# Implementation of a specialized inpatient HIV care model and in-hospital mortality in South Brazil: a before-after study

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## Summary

**Background** Advanced HIV disease (AHD) remains a major cause of hospitalization and mortality among people living with HIV (PLHIV). We evaluated the association between implementation of a structured specialist-led inpatient HIV care model and clinical outcomes among hospitalized PLHIV in southern Brazil.

**Methods** We conducted an observational before–after study at a tertiary public hospital in Porto Alegre, Brazil, comparing a pre-intervention period (January 2023–April 2024) with a post-intervention period (May 2024–August 2025). The intervention included a dedicated infectious diseases team, standardized protocols for AHD and opportunistic infections, and rapid antiretroviral therapy (ART) initiation during hospitalization. Adults admitted with AHD were included. Adjusted risk ratios (aRR) for mortality, ICU admission, and a composite adverse outcome were estimated using modified Poisson regression.

**Findings** A total of 963 hospitalizations among 899 unique patients were included (406 pre-intervention; 557 post-intervention). Baseline characteristics were similar between periods. In-hospital mortality declined from 24% to 17% ($p = 0.014$). In adjusted analyses, the post-intervention period was associated with lower risks of in-hospital mortality (aRR 0.74, 95% CI 0.57–0.96), ICU admission (0.70, 0.57–0.86), and composite adverse outcomes (0.78, 0.67–0.92). Opportunistic infection screening increased, lumbar puncture was performed more frequently, and ART was initiated earlier.

**Interpretation** Implementation of a structured inpatient HIV care model was associated with improved clinical outcomes among PLHIV with AHD. Structured multidisciplinary inpatient HIV care may represent a promising approach to strengthen delivery of WHO-recommended AHD care in hospital settings and warrants further evaluation in controlled studies.

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**Keywords:** HIV infections; Acquired immunodeficiency syndrome; Hospitalization; Patient care team; Delivery of health care; Mortality

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## Research in context

### Evidence before this study

Advanced HIV disease (AHD) remains a major cause of HIV-related morbidity and mortality globally, particularly among people diagnosed late or re-engaging in care after treatment interruption. WHO recommends a package of care for AHD that includes systematic screening, diagnosis and treatment of opportunistic infections (OIs), prophylaxis, and timely antiretroviral therapy (ART) initiation. However, implementation of these interventions remains inconsistent in routine hospital settings. We searched PubMed, Embase and regional databases from January 1, 2000, to June 30, 2025, for studies evaluating inpatient HIV care, AHD, OIs, and mortality among people living with HIV (PLHIV). Existing evidence supports the use of point-of-care diagnostic strategies for tuberculosis, cryptococcosis, and histoplasmosis among people with AHD, as well as timely lumbar puncture when central nervous system infection is suspected. However, most studies have evaluated individual diagnostic or treatment components, often in outpatient or program settings. Only a limited number of studies have evaluated integrated inpatient AHD care models, and few have examined the impact of broader hospital-level services reorganization on mortality and other clinical outcomes. Evidence on whether reorganizing inpatient HIV care at the hospital level improves clinical outcomes remains limited, particularly in Latin America and other high-burden settings.

### Added value of this study

This study provides real-world evidence from a high burden setting in southern Brazil on the implementation of a multicomponent inpatient HIV care model. The intervention integrated centralized inpatient HIV care, multidisciplinary specialist support, standardized diagnostic and treatment protocols for AHD and OIs, and timely ART initiation during hospitalization. Compared with previous studies focusing on single interventions, this study evaluates a multicomponent, health systems–level reorganization of inpatient HIV care implemented under routine care conditions in a high HIV burden urban setting in southern Brazil. The post-intervention period was associated with substantial increases in OI screening, including TB-LAM, cryptococcal antigen, and Histoplasma antigen testing, greater use of lumbar puncture; a higher proportion of microbiologically confirmed TB diagnoses; and earlier and more frequent ART initiation during hospitalization. Importantly, the post-intervention period was also associated with lower in-hospital mortality, ICU admission, and composite adverse outcomes, even after adjustment for baseline characteristics.

### Implications of all the available evidence

Together with existing evidence on AHD care, these findings suggest that strengthening hospital level organization of HIV care may represent an important strategy to reduce preventable mortality among PLHIV with AHD. Even in settings with universal ART access, fragmented inpatient care, delayed diagnosis of OIs and barriers to timely ART initiation may contribute to poor outcomes. These findings support further evaluation of the implementation of WHO-recommended AHD care packages within hospital settings suggest a potential role for strengthening inpatient service delivery models.

## Introduction

Human immunodeficiency virus (HIV) remains a major global public health challenge despite substantial advances in early diagnosis and antiretroviral therapy (ART). Although expanded access to ART has significantly reduced AIDS-related morbidity and mortality, important disparities persist, particularly in settings affected by social and structural vulnerabilities.[1] Late diagnosis and disengagement from care continue to drive morbidity and mortality among people living with HIV (PLHIV).[2]

Brazil has been recognized for its comprehensive HIV response, including universal access to ART through the Unified Health System (Sistema Único de Saúde, SUS), robust surveillance system, and sustained public health interventions.[3,4] Nevertheless, 39,216 new HIV diagnoses were reported nationally in 2024 (18.4 cases per 100,000 inhabitants), highlighting the ongoing burden of HIV in Brazil. Since the beginning of the epidemic, more than 1.6 million HIV or AIDS cases have been recorded in the country.[5] Despite these achievements, a substantial proportion of PLHIV in Brazil remain outside continuous care, limiting viral suppression and contributing to ongoing transmission and inequalities in health outcomes.[6]

HIV burden and outcomes are unevenly distributed across Brazil. The southern region, including the states of Paraná, Santa Catarina, and Rio Grande do Sul (RS), accounts for approximately 19% of cumulative national cases and has consistently reported among the highest AIDS-related mortality rates nationwide. In RS, more than 4300 new HIV cases were reported annually in 2023 and 2024.[7] Porto Alegre, the state capital, has persistently ranked among the Brazilian capitals with the highest HIV incidence and has reported the highest HIV-related mortality among Brazilian state capitals. In 2024, it recorded the highest AIDS-related mortality rate among Brazilian capitals (12.0 deaths per 100,000 inhabitants), more than three times the national average (3.4 deaths per 100,000 inhabitants).[7,8]

