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Factors influencing the survival of patients with advanced HIV disease in Guinea from 2015 to 2024

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Abstract:

Introduction: Advanced HIV disease (AHD) remains associated with substantial mortality in routine care settings. We aimed to describe survival patterns and identify predictors of mortality among patients with AHD managed in Guinea, while also examining programmatic pathway variables relevant to continuity of care, including transfer into one of the nine specialized AHD sites, return after previous loss to follow-up, and visit intensity during follow-up. **Methods:** We conducted a retrospective cohort study using routine program data from patients with AHD enrolled in nine AHD care sites in Guinea between January 2015 and December 2024. Cohort entry was defined as the first documented AHD care visit at one of the nine study sites after AHD criteria were met. Follow-up was defined at the individual level from AHD cohort entry to death or censoring and was summarized in months

and person-years. Median documented follow-up among analyzable individual follow-up intervals was summarized as median and interquartile range. Kaplan–Meier methods were used to describe survival patterns, and log-rank tests were used to compare curves. A principal multivariable Cox model was specified a priori using baseline predictors measured at cohort entry, and a secondary extended model additionally examined care-process variables accrued during follow-up. Programmatic pathway variables describing transfer into one of the nine study sites and return after previous loss to follow-up were examined descriptively and in exploratory analyses but were excluded from the principal prognostic model. **Results:** Among 24,090 individuals diagnosed with HIV during 2015–2024, 10,645 met the AHD definition and 1,289 died. Median documented follow-up was 2 months (IQR 1–5), corresponding to 2,529.8 person-years; the overall mortality incidence was 50.95 deaths per 100 person-years. In the principal multivariable model, mortality was higher among men (aHR 1.18, 95% CI 1.06–1.33), patients aged >40 years (aHR 1.56, 95% CI 1.29–1.88), and those with WHO stage 3 (aHR 2.18, 95% CI 1.68–2.83) or stage 4 disease (aHR 4.20, 95% CI 3.19–5.52). Compared with new patients, transferred patients by ART initiation method had lower mortality (aHR 0.55, 95% CI 0.44–0.69). In the secondary extended model, confirmed TB or no documented TB screening at the last visit, fewer visits, and hospitalization during follow-up were associated with mortality in secondary exploratory care-process analyses. Exploratory pathway analyses showed lower observed hazards among patients transferred into the nine study sites and among those who returned after prior loss to follow-up; these findings were interpreted as referral, survivor selection, and re-engagement phenomena rather than as protective effects. **Conclusion:** Mortality among patients with AHD in Guinea remained high and was

concentrated in the earliest documented period after cohort entry. Male sex, older age, and advanced WHO stage were the most consistent baseline predictors of death. The analyses also highlight the operational importance of continuity-of-care markers such as visit intensity, inter-site transfer, and return after interruption of follow-up, all of which can signal episodes during which adherence may be compromised in patients already presenting with advanced disease. These findings support earlier diagnosis, stronger implementation of the AHD package of care, improved TB screening and management, closer early follow-up, and stronger coordination of transfer and re-engagement pathways.

Keywords: advanced HIV disease; mortality; survival analysis; retrospective cohort; Guinea; tuberculosis.

Introduction

The World Health Organization (WHO) defines advanced HIV disease (AHD) as a cluster of differentiation 4 (CD4) cell count <200 cells/mm3 or WHO stage 3 or 4 disease in adults and adolescents. This definition includes both people who present to care and have never received antiretroviral therapy (ART) and those who return to care after interrupted treatment [1]. Although CD4+ T-cell counts are no longer required to start treatment, they are still an essential tool for identifying people with AHD. All children under 5 years of age living with HIV are considered to have AHD because of their increased risk of disease progression and mortality [1].

Nearly half of all people living with HIV worldwide often seek care late [2,3]. The proportion of people with AHD has remained relatively unchanged over the past five years, although the number of PLHIV receiving antiretroviral therapy in low- and middle-income countries (LMICs) has more than doubled over this period [4–6]. In 2020, 21.6% of people newly diagnosed with HIV in the United States were late

presentations of advanced HIV disease [7]. Studies in sub-Saharan Africa have shown that AHD is prevalent in this area, with proportions between 32% and 71% of patients starting care with AHD and up to 60% of patients presenting for care with AHD after returning to care [4,8,9]. AHD is characterized by increased susceptibility to malignancies and opportunistic infections, such as bacterial infections, cryptococcal infections, and mycobacterial diseases, such as *Mycobacterium tuberculosis* and nontuberculous mycobacteria [10,11]. In addition, AHD is often associated with anemia and weight loss [12]. Many people living with HIV may remain asymptomatic during disease progression, which can delay care-seeking and contribute to late presentation, particularly among people with AHD [10,13,14].

WHO recommends an AHD package of care that combines rapid ART initiation with CD4 testing to identify advanced disease, systematic screening for tuberculosis and cryptococcal disease, prevention and treatment of severe bacterial infections, prophylaxis where indicated, and close clinical follow-up [1,15]. In practice, the value of this package is greatest when patients are identified early and rapidly linked to structured care pathways, because mortality in AHD is concentrated in the earliest period after presentation.

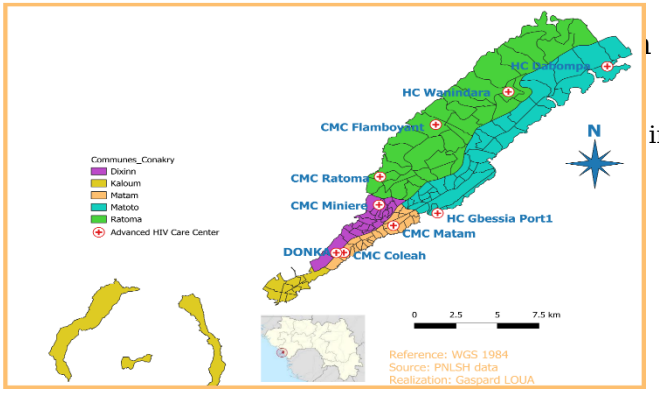
In 2024, approximately 630,000 [490,000–820,000] people died from HIV-related causes worldwide, and the WHO African Region remained the most affected region [16]. Late presentation is associated with increased healthcare costs, poor treatment outcomes, ongoing HIV transmission, and increased morbidity and mortality [17,18]. In Guinea, a tertiary-hospital study among patients hospitalized for advanced HIV disease reported a case-fatality rate of 33.6% [19], but multicentre program data on survival after AHD cohort entry remain scarce.

