positive individuals can transmit HIV before the transmission risk is potentially eliminated through HIV treatment [31]. Our results indicate that substantial linkage improvements will be needed to maximize population-level benefits of both HIV treatment and HIV treatment-as-prevention.

With close to a quarter of patients dying within their first year on ART [31], not only is earlier initiation required, but also earlier diagnosis. We estimated that the median CD4⁺ cell counts at linkage-to-care was of 370 cells/μl for individuals linking within 1 year of HIV infection and 290 cells/μl for those linking 5 years or more after HIV infection. Several reasons could explain that the median CD4⁺ cell count for individuals linking to care within 1 year was below 500 cells/μl. First, the observed time lag between the last negative and first positive HIV test had a median of 2 years. Nondifferential misclassification of the date of HIV infection could have biased our results toward the overall median CD4⁺ cell count of individuals linking to care. Second, rates of decline in CD4⁺ cell counts follow an unobserved distribution that we can estimate only among those individuals who linked to care. If linkage is a function of health status, which has been shown in other studies [15, 32], those with rapid disease progression and lower CD4⁺ cell counts will link to care faster. The resulting median CD4⁺ cell count since time from HIV infection is thus likely lower among those who have linked to care than the median CD4⁺ cell count since time from HIV infection among all HIV-positive people.

In this mostly poor and rural population, rates of linkage-to-care were twice as high for women than for men, substantiating previous research [5, 6, 33]. Age was another important determinant of time to linkage-to-care. HIV seroconverters in the 40–49-year-old range had the highest rates of linkage-to-care. Having other household members who previously initiated ART tended to reduce time to linkage-to-care. This finding provides some limited evidence that family and social exposure to HIV treatment could facilitate linkage and ART uptake.

Diagnosing HIV is the first and a necessary step on the HIV treatment cascade. We estimated that 63% of individuals were aware of their HIV status at their first positive HIV test during the annual serosurveys, and HIV status knowledge was a predictor of linkage-to-care. Yet, linkage-to-care was low and delayed in this cohort of HIV seroconverters. This finding could be partly due to the clinical eligibility criteria for ART applied from 2004 to 2010. During those years, individuals with CD4⁺ cell count less than 200 cells/μl were eligible for ART initiation, while individuals with higher CD4⁺ counts were not eligible unless they suffered from additional morbidities. Compounding the slow linkage are the previously described low pre-ART retention rates [16] and high disengagement from care in this cohort [11]. These findings are corroborated by those from the first phase of the ANRS 12249 treatment-as-prevention trial, conducted in the same district as this study, which showed that delays in linkage-to-care can compromise the population-level effectiveness of treatment-as-prevention [8, 9]. Preliminary results from the trial suggest that treatment-as-prevention did not substantially reduce HIV incidence because ART coverage in both arms of the trial were similar [8, 9]. The likely reason for the similarity in ART coverage was slow linkage-to-care among people in early HIV infection stages (who would have been eligible for ART in the intervention but not in the control arm of this trial).

Great challenges will need to be overcome to maximize the public health benefits of ART in settings such as the community in which this study took place. Several potential solutions have been proposed, from point-of-care CD4⁺ testing with home-based counseling and testing to financial incentives [34, 35]. Yet, the quality of evidence for these proposed

interventions is low, and interventions often only target a single point in the HIV care continuum [34–36]. More health systems research is needed into multipronged approaches that would mitigate the individual, community, and structural barriers that delay linkage-to-care.

The current study has several limitations. First, the exact date of HIV infection remains unknown and was estimated on the basis of individuals who repeatedly participated in the annual population HIV surveillance surveys. Yet, random imputation of infection dates, resulting in nondifferential measurement errors in time-to-event, generally introduces only small bias in the hazard ratio estimates [37, 38]. Further, we randomly imputed 10 datasets, and the summary estimates we present included this uncertainty. Second, we cannot completely rule out that some of the recent HIV seroconverters in this population sought care outside of the local *Hlabisa Treatment and Care Program*, which was the source for our data on linkage. Nevertheless, it is unlikely that the proportion of HIV-positive individuals accessing ART outside of this public-sector program is higher than a few percentage points [24].