Despite overall declines in mortality, advanced HIV disease (AHD), defined by severe immunosuppression (CD4<200 cells/mm$^3$) or World Health Organization (WHO) clinical stage 3 or 4, remains a major driver of

HIV-related deaths. Individuals presenting with AHD at diagnosis or re-engaging in care after prolonged interruption face a markedly increased risk of hospitalization and mortality.[9] These outcomes are largely driven by severe opportunistic infections (OIs) including tuberculosis (TB), disseminated fungal infections, and other co-infections.[10] The WHO recommends a comprehensive package of care for AHD, including rapid diagnosis and treatment of OIs, prompt ART initiation, and intensified clinical management; however, implementation of these approaches in routine hospital settings remains inconsistent, particularly in high-burden urban contexts in Latin America.[2]

Although WHO-recommended interventions for AHD are well established, implementation in routine inpatient settings remains challenging. Fragmented care pathways, delayed diagnosis of OIs, inconsistent application of standardized protocols, and barriers to timely ART initiation may contribute to preventable morbidity and mortality among hospitalized PLHIV with AHD. Hospital-level re-organization of care may therefore facilitate coordinated multidisciplinary management and more timely delivery of evidence-based interventions.

In this context, hospital-level organization of care may play a critical role in improving outcomes. In May 2024, a structured inpatient HIV care model was implemented in a tertiary public hospital in Porto Alegre to reorganize inpatient HIV care. The intervention aimed to strengthen specialist-led management, standardize diagnostic and therapeutic algorithms, and facilitate rapid ART initiation among hospitalized PLHIV, particularly those with AHD. Operational details of the institutional inpatient AHD diagnostic and treatment protocol implemented during the intervention period are provided in Supplementary Appendix S1. However, evidence on the effectiveness of such service reorganization in reducing mortality in real-world settings in Latin America remains limited. This study aimed to evaluate the association between this care reorganization and in-hospital mortality among PLHIV in a high-burden urban setting in southern Brazil.

## Methods

### Study design and setting

We conducted an observational before–after study to evaluate changes in in-hospital mortality following the implementation of the specialized ID team established in May 2024. The analysis compared two consecutive 16-month periods: a pre-intervention period (January 2023–April 2024) and a post-intervention period (May 2024–August 2025). The study was conducted at a tertiary public hospital in Porto Alegre, Rio Grande do Sul (RS), Brazil, a high HIV-burden urban setting within the Unified Health System. The hospital serves as a referral center for the management of AHD and associated OIs.

HIV/AIDS cases were identified using multiple data sources within the hospital's Epidemiological Surveillance Service. At our institution, HIV serological testing is routinely performed as part of standard care, irrespective of clinical presentation. Case identification was based on at least one of the following: documented positive HIV serology, detectable HIV viral load, or HIV/AIDS-related ICD-10 diagnostic codes recorded during hospitalization. This combined approach was used to enhance case ascertainment and reduce misclassification.

HIV infection was confirmed through reactive rapid testing followed by confirmatory assays, including enzyme-linked immunosorbent assay (ELISA) for anti-HIV antibodies and/or immunoblot testing for HIV-1 (p24, gp41, gp120, gp160) and HIV-2 (gp36) antigens. HIV viral load was measured at a certified reference laboratory using a real-time polymerase chain reaction (RT-PCR) assay (cobas 5800 system, Roche Diagnostics) and expressed as HIV RNA copies per milliliter.

Clinical and laboratory data, including CD4+ T-cell counts and viral load measurements, were extracted from electronic medical records and cross-checked with the Brazilian Laboratory Test Control System (SISCEL), a national database that compiles laboratory data for all PLHIV receiving care in the Brazilian public health system, and the Logistic Control System for Medications (SICLOM), which records ART dispensing information.[11,12] Deterministic record linkage was performed using each patient's unique SUS identification number. Personal identifiers were used solely for linkage purposes and were removed prior to statistical analysis.

Completeness of key study variables was high due to linkage between institutional electronic medical records and national HIV information systems (SISCEL and SICLOM). Missing data were minimal (<1% across variables), and complete -case analyses were therefore performed without imputation.

Participants were classified as having AHD at admission if they had a CD4+ T-cell count <200 cells/μL and/or a documented WHO stage 3 or 4 condition, consistent with WHO definitions. Classification was based exclusively on clinical and laboratory information recorded in medical records at the time of admission. The list of WHO stage 3 and 4 conditions is provided in the Supplementary Table S1.

All adult patients aged ≥18 years with confirmed AHD requiring hospital admission during the study periods were eligible for inclusion. To minimize overrepresentation of individuals with multiple hospitalizations, patients with more than one admission within the same period were included only once. Patients admitted in both pre- and post-intervention periods were included once in each period and treated as independent observations, reflecting exposure to different models of care.

As an observational before–after study without a concurrent control group, the design cannot fully

exclude the influence of secular trends, unmeasured confounding, or other institutional changes occurring during the study period.

### Description of the intervention

The intervention comprised three components: (1) implementation of a dedicated inpatient infectious diseases team for the management of PLHIV; (2) introduction of standardized diagnostic and treatment protocols for AHD and OIs; and (3) establishment of a structured process to enable timely initiation of ART during hospitalization.

Before implementation, PLHIV were admitted across multiple general medical wards without a dedicated ID team or fixed nursing staff. Clinical management relied primarily on an informal consultation-based model, in which ID specialists were consulted on demand while primary responsibility remained with non-specialized teams.

Following the creation of a dedicated ID ward, patient care was centralized and delivered by a multidisciplinary team including ID physicians, nurses, pharmacists, physiotherapists, nutritionists, psychologists, and social workers trained in the management of complex infectious diseases. In addition to managing patients within the ward, the ID team also provided consultation and co-management for PLHIV admitted to other specialized units, including the intensive care unit, psychiatric wards, and the prison healthcare unit.

The intervention did not involve construction of a new hospital ward, but rather the reorganization and centralization of inpatient HIV care within an existing clinical unit. New staffing consisted primarily of five ID physicians and one anthropologist focused on communication and support for socially vulnerable populations. Most multidisciplinary professionals were already employed by the hospital and were reassigned to the inpatient HIV unit, where they received targeted training in AHD management, protocol-based care, OIs, and people-centered communication approaches. The reorganized care model integrated dedicated nurses, fixed nursing technician teams, physiotherapists, psychologists, social workers, nutrition support, and speech therapists integrated into routine multidisciplinary reassessment according to clinical complexity.