In Guinea, national evidence on survival patterns and predictors of mortality among patients with advanced HIV disease remains limited, particularly beyond single-center hospital studies. We therefore sought to characterize outcomes across the national AHD platform supported in nine specialized care sites, while distinguishing baseline prognostic factors from programmatic pathway variables that may arise during follow-up. The specific objectives were to describe survival from AHD cohort entry over observed follow-up, quantify individual follow-up time, person-years and incidence rates of death, identify baseline predictors of mortality in a principal multivariable model, and examine the contribution of programmatic pathway variables—including transfer into one of the nine study sites and return after previous loss to follow-up—in secondary and exploratory analyses.

Methods

Study Setting:

The study was conducted in eight (08) centers providing screening and management of advanced HIV disease in Guinea and the Unité de Soins et de Formation Specialises (USFR) of Donka, which provides inpatient care for PLHIV. Together, these nine facilities comprised one university hospital (Donka University Hospital), five communal medical centres (CMCs: Coléah, Flamboyant, Matam, Minière, and Dabompa), and three health centres (Gbessia Port 1, Tombolia, and Wanindara). All were supported by Médecins Sans Frontières (MSF) to deliver the full advanced HIV



WHO guidance.

included in the study in Guinea - Conakry.

This was a retrospective cohort study based on routine program data from patients with advanced HIV disease enrolled between January 2015 and December 2024. Data extraction and statistical analyses for this manuscript were conducted in 2025 after administrative authorization to access the program database.

Study population:

The study population included people living with HIV who were recorded in the AHD program database at one of the nine study sites between January 2015 and December 2024 and who met the operational AHD definition. Inclusion was based on clinical and program criteria recorded in the database, irrespective of nationality, place of residence, or presumed place of HIV acquisition.

Sampling technique

We performed a complete enumeration of all eligible patient records in the AHD program database. No probabilistic, purposive, or sample-based selection procedure was used; all eligible records reported in the database from 2015 to 2024 were included.

AHD was operationalized according to WHO criteria: CD4 count <200 cells/mm³ or WHO clinical stage 3 or 4 among adults, adolescents, and children aged ≥5 years; all children younger than 5 years were classified as having AHD. When CD4 count and WHO stage were discordant, either criterion was sufficient for AHD classification. Therefore, patients with CD4 counts ≥500 cells/mm³ were retained if they had documented WHO stage 3 or 4 disease or were younger than 5 years.

The national database for the longitudinal follow-up of patients with AHD was established in 2015 by the PNLSH, with technical and financial support from MSF Belgium, to strengthen management of AHD in Guinea.

Data collection

The database already exists. Access was obtained through an administrative procedure involving the PNLSH and MSF, which provides technical management of the database.

The PNLSH issued an official letter (N200/PNLSH/CN/MSHP/2025) to MSF authorizing access to the data for this research project.

Data analysis

R software (version 4.3.2) was used for all analyses. The primary endpoint was death, as coded in the outcome field. A sensitivity analysis used terminal outcome coding from the detailed outcome variable when the terminal state was explicitly recorded as death. Cohort entry, or time zero, was defined as the first documented AHD care visit at one of the nine study sites after AHD criteria were met. Follow-up started at cohort entry and ended at death or censoring. Patients were censored at the last date known alive, the documented transfer-out date when no subsequent outcome was available, or the administrative end of follow-up, whichever occurred first. ART initiation date was used to describe treatment history and prior ART exposure but was not used as the time origin for the primary survival analysis. Because the underlying database was created for routine longitudinal monitoring of patients with AHD, person-time reflects documented individual follow-up intervals rather than a fixed administrative 10-year exposure for each patient.

Median documented follow-up among analyzable individual follow-up intervals was summarized as median and interquartile range. Overall mortality incidence and incidence rates by selected covariates were calculated as deaths divided by accumulated person-years and expressed per 100 person-years. Bivariate descriptive tables presented continuous variables as means (standard deviation [SD]) and categorical variables as n/N (%), with percentages calculated among non-

missing observations. For care-process variables in which the absence of testing was intrinsically meaningful, the category “Not done” was retained; otherwise, missing and unknown values were excluded from analytic categories and documented separately in dedicated missingness tables. The 2015–2024 period denotes the calendar period of cohort inclusion, whereas the 2-month median follow-up refers to patient-level documented observation time after AHD cohort entry.

A principal multivariable Cox model was specified a priori using baseline variables measured at cohort entry: sex, age at diagnosis group, WHO clinical stage before ART, baseline CD4 group, method of ART initiation, prior ART category, and time from diagnosis to first visit. Because the subgroup “Under TARV Before PMTCT” contained sparse events, prior ART categories were collapsed for Cox modelling into a PMTCT-related ART exposure group to avoid unstable coefficient estimation. Variables measured after cohort entry, including TB status at the last visit, number of visits, hospitalization during follow-up, last CD4 count, and last viral load, were not treated as baseline predictors; they were examined only in secondary exploratory care-process analyses.

Two programmatic pathway variables were handled separately from the principal prognostic model. “Transferred” denoted patients transferred from another site into one of the nine study sites where AHD data were collected. “Lost_Sight” denoted patients who had previously been lost to follow-up and later returned to the active cohort. These variables were examined explicitly because transfer, interruption of care, and return to follow-up are operationally crucial situations in advanced HIV disease: during such periods, delayed drug refills, poor adherence, interrupted monitoring, and treatment gaps may increase clinical vulnerability and may contribute to resistance selection in patients already at an advanced stage. Because

these variables also reflect referral, re-engagement, and survivor selection processes rather than pure baseline prognosis, they were described in bivariate tables, Kaplan–Meier analyses, incidence-rate summaries, and a dedicated exploratory pathway model, but were not retained in the principal Cox model.

The proportional hazards assumption was assessed using Schoenfeld residuals and log-minus-log survival plots. Because some departures from proportional hazards were detected for selected covariates, Cox estimates were interpreted as average hazard ratios over the observed follow-up rather than as strictly constant effects over time.

Potential facility-level clustering and calendar-year effects were considered during model specification but were not explicitly modelled in the principal Cox analysis, which was intentionally restricted to patient-level baseline prognostic factors; therefore, effect estimates are interpreted as patient-level associations over the observed follow-up rather than as facility- or period-specific effects.