An important strength of this research is the use of population-based data from one of Africa's largest population-based HIV incidence cohorts, to estimate the time from HIV infection to linkage-to-care. Such estimates are likely more representative of the HIV-positive population than those derived from facility-based data. Another important strength of our study is that we use a cohort of repeated HIV testers to estimate the HIV infection date, which is more accurate than other approaches to estimate this date, such as back-calculation of the seroconversion date based on CD4⁺ cell counts at ART initiation or estimations based on tests for recent HIV infections [39, 40]. Finally, we addressed a key limitation of the extant literature on the determinants of linkage-to-care. Because HIV testing and diagnosis can, at least partly, be a function of health status and treatment-seeking behavior, using the date of diagnosis in survival analysis is likely to lead to substantial endogeneity bias. Our approach, based on the date of HIV infection rather than the diagnosis date, corrects for this bias.

In conclusion, large reductions in the time from HIV infection to linkage-to-care are required to realize the full potential of HIV treatment and HIV treatment-as-prevention in improving population health. Novel approaches to encourage HIV testing and ART uptake are urgently needed to achieve such reductions, in particular for men and young adults [41].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Pooled Kaplan-Meier estimates of time from HIV infection to linkage-to-care in rural KwaZulu-Natal, South Africa (2004–2013) for (a) all seroconverters and (b) stratified by sex.

Table 1

Baseline characteristics of recent seroconverters (using midpoint imputation; $N = 1733$) residing in the AHRI surveillance area, South Africa (2004–2013).

Variables	Mean (SD) or total (%)
Sex	
Female	1333 (76.9%)
Male	400 (23.1%)
Age (years)	26.8 (10.5)
Education level	
None or less than 1 year	103 (5.9%)
Some or completed primary	269 (15.5%)
Some or completed secondary	1289 (74.4%)
Missing	72 (4.2%)
Socioeconomic status	
Poorest	374 (21.6%)
Poor	435 (25.1%)
Rich	488 (28.2%)
Richest	435 (25.1%)
Missing	1 (0.1%)
Food security	
Never (or some months) missed meals	1675 (96.7%)
Missing meals almost every month	47 (2.7%)
Missing	11 (0.6%)
Uptake of ART by household members	
No household members on ART	1463 (84.4%)
At least one household member on ART	270 (15.6%)
Knowledge of HIV status ^a	
Aware	917 (63.3%)
Unaware/refused	537 (36.7%)
Area of residence	
Urban	53 (3.1%)
Periurban	619 (35.7%)
Rural	1061 (61.2%)
Distance to closest health facility (km)	6.0 (9.1)
Calendar year of HIV infection	
2004	81 (4.7%)
2005	198 (11.4%)
2006	240 (13.8%)
2007	259 (14.9%)
2008	262 (15.1%)
2009	207 (11.9%)
2010	180 (10.4%)

Variables	Mean (SD) or total (%)
2011	153 (8.8%)
2012	129 (7.4%)
2013	24 (1.4%)

AHRI, Africa Health Research Institute; ART, antiretroviral therapy.

^aThe question about knowledge of HIV status from previous testing was not asked in 2004 and 2005 (279 seroconverters were excluded).

Table 2

Median CD4⁺ cell count (cells/μl) at linkage, stratified by linkage time since HIV infection, with 95% bootstrapped confidence intervals.

Time from HIV infection to linkage-to-care	Median CD4 ⁺ cells/μl (95% CI ^a)
Less than 1 year	370 (320–410)
Between 1 and 2 years	380 (340–420)
Between 2 and 3 years	360 (290–430)
Between 3 and 4 years	310 (230–390)
Between 4 and 5 years	320 (220–410)
More than 5 years	290 (160–430)
Overall	350 (330–380)

^a95% CI, 95% confidence interval. These are based on 9999 bootstrap replicates.