Standardized diagnostic protocols were implemented at hospital admission, including systematic screening for OIs such as TB (using urine lipar-abinomann [LAM] antigen testing and Xpert MTB/RIF), cryptococcosis (using cryptococcal antigen [CrAg] testing), and histoplasmosis (using antigen detection assays [ELISA or LFA], in accordance with national guidelines and locally available diagnostics. Lumbar puncture was performed when clinically indicated in patients with suspected central nervous system (CNS) infection or positive CrAg results.

Rapid ART initiation was integrated into inpatient care to enable timely treatment initiation during hospitalization. Management of OIs followed protocol-based treatment regimens, with attention to drug–drug interactions, immune reconstitution inflammatory syndrome, and treatment-related toxicities.[2,3,13] The intervention also included coordination with public health authorities to ensure uninterrupted ART supply through the Brazilian federal HIV program.

Fig. 1 illustrates the transition from a fragmented model of inpatient HIV care to a structured multidisciplinary HIV unit, including the principal components of the intervention and associated changes in diagnostic and treatment practices.

Because the intervention was implemented as an integrated hospital-level reorganization of inpatient HIV care, analyses assessed the association between the overall care model and clinical outcomes rather than the independent effects of individual intervention components.

### Data sources and variables

We collected demographic, clinical, and HIV care–related variables, including age at admission, sex, race, and comorbidity burden assessed using the Charlson Comorbidity Index (CCI). The CCI was systematically recorded for all patients at hospital admission as part of institutional protocol and was used without modification.

HIV-related variables included ART status at admission, categorized as: (1) ART-naïve, defined as individuals with no prior history of ART; (2) re-engaged after ART discontinuation, defined as PLHIV who had interrupted ART and were not receiving treatment at the time of admission; and (3) ART at admission, defined as PLHIV receiving ART at the time of admission.

Additional HIV-related variables included plasma HIV viral load (log-transformed; undetectable values were assigned 50 copies/mL prior to transformation; maximum observed value: 10,000,000 copies/mL [log10 = 7]), CD4 cell count at presentation (<50, 50–199, and ≥200 cells/mm$^3$), and ART use during hospitalization (not prescribed, continued, or initiated). Time to ART initiation was defined as the number of days from hospital admission to ART prescription among those who initiated therapy during hospitalization. Diagnostic and management variables included performance of inpatient lumbar puncture and results of OIs screening tests (CrAg, histoplasma antigen, and TB-LAM), categorized as positive, negative, or not performed. TB co-infection was classified as confirmed (microbiologically) or empirically diagnosed. Detailed diagnostic and treatment algorithms used during the intervention period are summarized in Supplementary Appendix S1.