Variables measured at cohort entry were handled using multiple imputation to reduce information loss and improve the stability of baseline prognostic estimates. No imputation was performed for the remaining variables. Descriptive percentages were calculated among non-missing observations, and when the absence of a test had clinical or programmatic meaning, it was retained as an explicit analytic category (“Not done”). In multivariable models, each analysis included only observations with the required data for the covariates entered in that model.

Ethical considerations

The protocol was submitted to the national ethics committee: Comite National d’Ethique pour la Recherche en Sante (CNERS) and approved (No: 123/CNERS/25) before the data were retrieved from the MSF database. The data were pseudo-

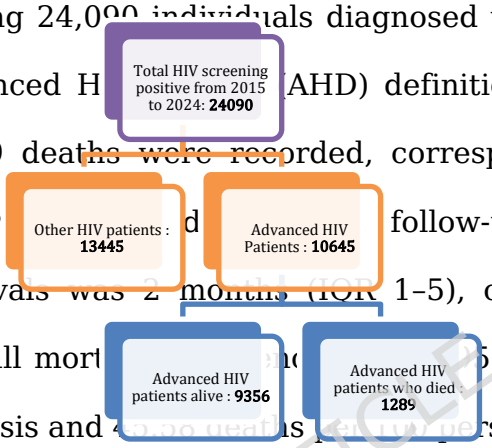
anonymized by patient codes, and confidentiality was guaranteed under Article 18 of Ordinance No. 56/2009/PRG/SGG on the Prevention, Management and Control of HIV/AIDS in the Republic of Guinea.

The dissemination and communication of data is performed only in a scientific context and in public policy orientation.

Results

Cohort profile and mortality incidence

Fig 2: Study profile showing the derivation of the analytic cohort of patients with advanced HIV disease in Guinea during 2015–2024 ***(Fig2: Must be placed on line 205)***



Among 24,090 individuals diagnosed with HIV during 2015–2024, 10,645 met the advanced H (AHD) definition and formed the analytic cohort. Overall, 1,289 deaths were recorded, corresponding to a crude mortality proportion of 12.1% d follow-up among analyzable individual follow-up intervals was 2 months (IQR 1–5), corresponding to 2,529.8 person-years. The overall mort 5 deaths per 100 person-years in the primary analysis and rson-years in the sensitivity analysis restricted to terminal outcome coding.

Factors influencing survival in bivariate analysis

Table 1: Baseline and selected care-process characteristics by vital status with advanced HIV disease in Guinea, 2015–2024 **(*Table 1: Must be placed on line 217)***.

In bivariate analyses, mortality was higher among men than women (14% vs 11%, p<0.001), among older patients, especially those aged >40 years (16% vs 9.4% in patients aged 15–24 years, p<0.001), and across WHO clinical stages, reaching 21% in stage 4 disease (p<0.001). Baseline CD4 group, method of ART initiation, prior ART category, last ART CD4 group, last ART viral load group, TB status at the last visit, number of visits, hospitalization during follow-up, and follow-up time were all

associated with the outcome in crude analyses. Variables measured after cohort entry (last documented CD4 count, last viral load, TB status at the last visit, number of visits, hospitalization during follow-up, and observed follow-up time) were examined as follow-up or care-process markers and were not interpreted as baseline predictors.

Patients classified as transferred patients by ART initiation method had lower crude mortality than new patients (9.7% vs 12.3%, p=0.018). In contrast, the programmatic pathway variable 'Transferred', which identified patients transferred from another site into one of the nine study sites, was associated with a lower crude mortality proportion than among non-transferred patients (4.5% vs 13.2%, p<0.001). Likewise, patients who had returned after previous loss to follow-up ('Lost_Sight' = Yes) had a lower crude mortality proportion than those without this history (1.8% vs 16.5%, p<0.001). These pathway variables were therefore interpreted descriptively rather than as baseline prognostic factors; however, they remain operationally important because they identify patients who experienced transitions or interruptions in care that may threaten continuity of ART in advanced disease.

TB status at the last visit was strongly associated with outcome. The crude mortality proportion was 6.8% among patients with no TB symptoms documented at last screening, 18.3% among those not screened, and 17.8% among those with confirmed TB (p<0.001). Mortality was also markedly higher among patients hospitalized during follow-up (43.4%) than among those not hospitalized (8.0%; p<0.001). These categories describe the last documented TB screening status and should not be interpreted as proving that screening status itself caused mortality.

Incidence-rate analyses supported the same pattern. Mortality incidence was higher among men than women (62.1 vs 45.1 deaths per 100 person-years), among patients aged >40 years (72.4 per 100 person-years), among patients with WHO stage 4 disease (110.3 per 100 person-years), among hospitalized patients (267.2 per 100 person-years), among patients with confirmed TB at the last visit (186.5 per 100 person-years), and among patients without documented TB screening at the last visit (132.1 per 100 person-years). Mortality incidence was lower among patients transferred into one of the nine study sites and among those who returned after previous loss to follow-up, again suggesting that these variables behave primarily as care-pathway and re-engagement markers rather than as biological protective factors.

Analysis of the different survival curves of patients with advanced HIV disease in Guinea