Table 3

Time from HIV infection (years) to linkage to care stratified by sex and calendar year of HIV infection.

Characteristics	Time from HIV infection for 25% of seroconverters to link to care (95% CI ^a)	Time from HIV infection for 50% of seroconverters to link to care (95% CI ^a)
Sex		
Females	1.7 (1.5–2.0)	4.2 (3.7–4.6)
Males	3.4 (2.4–4.4)	NA ^b
Calendar year of HIV infection		
2004	3.7 (2.4–5.0)	6.1 (3.7–8.5)
2005	3.1 (2.4–3.8)	5.6 (4.2–7.1)
2006	2.3 (1.7–2.9)	4.6 (3.3–6.0)
2007	1.6 (1.0–2.3)	4.0 (2.7–5.4)
2008	1.5 (1.0–2.0)	NA ^b
2009	1.6 (1.0–2.2)	NA ^b
2010	1.4 (0.6–2.2)	NA ^b
Overall	2.0 (1.8–2.2)	4.9 (4.2–5.7)

^a95% CI, 95% confidence interval. The CIs are based on 9999 bootstrap replicates.^bNA, not available (the follow-up time was not long enough to observe 50% of seroconverters linking to care).

Table 4

Univariable and multivariable effect size estimates from Cox proportional hazard models of determinants of time from HIV infection to linkage-to-care in rural KwaZulu-Natal, South Africa.

Variables	Univariable HR (95% CI)	Multivariable ^a aHR (95% CI)
Sex		
Male	0.49 (0.39–0.61)	0.49 (0.37–0.64)
Age		
15–29 years	1.00	1.00
30–39 years	1.22 (0.96–1.55)	1.16 (0.86–1.57)
40–49 years	1.92 (1.53–2.40)	1.54 (1.14–2.08)
50+ years	1.15 (0.80–1.64)	0.87 (0.53–1.44)
Education level		
None or less than 1 year	1.00	1.00
Some or completed primary	0.87 (0.61–1.25)	0.75 (0.46–1.22)
Some or completed secondary	0.68 (0.50–0.93)	0.63 (0.39–1.00)
Food security		
Missing meals almost every month (financial reasons)	1.56 (0.88–2.79)	1.37 (0.67–2.80)
Socioeconomic status		
Poorest	1.00	1.00
Poor	1.15 (0.90–1.46)	1.21 (0.91–1.61)
Rich	1.14 (0.90–1.44)	1.19 (0.75–1.90)
Richest	1.00 (0.78–1.29)	1.05 (0.62–1.79)
Other household members using ART		
At least one (versus ‘none’)	1.16 (0.96–1.41)	1.23 (0.98–1.55)
Knowledge of HIV status ^a		
Yes (versus ‘no/refused’)	1.52 (1.24–1.87)	1.35 (1.09–1.68)
Area of residence		
Urban	1.00	1.00
Periurban	0.65 (0.42–1.02)	0.73 (0.43–1.24)
Rural	0.77 (0.49–1.21)	0.76 (0.45–1.30)
Distance to health facility		
<2km	1.00	1.00
2–4km	1.04 (0.86–1.25)	1.00 (0.79–1.26)
>4km	1.16 (0.93–1.45)	1.10 (0.84–1.44)
Calendar year of HIV infection	Included as strata	Included as strata

95% CI, 95% confidence interval; aHR, adjusted hazard ratio; HR, hazard ratio. Results are presented after pooling the analyses of the 10 imputed datasets, as described in the text. All models were stratified using the calendar year of HIV infection to ensure that the proportional hazards assumption was met. The outcome variable was the time from HIV infection to linkage-to-care. We used the date of the first CD4⁺ cell count test performed in the local HIV treatment and care program to identify the time from infection to linkage.

^aThe question about knowledge of HIV status from previous testing was not asked in 2004 and 2005; hence, observations from these years were not included in the multivariable model.