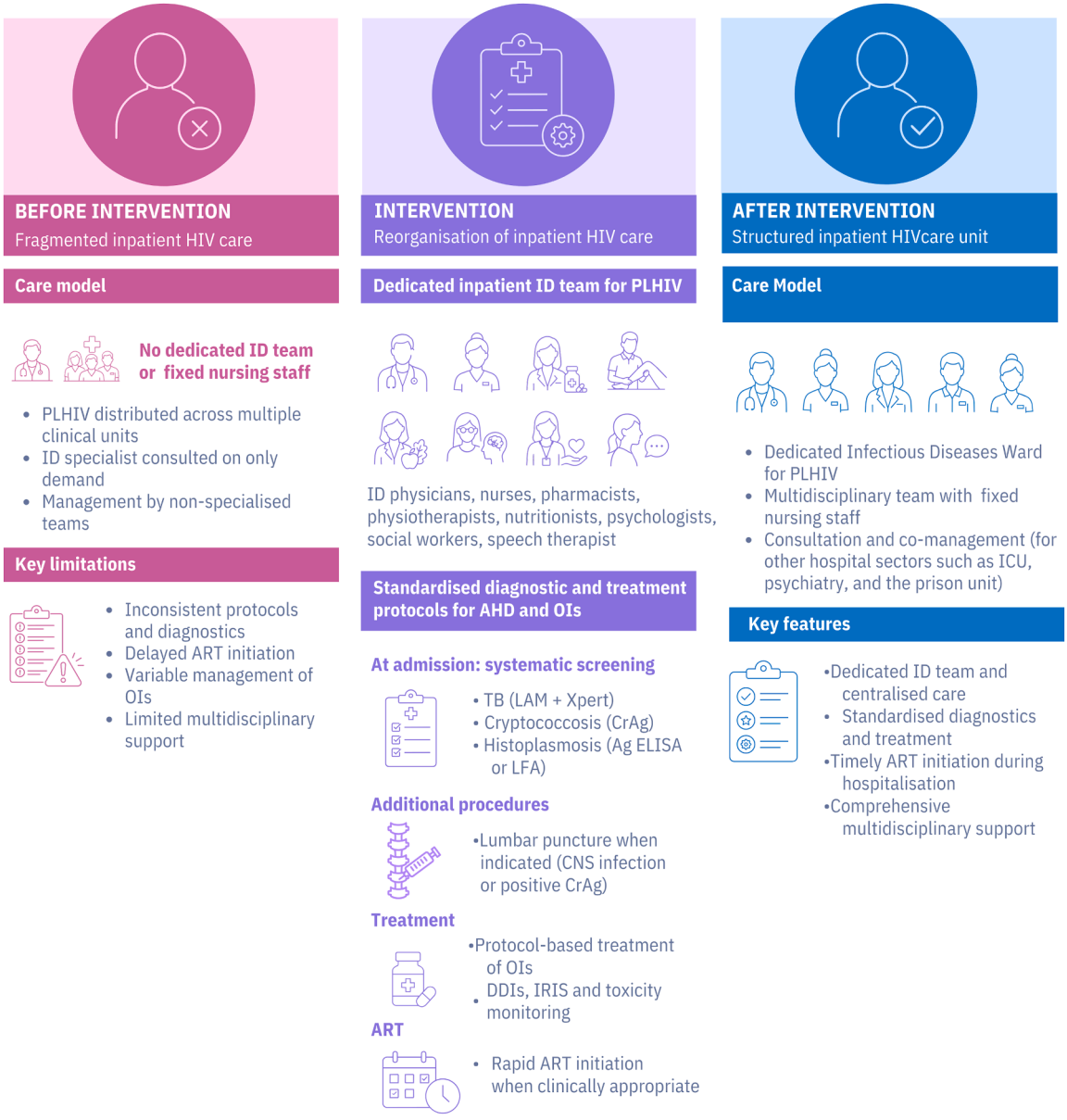


***Fig. 1:* Components of the Specialized Inpatient HIV Care Model Implemented at Hospital Vila Nova, Porto Alegre, Brazil.** The figure summarizes the reorganization of inpatient care for PLHIV, from a fragmented pre-intervention model to a centralized model led by a dedicated ID team. The intervention included dedicated inpatient HIV care, multidisciplinary support with fixed nursing staff, standardized diagnostic and therapeutic protocols for AHD, systematic screening for OIs, specialist consultation and co-management across hospital sectors, and rapid ART initiation when clinically appropriate. The intervention was implemented pragmatically as part of routine service reorganization; components were introduced simultaneously and were not prospectively designed for isolated effect evaluation. AHD = advanced HIV disease; ART = antiretroviral therapy; CNS = central nervous system; CrAg = cryptococcal antigen; DDIs = drug–drug interactions; ELISA = enzyme-linked immunosorbent assay; HIV = human immunodeficiency virus; ICU = intensive care unit; ID = infectious diseases; IRIS = immune reconstitution inflammatory syndrome; LFA = lateral flow assay; LP = lumbar puncture; TB = tuberculosis; TB-LAM = tuberculosis lipoarabinomannan.

The primary outcome was in-hospital mortality, defined as death occurring during the index hospitalization. Secondary outcomes included intensive care unit (ICU) admission and a composite adverse outcome (ICU admission and/or in-hospital death). The composite adverse outcome was intended to capture severe clinical deterioration during hospitalization, recognizing that ICU admission and in-hospital death

| Characteristic | Before (n = 406) | After (n = 557) | p-value[a] |
|---|---|---|---|
| Age | | | |
| Median (IQR) | 44 (36–51) | 43 (34–52) | 0.34 |
| Sex | | | |
| Male | 242 (60%) | 319 (57%) | 0.46 |
| Female | 164 (40%) | 238 (43%) | |
| Race | | | |
| White | 221 (54%) | 331 (59%) | 0.09 |
| Black | 124 (31%) | 134 (24%) | |
| Mixed | 61 (15%) | 92 (17%) | |
| Charlson Comorbidity score | | | |
| Median (IQR) | 7 (6–8) | 7 (6–8) | 0.48 |
| Antiretroviral therapy adherence | | | |
| ART naïve | 115 (28%) | 132 (24%) | 0.24 |
| Previously diagnosed, reengaged after ART discontinuation | 264 (65%) | 382 (69%) | |
| Previously diagnosed, on ART | 26 (6%) | 43 (8%) | |
| Viral Load (Log) | | | |
| Median (IQR) | 5.2 (4.3–5.8) | 5.1 (3.9–5.8) | 0.23 |
| CD4 count at presentation | | | |
| <50 | 119 (29%) | 162 (29%) | 0.51 |
| 50–199 | 192 (47%) | 281 (51%) | |
| ≥200 | 95 (23%) | 114 (21%) | |
| Tuberculosis co-infection | | | |
| Confirmed | 105 (26%) | 228 (41%) | <0.001 |
| Empiric diagnosis | 85 (21%) | 54 (10%) | |

[a]P-values were calculated using the Wilcoxon rank-sum test for continuous variables and joint Wald tests of all category coefficients for categorical variables.

***Table 1:*** **Sociodemographic and clinical characteristics of hospitalizations among PLHIV before and after implementation of the structured inpatient HIV care model in South Brazil.**

represent related but distinct markers of adverse prognosis. The CCI is a validated clinical tool used to quantify an individual's burden of chronic disease by assigning weighted scores to predefined conditions associated with mortality risk. The total score reflects overall comorbidity severity and has been widely used to predict survival. The full list of included conditions is presented in Supplementary Table S2.[14]

### Statistical analysis

Continuous variables were summarized as medians with interquartile ranges (IQR), and categorical variables as counts and percentages. Viral load values were summarized using medians and IQR and compared between pre- and post-intervention periods using the Wilcoxon rank-sum test. Most patients contributed a single hospitalization, with a minority (7.1%) contributing two observations (mean 1.1 per patient), resulting in minimal within-patient clustering.

Modified Poisson regression with robust standard errors was used to estimate relative risks (RR) for outcomes. This approach provides consistent estimates under mild violations of independence, including limited within-patient clustering.[15,16] Accordingly, all models were fitted using cluster-robust standard errors at the patient level. P-values for Table 1 and Table 2 were derived using joint Wald tests of all category coefficients (testparm) for categorical variables. To examine outcomes of interest and independent associations, multivariable models were constructed a priori based on clinical relevance and potential confounding. Covariates included age, sex, CCI, CD4 count, ART status at admission, TB co-infection, and timing of intervention. Variables representing in-hospital processes of care were excluded from primary models to avoid adjustment for potential mediators. All tests were two-sided, and a p-value <0.05 was considered statistically significant. Analyses were conducted using Stata (version 14; StataCorp, College Station, TX).

As a complementary analysis, interrupted time-series analyses were conducted for in-hospital mortality and ICU admission using the pre-intervention trends to estimate counterfactual trajectories and compare them with observed post-intervention outcomes. To evaluate whether associations were sustained over time, follow-up for these outcomes was extended through April 2026. Extended follow-up was restricted to mortality and ICU admission because routinely collected aggregated data were available only for these endpoints.

### Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the institutional Research Ethics Committee of Hospital Ernesto Dornelles under CAAE number 89594725.5.0000.5304. As a retrospective observational study based on anonymized secondary data, the requirement for individual informed consent was waived.

### Role of funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

## Results

A total of 963 hospitalizations were recorded across the pre- and post-intervention periods (406 pre-intervention; 557 post-intervention), corresponding to 899 unique patients; no additional exclusion criteria were applied. Among these, 64 (7%) contributed hospitalizations in both periods. Patients had a median age of 43–44 years, with a predominance of males (~58%), median CCI index of 7, and severe immunosuppression, with nearly one-third presenting with CD4 counts <50 cells/mm$^3$. Most patients were either ART-naïve or reengaged after ART discontinuation, and baseline characteristics were comparable between periods. Sociodemographic and clinical characteristics are summarized in Table 1.