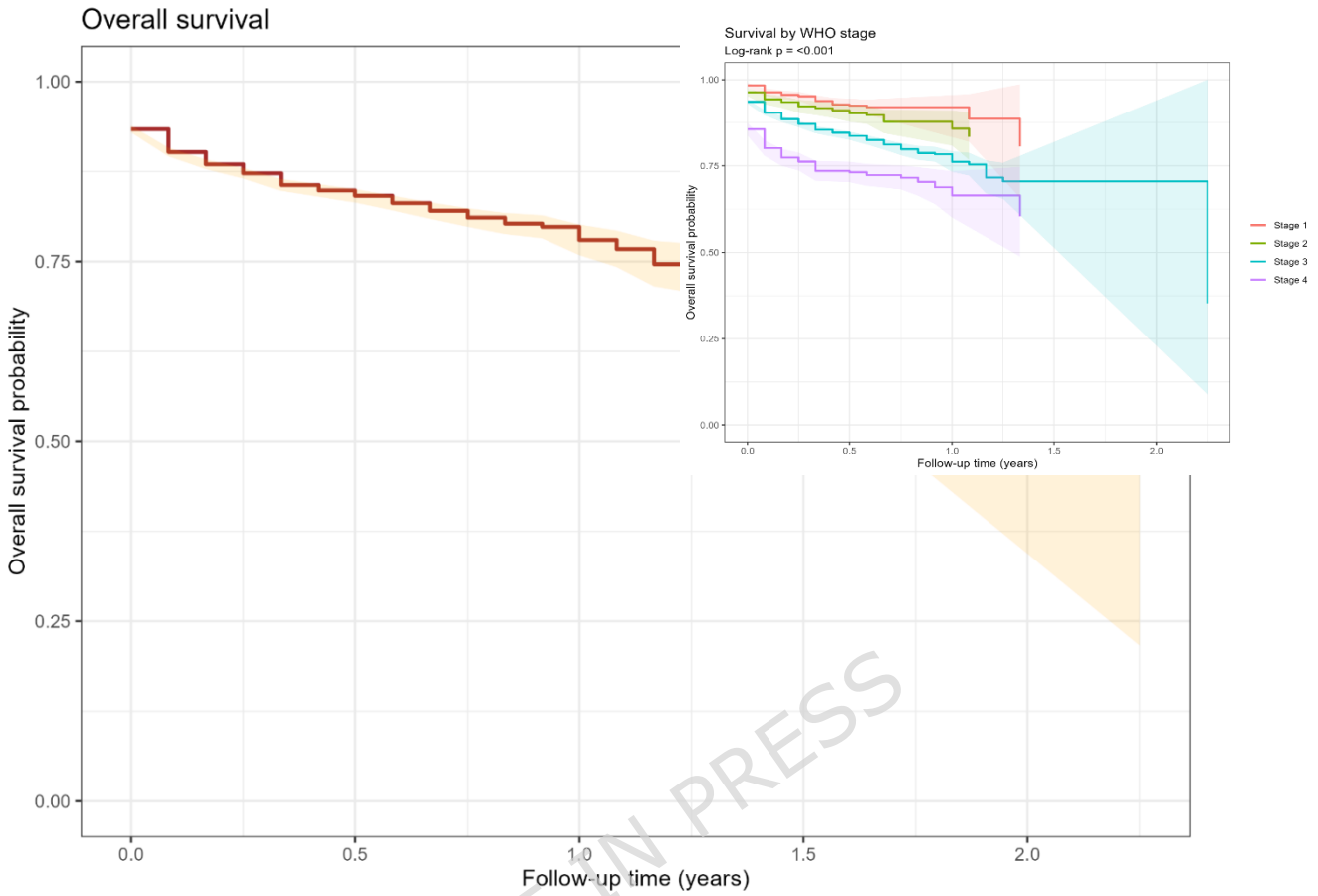
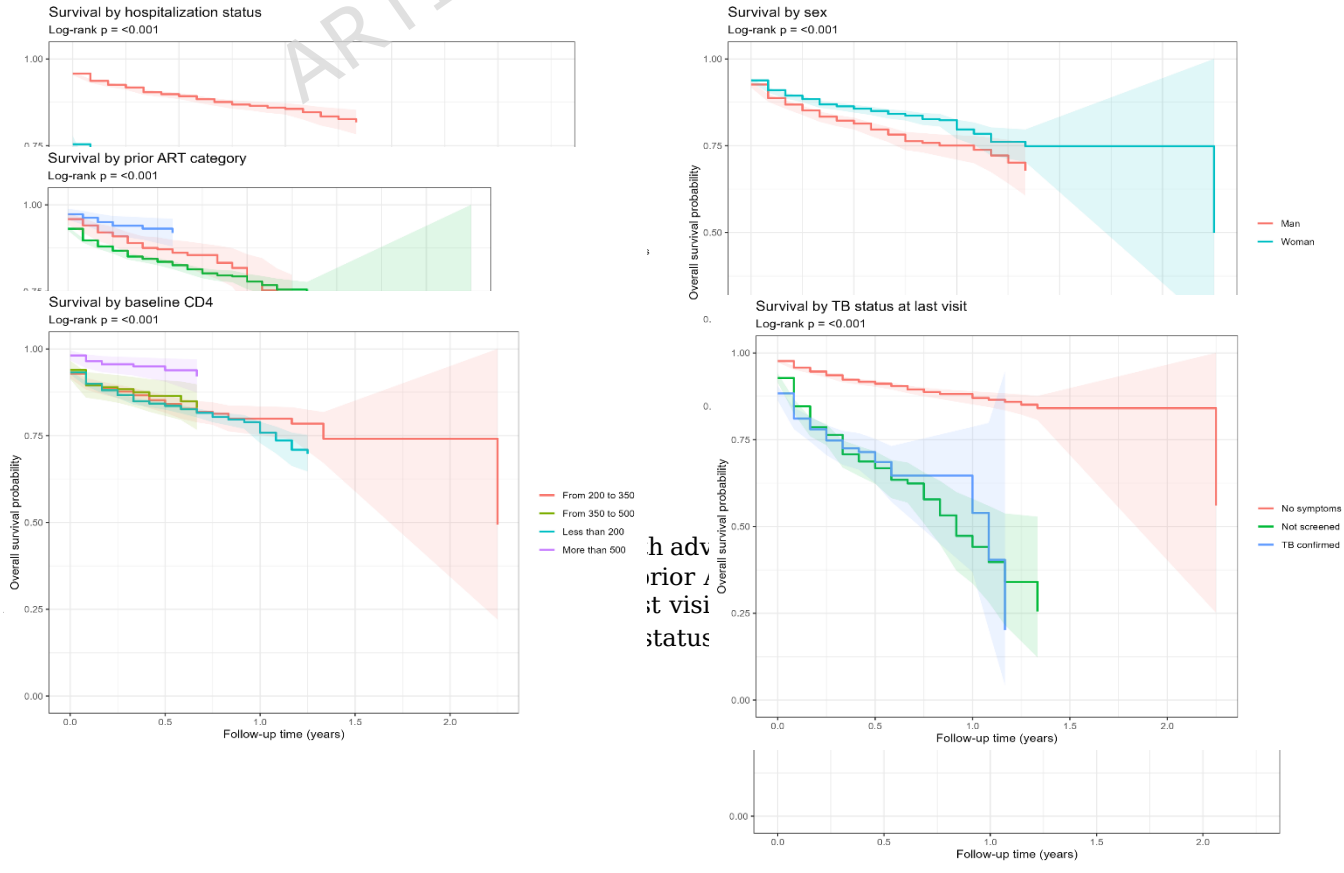


Fig. 3 Overall Kaplan-Meier survival curve of patients with advanced HIV disease in Guinea. **(*Fig3: Must be placed on line 252)***



line 255; (c) & (d) Must be placed on line 256; (e) & (f) Must be placed on line 257; (g) & (h) Must be placed on line 258)

Kaplan–Meier analyses showed lower survival among men than women, among patients with more advanced WHO stage, among patients without prior treatment compared with those with prior ART or PMTCT-related exposure, among patients with confirmed TB or no documented TB screening at the last visit, and among patients hospitalized during follow-up. Survival curves also suggested that patients transferred into one of the nine study sites and patients who returned after previous loss to follow-up experienced more favorable observed survival than their counterparts.

These pathway-related patterns were not interpreted as protective biological effects. Rather, they were considered compatible with referral into specialized AHD services, re-engagement in care, and survivor selection. At the same time, transfer episodes, prior disengagement, and return after interruption remain highly relevant programmatically because they may coincide with periods of suboptimal adherence, delayed treatment resumption, and increased vulnerability to resistance among patients already presenting with advanced HIV disease. Because event density becomes sparse in the far-right tail of the curves, no causal interpretation was made from the extreme tail of the Kaplan–Meier plots.

Table 2: Bivariate characteristics associated with death among hospitalized patients with advanced HIV disease **(*Table 2: Must be placed on line 279)***.

Among 1,241 hospitalized patients with AHD, crude mortality was 43.4%. In bivariate analyses, sex, CD4 at admission, last CD4 during hospitalization, TB-LAM, blood CrAg, CSF CrAg, hemoglobin at admission, and viral load at admission group were not clearly associated with death. By contrast, skin signs, respiratory signs, general signs, reduced consciousness, meningeal signs, GenXpert result, and length of stay were associated with outcome.

Mortality was higher among patients with respiratory signs than among those without respiratory signs (48% vs 36%, p<0.001), among patients with general signs (51% vs 41%, p=0.003), among patients with reduced consciousness (57% vs 41%, p=0.002), and among patients with meningeal signs (50% vs 42%, p=0.036). Patients with a GenXpert result categorized as not done had the highest crude mortality proportion (52%) compared with those with negative TB (40%) or resistant TB (38%) (p=0.001). ART interruption before hospitalization was also associated with outcome and should be viewed as an operational warning sign in this particularly vulnerable subgroup.

These findings are consistent with severe clinical presentation during hospitalization and support the interpretation of the hospital model as exploratory and severity-oriented rather than as a baseline prognostic model.

Multivariate analysis

Table 3: Principal multivariable Cox model of baseline factors associated with death among patients with advanced HIV disease ***(Table 3: Must be placed on line 298)***

Fig. 5: Adjusted hazard ratios from the corrected secondary extended multivariable Cox model of mortality among patients with advanced HIV disease ***(Fig. 5: Must be placed on line 299 just after Table 3)***

In the principal multivariable Cox model, mortality was independently associated with male sex (aHR 1.18, 95% CI 1.06–1.33), age >40 years compared with 15–24 years (aHR 1.56, 95% CI 1.29–1.88), WHO stage 3 disease (aHR 2.18, 95% CI 1.68–2.83), and WHO stage 4 disease (aHR 4.20, 95% CI 3.19–5.52). Patients classified as transferred patients by method of ART initiation had lower mortality than new patients (aHR 0.55, 95% CI 0.44–0.69).

Baseline CD4 showed no clear monotonic gradient after adjustment. Compared with the <200 cells/mm³ reference category, the 200–349 cells/mm³ category remained

associated with higher mortality (aHR 1.31, 95% CI 1.11–1.55), whereas the 350–499 and ≥500 cells/mm³ categories were not statistically different from the reference. Prior ART grouping and time from diagnosis to first visit were not independently associated with mortality after adjustment.

Figure 5 presents the secondary extended model, which incorporated care-process variables accrued during follow-up. In that model, confirmed TB or no documented TB screening at the last visit, fewer visits, and hospitalization during follow-up were additionally associated with mortality. These variables were retained in secondary analyses because they are highly relevant operationally in AHD follow-up, even though they cannot be interpreted as pure baseline exposures.

In a dedicated exploratory pathway model, transferred status into one of the nine study sites and return after previous loss to follow-up were both associated with lower observed hazards of death, a pattern interpreted as survivor selection and re-engagement in care rather than as protection. A sensitivity Cox model using terminal outcome coding yielded effect estimates that were directionally similar to those of the principal model, supporting the robustness of the main baseline findings despite some departures from the proportional hazard's assumption for selected covariates.

Discussion

This study provides one of the first national-level analyses of survival patterns and predictors of mortality among patients with advanced HIV disease in Guinea using routine data from nine specialized AHD care sites. Two broad messages emerge from the corrected analyses. First, mortality remained high and was concentrated in the earliest documented period after cohort entry, as reflected by the distribution of recorded follow-up intervals and person-time. Second, male sex, older age, and

advanced WHO stage were the most consistent baseline predictors of death in the principal multivariable model.

The burden of advanced HIV disease in our cohort was substantial, with 44.2% of patients meeting the AHD definition among all individuals diagnosed with HIV during 2015–2024. This proportion remains comparable to the high AHD prevalence reported in Guangdong Province in China [14], South Africa [4], and rural Tanzania [26]. Our crude mortality proportion of 12.1% appears lower than that reported in some inpatient or referral cohorts, such as the studies by Stöger et al. in Tanzania [26] and Li et al. in southwestern China [27], but such comparisons should be interpreted cautiously because the documented person-time in our cohort was concentrated early after cohort entry, with early deaths contributing substantially to the observed incidence.

Male sex and older age were robustly associated with mortality. The higher mortality among men is consistent with the broader literature on late presentation and delayed care engagement in HIV care [17,18], whereas the excess hazard observed after age 40 years is clinically plausible in a population already burdened by advanced disease and comorbidity. Findings in children and adolescents were less stable, which is also in line with the complex age patterns described by Chabikuli et al. [28] and the concerns raised by Frigati et al. for children with advanced HIV disease [29].