Diagnostic practices, inpatient care processes, and clinical outcomes before and after implementation of the intervention are summarized in Table 2 and Fig. 2. Use of point-of-care diagnostics increased substantially, including TB-LAM 154/406 (38%) vs 490/557 (88%), CrAg testing 163/406 (40%) vs 464/557 (83%), and Histoplasma antigen testing 171/406 (42%) vs 347/557 (62%) (all p < 0.001) (Fig. 2). Positivity rates among performed diagnostic tests were also evaluated. While CrAg positivity remained stable between periods, positivity rates for urine TB-LAM and Histoplasma antigen testing increased despite broader post-intervention test utilization (see Supplementary Table S3). This coincided with a higher proportion of microbiologically confirmed TB diagnoses [228/557 (41%) vs 105/406 (26%)] and fewer empiric TB diagnoses [54/557 (10%) vs 85/406 (21%); p < 0.001]. The proportion of patients undergoing lumbar puncture nearly doubled [198/557 (36%) vs 79/406 (20%); p < 0.001]. Inpatient ART initiation increased from 97/406 (24%) to 400/557 (72%) (p < 0.001), while median time to ART initiation decreased from 10 to 6 days (p < 0.001) (Fig. 2). Median length of stay did not differ significantly between periods (11 [IQR 7–21] vs 12 days [IQR 7–21]; p = 0.19). Following implementation of the intervention, ICU admissions (114/557 (21%) vs 125/406 (31%); p < 0.001), in-hospital mortality [93/557 (17%) vs 96/406 (24%); p = 0.014] and the composite adverse outcome [183/557 (33%) vs 178/406 (44%); p < 0.001] were significantly lower (see Figs. 3 and 4).

| Variable | Before (n = 406) | After (n = 557) | p-value[a] |
|---|---|---|---|
| Length of stay, days Median (IQR) | 11 (7–21) | 12 (7–21) | 0.19 |
| ART provided during hospitalization | | | |
| Not prescribed | 265 (65%) | 91 (16%) | <0.001 |
| Previously on ART | 44 (11%) | 66 (12%) | |
| Initiated inpatient | 97 (24%) | 400 (72%) | |
| Days elapsed until ART provided during hospitalization[b] Median (IQR) | 10 (5–19) | 6 (3–8) | <0.001 |
| Inpatient lumbar puncture | | | |
| Performed | 79 (20%) | 198 (36%) | <0.001 |
| Cryptococcal Antigen | | | |
| Negative | 149 (37%) | 431 (78%) | <0.001 |
| Positive | 14 (4%) | 33 (6%) | |
| Not performed | 243 (60%) | 92 (17%) | |
| Histoplasma Antigen | | | |
| Negative | 159 (39%) | 288 (52%) | <0.001 |
| Positive | 12 (3%) | 59 (11%) | |
| Not performed | 235 (58%) | 209 (38%) | |
| TB Lipoarabinomannan screen | | | |
| Negative | 118 (29%) | 313 (56%) | <0.001 |
| Positive | 36 (9%) | 177 (32%) | |
| Not performed | 252 (62%) | 67 (12%) | |
| Tuberculosis diagnostic modalities[c] | | | |
| Rapid Molecular Test | 71 (18%) | 90 (16%) | 0.38 |
| Culture | 13 (3%) | 4 (1%) | 0.003 |
| TB Lipoarabinomannan screen | 36 (9%) | 177 (32%) | <0.001 |
| Intensive Care Unit | | | |
| Yes | 125 (31%) | 114 (21%) | <0.001 |
| In-hospital mortality | | | |
| Yes | 96 (24%) | 93 (17%) | 0.014 |
| Composite adverse outcome[d] | | | |
| Yes | 178 (44%) | 183 (33%) | <0.001 |

[a]P-values for continuous variables were calculated using the Wilcoxon rank-sum test. For categorical variables with more than two categories, p-values were derived using joint Wald tests of all category coefficients. [b]Among those who were initiated on ART during hospitalization. [c]Microbiologically confirmed tuberculosis included cases with positive Xpert MTB/RIF, mycobacterial culture, smear microscopy, TB-LAM, histopathology, or other microbiological confirmation documented in the medical record. Diagnostic modalities presented in Table 1 were not mutually exclusive and do not encompass all confirmatory methods. [d]Composite adverse outcome was defined as experiencing ICU and/or mortality during hospitalization.

***Table 2:*** **Changes in diagnostic practices, inpatient HIV care processes, and clinical outcomes following implementation of the structured inpatient HIV care model.**

### Intensive care unit (ICU) admission

In unadjusted analyses, hospitalization during the post-intervention period was associated with a lower risk of ICU admission (IRR 0.66, 95% CI 0.54–0.81, p < 0.001). Positive CrAg results (IRR 1.64, 95% CI 1.08–2.48), empiric TB diagnosis (IRR 1.44, 95% CI 1.08–1.94), and higher CCI scores (IRR 1.11 per point, 95% CI 1.05–1.16) were associated with a higher risk of ICU admission, whereas receipt of ART during hospitalization was associated with a lower risk (IRR 0.61 95% CI 0.48–0.76). Detailed unadjusted analyses are presented in Supplementary Table S4.

In adjusted analyses, the association between the post-intervention period and a lower risk of ICU admission remained significant (aIRR 0.70, 95% CI 0.57–0.86; p = 0.001) (Fig. 3). Higher CCI scores and lower CD4 cell counts remained independently associated with ICU admission (IRR 1.11, 95% CI 1.05–1.18 and IRR 0.75, 95% CI 0.59–0.95, respectively). Empiric tuberculosis treatment was also independently associated with an increased risk of ICU admission (aIRR 1.38, 95% CI 1.02–1.86).

### In-hospital mortality

In unadjusted analyses, hospitalization during the post-intervention period was associated with a lower risk of in-hospital mortality (IRR 0.71, 95% CI 0.55–0.91, p = 0.008) (Fig. 3). Higher CD4 cell counts were associated with lower mortality, whereas increasing age, higher CCI scores, and higher viral load were associated with increased mortality. Detailed unadjusted analyses are presented in Supplementary Table S4. Compared with ART-naïve individuals, those re-engaged in care after ART discontinuation and those with a previous HIV diagnosis receiving ART had lower mortality (see Supplementary Table S5).