WHO clinical stage before ART was one of the strongest predictors of mortality, with a stepwise increase from stage 2 to stage 4 and the highest hazards observed for stage 4 disease. This is consistent with the natural history of advanced disease and with studies emphasizing the prognostic importance of severe clinical presentation despite ART availability [20,26,30]. In contrast, baseline CD4 group did not show a

fully monotonic adjusted gradient after correction. We therefore avoid overstating a specific protective effect of individual CD4 strata. Our interpretation is aligned with the broader literature showing that low CD4 remains clinically important for identifying high-risk AHD patients, while the adjusted association may become less orderly once severe clinical stage and other baseline factors are considered [30–32]. The corrected analyses also refine the interpretation of ART-related variables. In the principal model, the method of ART initiation remained associated with outcome, with transferred patients by ART initiation method showing lower observed mortality than new patients. This pattern is compatible with the observation by Li et al. that treatment-experienced AHD patients can have lower mortality than treatment-naïve patients in some contexts [27]. By contrast, prior ART category itself was not a robust independent predictor after regrouping sparse categories for model stability. The subgroup 'Under TARV Before PMTCT' contained only 14 women and no deaths, making separate estimation unstable. The regrouping applied in the corrected model was therefore methodologically necessary and is reported transparently. This association should be interpreted as a care-pathway pattern rather than a biological protective effect.

TB remained central to prognosis. In crude analyses, both confirmed TB and no documented TB screening were associated with markedly worse outcomes, and incidence rates were especially high among these subgroups. In the extended model, both 'TB confirmed' and 'Not screened' remained strongly associated with mortality. These findings are coherent with the large literature on TB/HIV comorbidity in AHD, including reports from Malawi [33] and Mozambique [34], and they reinforce the operational importance of the WHO AHD package, particularly systematic TB screening and rapid management [15]. The high hazard in the 'Not screened' group

is particularly concerning because it likely reflects missed diagnostic opportunities in a clinically vulnerable subgroup. Because TB status was recorded at the last visit, this variable may reflect illness severity, missed diagnostic opportunities, or incomplete documentation rather than a purely causal exposure.

Hospitalization and visit frequency require careful interpretation. Crude mortality among hospitalized patients was 43.4%, and in the extended model hospitalization during follow-up was strongly associated with death. We do not interpret this as a causal effect of hospitalization itself, but rather as a marker of clinical severity and deterioration during follow-up. Similarly, the inverse association between number of visits and mortality is best understood as a marker of continuity of care and sustained contact with the health system. In patients already at advanced stage, missed visits, delayed return, and fragmented follow-up may correspond to periods of treatment interruption, poor adherence, and increased vulnerability to virological failure or resistance, making visit intensity a clinically meaningful operational signal rather than a simple behavioral count.

The pathway variables 'Transferred' and 'Lost_Sight' require a distinct interpretation. By definition, 'Transferred' described patients transferred from another site into one of the nine study sites, while 'Lost_Sight' identified patients who had previously been lost to follow-up and later returned to the active cohort. In both descriptive and exploratory pathway analyses, these variables were associated with lower observed mortality than their counterparts. This should not be interpreted as a protective biological effect. Instead, these variables likely capture referral into specialized AHD services, re-engagement in care, and survivor selection. At the same time, they remain highly important programmatically because transfer episodes and care interruptions are precisely the moments at which

treatment continuity may fail, adherence may weaken, and resistance may emerge in patients with advanced HIV disease. This interpretation is more consistent with the literature on disengagement and re-engagement in HIV care, including the work of Mesic et al. [35], Kaplan et al. [36], Mills et al. [37], Moolla et al. [38], and Rivera-Villegas et al. [39], than the earlier interpretation in the initial manuscript that these statuses directly increased mortality.

Limitations

This study has limitations. First, it relied on routine longitudinal program data, and some variables had missing or incomplete documentation, as is common in real-world cohort analyses. Second, the hospitalized-patient Cox model remains exploratory and should be interpreted cautiously because several clinical and process variables reflect evolving inpatient severity rather than baseline comparability. Finally, our analyses did not explicitly stratify by key populations or post-discharge outcomes, which remain important priorities for future work.

Conclusions

This retrospective cohort study included patients managed across nine specialized AHD care sites in Guinea, providing a large routine-program cohort. This retrospective cohort study adds national evidence on advanced HIV disease outcomes in Guinea by quantifying individual follow-up, person-years, incidence rates, and adjusted predictors of mortality across nine specialized AHD care sites. The corrected analyses show that mortality remains high and is concentrated in the earliest observed period after cohort entry, and that male sex, older age, and advanced WHO stage are the most consistent baseline predictors of death. Secondary analyses further identify confirmed TB or no documented TB screening, low visit intensity, hospitalization during follow-up, inter-site transfer, and return

after previous loss to follow-up as operational markers of patients requiring close attention.

These findings support three immediate priorities. First, the AHD package of care should be strengthened through earlier identification of AHD, systematic CD4 assessment where available, and rapid implementation of screening and treatment algorithms, particularly for tuberculosis. Second, the program should intensify early follow-up, appointment adherence, and retention efforts during the first months after cohort entry, while also strengthening coordination of transfers and rapid re-engagement after interrupted follow-up. Third, hospitalized AHD patients should remain a priority subgroup for comprehensive clinical assessment and close monitoring because hospitalization is a clear marker of severe disease and poor prognosis.

Future research should focus on time-varying models of care processes, post-hospital outcomes, treatment continuity during transfers and re-engagement after interruption, and quality-of-life trajectories among patients with advanced HIV disease in Guinea. Such work would help distinguish baseline predictors from events that arise during follow-up and would further improve programmatic targeting of the most vulnerable patients.

Declarations

Abbreviations

acquired immunodeficiency syndrome: (AIDS) 4
advanced HIV disease: (AHD) 3
Akaike Information Criterion: (AIC) 6
antiretroviral therapy: (ART) 1
Antiretrovirals: (ARV) 2
Centre d’excellence africain pour la prévention et le contrôle des maladies transmissibles: (CEA-PCMT) 1
cluster of differentiation 4: (CD4) 3
communal medical centers: (CMCs) 4
Faculté des Sciences et Techniques de la Santé: (FSTS) 1
Hazard Ratio: (HR) 2

health centers: (HC) 4
human immunodeficiency virus: (HIV) 1
low- and middle-income countries: (LMIC) 3
Médecins Sans Frontières: (MSF) 4
Multidrug-resistant tuberculosis: (MDR-TB) 6
Person living with HIV: (PLHIV) 4
Prevention of mother-to-child transmission: (PMTCT) 6
Programme National de Lutte contre le Sida et les Hépatites: (PNLSH) 1
tuberculosis: (TB) 6
Unité d'Appui à la Gestion et à la Coordination des Programmes: (UAGCP) 1
Unite de Soins et de Formation Specialises (USFR) 4
Universite Gamal Abdel Nasser de Conakry: (UGANC) 1
World Health Organization: (WHO) 1

Ethical approval and consent to participate

The need for individual informed consent to participate was waived by the Institutional Review Board: The Comité National d'Ethique pour la Recherche en Santé (CNERS) of the Republic of Guinea after review and approval of the research protocol. Approval letter reference: No.123/CNERS/25.