In adjusted analyses, the association between the post-intervention period and reduced in-hospital mortality remained significant (aIRR 0.74, 95% CI

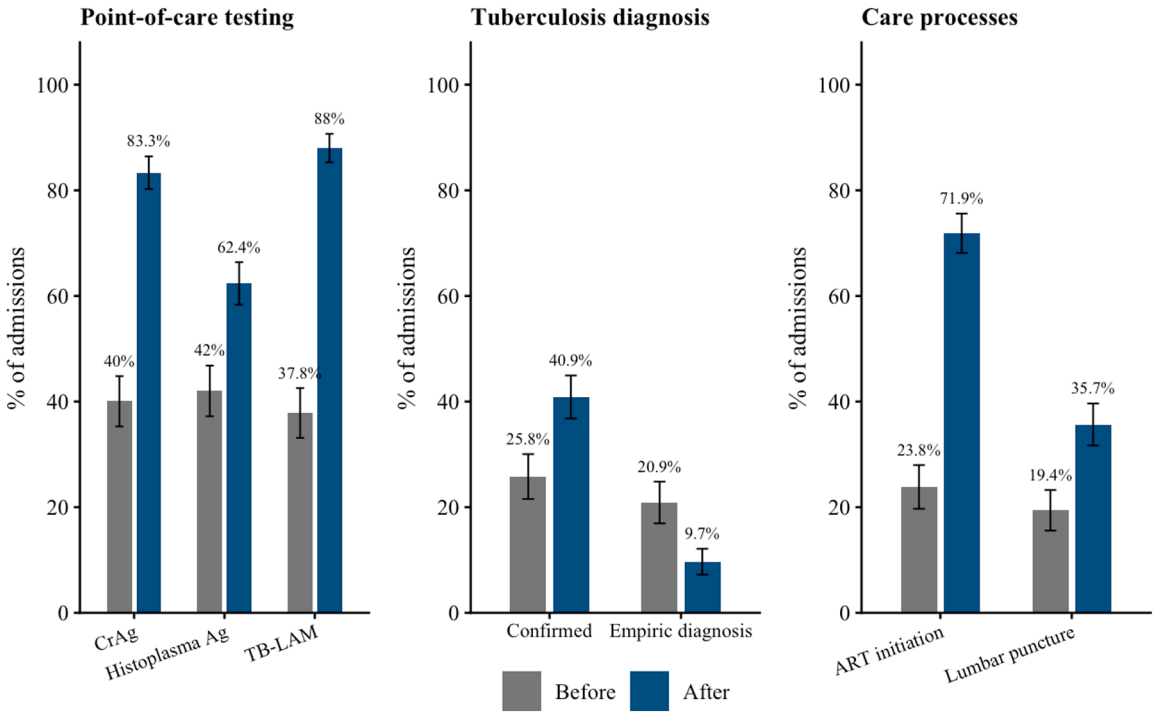


***Fig. 2:* Changes in Opportunistic Infection Diagnostic Testing and HIV Care Processes Following Implementation of the Specialized Inpatient HIV Care Model.** Changes in diagnostic practices and inpatient HIV care processes before and after implementation of a structured inpatient HIV care model. Bars represent the proportion of admissions in which each diagnostic test or clinical process was performed during the pre-intervention ("Before") and post-intervention ("After") periods. Error bars indicate 95% confidence intervals. TB-LAM = urine lipoarabinomannan assay; CrAg = cryptococcal antigen; ART = antiretroviral therapy.

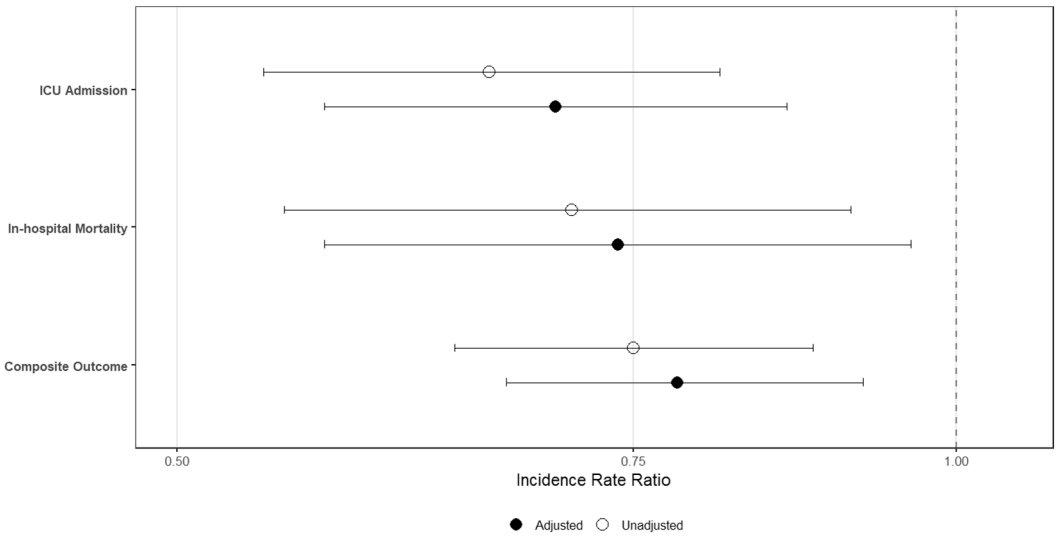


***Fig. 3:* Adjusted and unadjusted risk estimates for ICU admission, in-hospital mortality, and composite adverse outcome.** Forest plot of adjusted and unadjusted incidence rate ratios for ICU admission, in-hospital mortality, and composite adverse outcome associated with hospitalization during the post-intervention period. Horizontal lines indicate 95% confidence intervals; the vertical dashed line indicates IRR = 1. IRR = incidence rate ratio; ICU = intensive care unit.

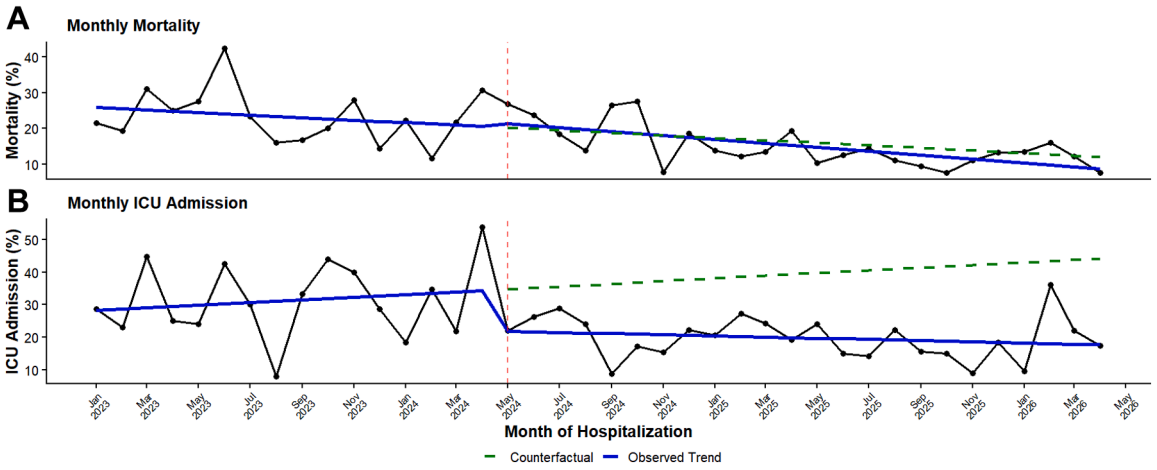


***Fig. 4:* Interrupted time-series analysis of monthly in-hospital mortality and ICU admission before and after implementation of the structured inpatient HIV care model.** Interrupted time-series analysis of monthly in-hospital mortality (panel A) and ICU admission (panel B) among hospitalized PLHIV before and after implementation of the structured inpatient HIV care model in May 2024. Black lines represent observed monthly outcome rates. Blue lines represent observed segmented regression trends, and green dashed lines represent counterfactual trends estimated from the pre-intervention period. The vertical red dashed line indicates timing of intervention implementation. ICU = intensive care unit.

0.57–0.96; p = 0.02). Higher CCI scores and lower CD4 cell counts also remained independently associated with mortality (aIRR 1.11, 95% CI 1.05–1.18 and aIRR 0.71, 95% CI 0.55–0.92, respectively).

### Composite adverse outcome

In unadjusted analyses, hospitalization during the post-intervention period was associated with a lower risk of the composite adverse outcome (IRR 0.75, 95% CI 0.64–0.88, p < 0.001). Higher CD4 cell counts were associated with lower risk (CD4 50–199 vs <50: IRR 0.80, 95% CI 0.68–0.96; CD4 ≥200 vs <50: IRR 0.66, 95% CI 0.51–0.84), whereas increasing age (IRR 1.01 per year, 95% CI 1.01–1.02) and higher CCI scores (IRR 1.15 per point, 95% CI 1.11–1.18) were associated with increased risk. ART Initiation during hospitalization was also associated with a lower risk of the composite outcome (IRR 0.74, 95% CI 0.62–0.88) (see Supplementary Table S4).

In adjusted analyses, the association between the post-intervention period and a lower risk of the composite adverse outcomes remained significant (aIRR 0.78, 95% CI 0.67–0.92; p = 0.002) (Fig. 3). Higher CCI scores and lower CD4 cell counts remained independently associated with the outcome (aIRR 1.13, 95% CI 1.09–1.17 and aIRR 0.82, 95% CI 0.69–0.98, respectively).

## Discussion

In this observational before–after study, the implementation of a specialized inpatient HIV care model was associated with reduced in-hospital mortality, ICU admission, and composite adverse outcomes among PLHIV. In adjusted analyses, hospitalization during the post-intervention period was associated with a 26% lower risk of in-hospital mortality. These improvements were observed despite persistent severe immunosuppression and high comorbidity burden. These findings provide real-world evidence that a structured inpatient HIV care model was associated with improved outcomes among hospitalized PLHIV. Interpretation of the composite adverse outcome requires caution, as ICU admission may be influenced by both disease severity and access to intensive care resources. However, the observed reductions in ICU admission and in-hospital mortality suggest that the intervention was associated with improvement across multiple indicators of severe inpatient outcomes.

Increased diagnostic intensity following implementation of systematic screening protocols likely altered ascertainment of OIs, particularly tuberculosis, and may have influenced the observed clinical characteristics of hospitalized patients across periods. As a result, differences in the apparent epidemiological profile of OIs between periods should be interpreted cautiously. Given the bundled nature of the intervention, it is not possible to isolate the relative contribution of individual components or fully disentangle the effect of changes in diagnostics, treatment, and timing of care. However, the observed improvements across multiple clinically relevant outcomes support a potential beneficial effect of the intervention on patient outcomes. The consistency of improvements across diagnostic practices, treatment initiation, and clinical outcomes suggests a plausible clinical pathway linking earlier diagnosis and timely ART initiation to improved survival.

A key component of the broader inpatient HIV care reorganization was the integration of rapid ART initiation into inpatient care. Early ART initiation during hospitalization, when clinically appropriate, has been associated with improved survival and reduced progression of AHD. Current guidelines recommend rapid ART initiation, while emphasizing the need to exclude CNS OIs to mitigate the risk of immune reconstitution inflammatory syndrome.[2,17] At the same time, patients with suspected TB initiating ART rapidly should undergo prompt diagnostic evaluation and close follow-up of microbiological results to ensure timely initiation of anti-TB therapy when indicated.[2,18] In our setting, structural barriers previously limited rapid ART initiation during hospitalization as medications were dispensed exclusively through outpatient systems. Following the intervention, ART was initiated more rapidly and consistently, with increased coverage during admission and shorter time to initiation. Although these care-process improvements were not independently associated with short-term in-hospital outcomes after adjustment, they remain essential components of comprehensive AHD care and may contribute to continuity of care beyond hospitalization.