Our research is in accordance with the Declaration of Helsinki.

Consent to publication

Not applicable

Availability of data and materials

The database exists. However, it is confidential. Getting it requires the approval of the National Program for the Fight against AIDS and Hepatitis (PNLSH) before it is released to MSF Belgium in Guinea, which manages it for the monitoring of HIV patients.

Conflicts of interest

The authors state that the research was conducted in the absence of any financial relationship that could be interpreted as a potential conflict of interest.

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Author contributions

Gaspard Loua: contributed to the entire writing process of this manuscript.

Amitabye Luximon-Ramma: contributed to the drafting of the protocol, commentary on the results, and review of the final document for amendments and suggestions.

Timothée Guilavogui: contributed to the method and the amendment of the final document

Ibrahima Barry: contributed to getting the data and amending the final document

Moussa Fanta Keita: contributed to cleaning the database, analyzing and amending the final document

Souleymane Chaloub: facilitated the administrative process of obtaining the data and amending the final document

Pascal Mweze: contributed to getting the data and amending the final document

Adelard Shyaka: contributed to getting the data and amending the final document

Honora A.B Djidonou: reading and amending the final document

Elie Sandy Massadouno: contributed to getting the data and amending the final document

Moussa Bill Keita: contributed to data extraction, cleaning, and reading of the final document

Abdourahamane Diallo: contributed to correcting the protocol, amending the results, and reviewing the final document

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Table 1: Baseline and selected care-process characteristics by vital status among patients with advanced HIV disease in Guinea, 2015–2024 ***(Table 1 Must be placed on line 217)***

Characteristic[1]	Alive N = 9,356	Dead N = 1,289	p-value1
Sex			**<0.001**
Woman	5,994/6,740 (89%)	746/6,740 (11%)	
Man	3,362/3,905 (86%)	543/3,905 (14%)	
Age at diagnosis (years)	30.85 (14.58)	35.00 (14.59)	**<0.001**
Age at diagnosis (group, years)			**<0.001**
Less than 5	779/827 (94%)	48/827 (5.8%)	
From 5 to 15	376/427 (88%)	51/427 (12%)	
From 15 to 25	1,499/1,654 (91%)	155/1,654 (9.4%)	
From 25 to 40	4,298/4,868 (88%)	570/4,868 (12%)	
More than 40	2,404/2,869 (84%)	465/2,869 (16%)	
WHO clinical stage before ART			**<0.001**
Stage 1	1,273/1,340 (95%)	67/1,340 (5.0%)	
Stage 2	936/1,012 (92%)	76/1,012 (7.5%)	
Stage 3	6,022/6,861 (88%)	839/6,861 (12%)	
Stage 4	1,125/1,432 (79%)	307/1,432 (21%)	
Baseline CD4 count (cells/mm³)	168.18 (232.05)	128.46 (137.96)	**<0.001**
Baseline CD4 count group (cells/mm³)			**<0.001**
Less than 200	7,460/8,519 (88%)	1,059/8,519 (12%)	
From 200 to 350	1,266/1,444 (88%)	178/1,444 (12%)	
From 350 to 500	277/312 (89%)	35/312 (11%)	
More than 500	353/370 (95%)	17/370 (4.6%)	
Method of ART initiation			**0.018**
New Patient	8,509/9,707 (88%)	1,198/9,707 (12%)	
Transferred Patient	847/938 (90%)	91/938 (9.7%)	
Prior ART category			**<0.001**
Anterior ARV >30 days	445/509 (87%)	64/509 (13%)	
No Treatment	8,515/9,719 (88%)	1,204/9,719 (12%)	

[1] Percentages are calculated among non-missing observations for each variable. Missingness is reported separately in the companion missingness table.

PMTCT	382/403 (95%)	21/403 (5.2%)	
Under TARV Before PMTCT	14/14 (100%)	0/14 (0%)	
Transferred from another site into one of the 9 study sites	1,288/1,349 (95%)	61/1,349 (4.5%)	**<0.001**
Returned after previous loss to follow-up	3,112/3,169 (98%)	57/3,169 (1.8%)	**<0.001**
Time from diagnosis to first visit (days grouped)			0.7
Less than a month	9,131/10,387 (88%)	1,256/10,387 (12%)	
From 1 to 3 months	117/131 (89%)	14/131 (11%)	
From 3 to 6 months	43/51 (84%)	8/51 (16%)	
From 6 to 12 months	15/18 (83%)	3/18 (17%)	
More than 12 months	50/58 (86%)	8/58 (14%)	
Last ART CD4 count (cells/mm³)	286.75 (292.17)	183.67 (199.44)	**<0.001**
Last ART CD4 group (cells/mm³)			**<0.001**
Less than 200	4,881/5,770 (85%)	889/5,770 (15%)	
From 200 to 350	1,814/2,018 (90%)	204/2,018 (10%)	
From 350 to 500	1,121/1,225 (92%)	104/1,225 (8.5%)	
More than 500	1,540/1,632 (94%)	92/1,632 (5.6%)	
Last ART viral load (copies/mL)	109,485.38 (643,008.88)	169,038.18 (742,233.59)	**<0.001**
Last ART viral load group (copies/mL)			**<0.001**
Less than 200	6,821/7,629 (89%)	808/7,629 (11%)	
From 200 to 500	354/401 (88%)	47/401 (12%)	
From 500 to 1000	274/321 (85%)	47/321 (15%)	
More than 1000	1,907/2,294 (83%)	387/2,294 (17%)	
TB status at last visit			**<0.001**
No TB symptoms documented at last screening	6,602/7,084 (93%)	482/7,084 (6.8%)	
No documented TB screening at last visit	1,212/1,484 (82%)	272/1,484 (18%)	
TB confirmed	769/935 (82%)	166/935 (18%)	
Number of visits during follow-up (count)	13.22 (12.90)	6.26 (8.46)	**<0.001**
Hospitalized during follow-up	703/1,241 (57%)	538/1,241 (43%)	**<0.001**
Observed Follow-up time (months)	3.06 (3.44)	1.36 (2.49)	**<0.001**

Continuous variables are presented as mean (SD), where SD denotes standard deviation.