The intervention was also associated with a marked increase in diagnostic capacity and a shift toward protocol-driven evaluation for OIs. Implementation of systematic screening for TB, cryptococcosis, and histoplasmosis resulted in higher rates of confirmed diagnoses and reduced reliance on empiric treatment. The increased positivity rates observed despite broader test utilization may reflect improved ascertainment of opportunistic infections among severely immunosuppressed individuals following implementation of systematic screening protocols, particularly given the high proportion of missed diagnostic evaluations during the pre-intervention period. These findings align with current recommendations for AHD management, which emphasize systematic screening for Ois.[2] Previous studies have shown that point-of-care diagnostic strategies increase detection of TB, cryptococcosis, and histoplasmosis, and may contribute to improved survival among PLHIV.[19–21]

The observed increase in TB diagnoses in the post-intervention period likely reflects improved case detection rather than a true increase in incidence. The use of rapid diagnostic tools, including molecular assays, culture, and urine LAM testing, has been shown to increase case detection and improve survival, particularly among high-risk populations.[22] In addition, urine-based screening strategies can identify a substantial proportion of otherwise undiagnosed TB cases, including among patients without classic symptoms or other methods of confirmation.[23] However, LAM testing may have cross-reactivity with non-TB mycobacteria, which can complicate interpretation in some settings.[24]

The proportion of hospitalized patients undergoing lumbar puncture nearly doubled during the post-intervention period. The increased use of lumbar puncture procedures likely contributed to earlier diagnosis and management of CNS infections, including cryptococcal and TB meningitis. The study however, captured only whether lumbar puncture was performed during hospitalization and could not distinguish diagnostic from therapeutic procedures or quantify repeated therapeutic lumbar punctures. Prior studies have demonstrated that prompt diagnosis and early initiation of treatment are critical for survival in AHD.[25,26] Delayed diagnosis has been independently associated with increased mortality,[25] while therapeutic lumbar punctures play a critical role in the management of cryptococcal meningitis and have been associated with improved survival.[26] These findings highlight the importance of early neurological assessment in patients with suspected central nervous system involvement.[27]

In adjusted analyses, empiric TB diagnosis remained independently associated with increased ICU admission, consistent with evidence that empiric TB treatment in high-burden settings is often associated with more advanced disease, diagnostic uncertainty, and poorer clinical outcomes.[28] Disseminated fungal infections such as histoplasmosis frequently mimic TB in this population, and misclassification may delay appropriate treatment.[29] In such cases, reliance on empiric therapy without microbiological confirmation may delay recognition of alternative OIs and detection of drug-resistant TB, thereby hindering timely optimization of treatment.[29,30]

Higher CD4 count at presentation was consistently associated with improved outcomes across all models, consistent with a biological gradient in risk. Patients with CD4 counts $\geq$200 cells/mm$^3$ had substantially lower mortality and adverse outcomes compared with those with severe immunosuppression, underscoring the role of immune status in prognosis among hospitalized PLHIV. Comorbidity burden was also a strong predictor of adverse outcomes across all models.

The need for structured inpatient care models for people with AHD has been increasingly recognized. The 2023 WHO policy brief recommends integrated inpatient approaches combining rapid HIV diagnosis, systematic OI screening, timely ART initiation, multidisciplinary management, and coordinated post-discharge follow-up.[31] Similar strategies have been described in Malawi, where an "in-reach" AHD model embedded within medical wards implemented routine inpatient HIV testing, point-of-care CD4 testing, systematic LF-LAM and CrAg screening, and inpatient ART initiation.[32] In contrast, our intervention involved a broader institutional reorganization, including centralized inpatient HIV care under a dedicated ID team and standardized diagnostic and treatment pathways.

Despite differences in context and implementation, both approaches share the goal of improving outcomes among hospitalized PLHIV with advanced disease through more structured and coordinated inpatient care.

In the present study, in-hospital mortality decreased from 96/406 (24%) before the intervention to 93/557 (17%) after implementation of the structured inpatient HIV care model, although mortality remained high in both periods, reflecting the severity of illness among hospitalized individuals with AHD. These findings should be interpreted within the broader global context of AHD hospitalizations. A recent systematic review and meta-analysis including more than 100,000 hospital admissions worldwide reported a pooled in-hospital mortality of approximately 17% among individuals hospitalized with AHD despite expanded access to ART in the universal treatment era.[33]

This study has several limitations. First, its observational before–after design is susceptible to residual confounding and cannot fully exclude the influence of secular trends or unmeasured differences in case-mix between periods. Changes in ICU admission practices over time cannot be excluded. The lower frequency of ICU admission observed during the post-intervention period may have resulted in a more severely ill subgroup of patients being admitted to ICU, introducing potential selection bias in comparisons of ICU-related outcomes between periods. Second, the use of routinely collected clinical data may introduce misclassification and variability in diagnostic coding. During the pre-intervention period, syndromic diagnoses were often recorded without etiologic confirmation, limiting retrospective characterization of OIs. As such, we were unable to perform a detailed comparison of specific OIs or causes of death across periods.

Despite these limitations, the direction and magnitude of observed associations support the contribution of a structured inpatient HIV care model to improved patient outcomes. Although conducted in a single urban referral center, the intervention reflects pragmatic changes in service delivery that may be applicable to other high-burden settings.

## Conclusion

From a health systems perspective, these findings have important implications for Brazil's Unified Health System and similar high-burden settings. The implementation of a structured inpatient HIV care model integrating multidisciplinary management, standardized diagnostic pathways, and timely ART initiation processes was associated with improved diagnostic capacity, more timely ART initiation, and reduced ICU admission and in-hospital mortality among PLHIV with AHD. These findings suggest that even in settings with universal ART access, preventable deaths may persist when care is fragmented or delayed. Strengthening inpatient HIV care through structured, multidisciplinary, and protocol-driven models may represent a potentially relevant approach to improve outcomes in high-burden settings.

### Contributors

PMF: conceptualization, methodology, formal analysis, investigation, project administration, supervision, and writing—original draft.

AN: methodology, investigation, data curation, and validation.

IA, GOB, AEB, and FDCA: investigation and data curation.

ET: data interpretation and writing—review & editing.

CJH: formal analysis and writing—review & editing.

FP: supervision, data interpretation, and writing—review & editing.

OS: data interpretation and writing—review & editing.

NR: conceptualization, methodology, supervision, and data interpretation.

PMF and AN directly accessed and verified the underlying data.

PMF, AN, and NR were responsible for the decision to submit the manuscript for publication.

All authors had access to the data reported in the study, contributed to data interpretation, critically reviewed the manuscript, approved the final version, and accept responsibility for the decision to submit for publication.

### Data sharing statement

The data underlying this study are not publicly available because they contain information derived from medical records and are subject to ethical and institutional restrictions. Deidentified data may be made available upon reasonable request to the corresponding author, subject to approval by the relevant ethics committees and institutional requirements.

### Declaration of interests

OS reports support from the International AIDS Society (IAS) for attendance at scientific conferences and participation on the Data Safety Monitoring Board of the El Dorado study and the HPTN Scientific Expert Committee. PMF, AN, IA, GOB, AEB, FDCA, ET, CJH, FP, and NR declare no competing interests.

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### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2026.101555.

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