Table 2: Bivariate characteristics associated with death among hospitalized patients with advanced HIV disease. ***(Table 2 Must be placed on line 279)***

Characteristic[2]	Alive N = 703	Dead N = 538	p-value1
Sex			0.6
Woman	412/735 (56%)	323/735 (44%)	
Man	291/506 (58%)	215/506 (42%)	
CD4 at admission (cells/mm³)	123.75 (202.96)	116.39 (197.36)	0.4
CD4 at admission group (cells/mm³)			0.7
Less than 200	602/1,068 (56%)	466/1,068 (44%)	
From 200 to 350	50/91 (55%)	41/91 (45%)	
From 350 to 500	22/34 (65%)	12/34 (35%)	
More than 500	29/48 (60%)	19/48 (40%)	
Last CD4 during hospitalization (cells/mm³)	137.58 (141.34)	135.13 (135.17)	0.8
Last CD4 during hospitalization group (cells/mm³)			0.7
Less than 200	272/527 (52%)	255/527 (48%)	
From 200 to 350	10/19 (53%)	9/19 (47%)	
From 350 to 500	18/39 (46%)	21/39 (54%)	
More than 500	15/24 (63%)	9/24 (38%)	
HIV status at admission			0.4
Known	20/33 (61%)	13/33 (39%)	
Child Exposed	3/7 (43%)	4/7 (57%)	
ART line at admission			0.7
Not on ARV	234/408 (57%)	174/408 (43%)	
First Line	339/617 (55%)	278/617 (45%)	
Second Line	18/33 (55%)	15/33 (45%)	
ART duration before admission			0.2
Not Initiated	215/367 (59%)	152/367 (41%)	
Initiation < 6 months	177/341 (52%)	164/341 (48%)	
6 to 12 months	38/76 (50%)	38/76 (50%)	
Initiation > 6 months	139/237 (59%)	98/237 (41%)	
Skin signs during hospitalization	677/1,208 (56%)	531/1,208 (44%)	**0.009**
Respiratory signs during hospitalization	355/685 (52%)	330/685 (48%)	**<0.001**
Malnutrition during hospitalization	393/682 (58%)	289/682 (42%)	0.7
General signs during hospitalization	117/240 (49%)	123/240 (51%)	**0.003**
Consciousness status during hospitalization			**0.002**
More than 12	622/1,062 (59%)	440/1,062 (41%)	
Less than 12	51/118 (43%)	67/118 (57%)	
Meningeal signs during hospitalization	103/204 (50%)	101/204 (50%)	**0.036**
TB-LAM result			0.4
Negative	272/484 (56%)	212/484 (44%)	

2 Percentages are calculated among non-missing observations for each variable. Missingness is reported separately in the companion missingness table. 'Not done' is retained only where absence of testing is a meaningful care-process category.

Positive	265/477 (56%)	212/477 (44%)	
Not done	134/221 (61%)	87/221 (39%)	
GenXpert result			**0.001**
Negative TB	369/619 (60%)	250/619 (40%)	
Resistant TB	123/198 (62%)	75/198 (38%)	
Not done	130/273 (48%)	143/273 (52%)	
Blood CrAg result			>0.9
Negative	580/1,015 (57%)	435/1,015 (43%)	
Positive	58/104 (56%)	46/104 (44%)	
Not done	46/82 (56%)	36/82 (44%)	
CSF CrAg result			0.7
Negative	178/318 (56%)	140/318 (44%)	
Positive	25/48 (52%)	23/48 (48%)	
Not done	347/600 (58%)	253/600 (42%)	
Hemoglobin at admission			0.3
Less than 6g/dl	127/236 (54%)	109/236 (46%)	
More than or equal to 6g/dl	554/962 (58%)	408/962 (42%)	
Not done	1/4 (25%)	3/4 (75%)	
Viral load at admission group			>0.9
Undetectable	44/71 (62%)	27/71 (38%)	
Detectable low	87/145 (60%)	58/145 (40%)	
Not suppressed	348/564 (62%)	216/564 (38%)	
Not done	6/10 (60%)	4/10 (40%)	
Length of stay (days)	11.91 (9.19)	11.91 (12.85)	**0.004**
ART interruption before hospitalization	301/442 (68%)	141/442 (32%)	**<0.001**

Continuous variables are presented as mean (SD), where SD denotes standard deviation.

Table 3: Principal multivariable Cox model of baseline factors associated with death among patients with advanced HIV disease. ***(Table 3 Must be placed on line 298)***

Characteristic	aHR	95% CI	p-value
Sex			
Woman	—	—	
Man	1.18	1.06, 1.33	**0.004**
Age at diagnosis group (years)			
From 15 to 25	—	—	
Less than 5	0.67	0.47, 0.95	**0.025**
From 5 to 15	1.10	0.80, 1.51	0.6
From 25 to 40	1.18	0.98, 1.41	0.075
More than 40	1.56	1.29, 1.88	**<0.001**
WHO clinical stage before ART			
Stage 1	—	—	
Stage 2	1.39	0.99, 1.93	0.055

Stage 3	2.18	1.68, 2.83	**<0.001**
Stage 4	4.20	3.19, 5.52	**<0.001**
Baseline CD4 count group (cells/mm³)			
Less than 200	—	—	
From 200 to 350	1.31	1.11, 1.55	**0.001**
From 350 to 500	1.33	0.94, 1.88	0.11
More than 500	0.70	0.41, 1.18	0.2
Method of ART initiation			
New Patient	—	—	
Transferred Patient	0.55	0.44, 0.69	**<0.001**
Prior ART Category			
Anterior ARV >30 days	—	—	
No Treatment	1.12	0.86, 1.45	0.4
PMTCT-related ART exposure	0.83	0.50, 1.38	0.5
Time from HIV diagnosis to first AHD-site visit			
From 1 to 3 months	—	—	
Less than a month	1.11	0.66, 1.89	0.7
From 3 to 6 months	1.33	0.56, 3.18	0.5
From 6 to 12 months	1.46	0.42, 5.10	0.5
More than 12 months	0.79	0.33, 1.89	0.6

Abbreviations: aHR = adjusted hazard ratio; CI = confidence interval. Hazard ratios are unitless. Units for grouped continuous variables are shown in row labels.