HHS Public Access
Author manuscript
J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2025 July 01.

Published in final edited form as:
J Acquir Immune Defic Syndr. 2024 July 01; 96(3): 223–230. doi:10.1097/QAI.0000000000003413.

Modeling the HIV cascade of care using routinely collected clinical data to guide programmatic interventions and policy decisions

Giorgos Bakoyannis, PhD[1,*], Batya Elul, PhD[2,*], Kara K. Wools-Kaloustian, MD[3], Steven Brown, MS[3], Aggrey Semeere, MBChB[4], Barbara Castelnuovo, MD[4], Lameck Diero, MBChB[5], Gertrude Nakigozi, MBChB[6], Rita Lyamuya, MD[7], Constantin T. Yiannoutsos, PhD[8,], for the East Africa IeDEA Regional Consortium.**

[1]Athens University of Economics and Business, Athens, Greece

[2]Columbia University, Mailman School of Public Health, New York, USA

[3]Indiana University School of Medicine, Indianapolis, USA

[4]Infectious Disease Institutes, College of Health Sciences, Makerere University, Kampala, Uganda

[5]Department of Medicine, Moi University School of Medicine, Eldoret, Kenya

[6]Rakai Health Sciences Program, Rakai, Uganda

[7]Morogoro Regional Hospital, Morogoro, Tanzania

[8]Indiana University Fairbanks School of Public Health, Indianapolis USA

Abstract

Background—The HIV care cascade is a framework to examine effectiveness of HIV programs and progress toward global targets to end the epidemic but has been conceptualized as a unidirectional process that ignores cyclical care patterns. We present a dynamic cascade that accounts for patient “churn,” and apply novel analytic techniques to readily available clinical data to robustly estimate program outcomes and efficiently assess progress towards global targets.

Methods—Data were assessed for 35,649 people living with HIV and receiving care at 78 clinics in East Africa between 2014–2020. Patients were aged ≥15 years and had ≥1 viral load measurements. We used multi-state models to estimate the probability of being in 1 of 5 *states* of a dynamic HIV cascade: (1) in HIV care but not on antiretroviral therapy (ART); (2) on ART; (3) virally suppressed; (4) in a gap-in-care; and (5) deceased; and compared these among subgroups. To assess progress towards global targets, we summed those probabilities across patients and generated population-level proportions of patients on ART and virally suppressed in mid-2020.

Results—One year following enrollment, 2.8% of patients had not initiated ART, 86.7% were receiving ART, 57.4% were virally suppressed,10.2% were disengaged from care, and 0.3% had died. At 5 years, the proportion on ART remained steady but viral suppression increased to 77.2%.

**Corresponding author.
*Joint first authors (names listed alphabetically)

Conflicts of interest: None

Of those aged 15–25, >20% had disengaged from care and <60% were virally suppressed. In mid-2020, 90.1% of the cohort was on ART, 90.7% of whom had suppressed virus.

Conclusion—Novel analytic approaches can characterize patient movement through a dynamic HIV cascade and, importantly, by capitalizing on readily available data from clinical cohorts, offer an efficient approach to estimate population-level proportions of patients on ART and virally suppressed. Significant progress towards global targets was observed in our cohort but challenges remain among younger patients.

Introduction

The HIV care cascade describes the spectrum of engagement in HIV services from diagnosis to the ultimate goal of viral suppression (VS)[1–5]. Since its conception, it has been used to measure the effectiveness of HIV testing and treatment programs and identify populations in need of targeted interventions. The cascade also forms the basis for the 95–95-95 targets set by the United Nations Joint Programme in HIV/AIDS (UNAIDS) to end the HIV epidemic which state that by 2030, 95% of people living with HIV (PLWH) will be diagnosed, 95% of those diagnosed will initiate antiretroviral therapy (ART) and 95% of those on ART will achieve VS[6].

In resource-limited settings, performance across the cascade and progress towards the UNAIDS targets have been measured cross-sectionally in nationally representative surveys, and in retrospective and prospective cohort analyses using longitudinal data from HIV care and treatment clinics[7]. Nationally representative cross-sectional surveys, such as the Population-based HIV Impact Assessments (PHIA), use the number of PLWH as the denominator to examine population-level progress towards all three UNAIDS targets in a given year[7–11]. However, given their high cost, they cannot be conducted widely or repeated with sufficient frequency to guide targeted interventions to end the epidemic[12]. On the other hand, cohort analyses examine individual-level progress across the cascade beginning with care enrollment. Of relevance for a chronic condition such as HIV, they can determine whether outcomes are sustained over time, and importantly, can be widely and regularly conducted as they draw on readily available data from HIV clinics[1, 4]. However, to date, most longitudinal analyses have considered the cascade as a linear, unidirectional procession across 5 steps from diagnosis to linkage to care, through ART initiation and retention in care, and ultimately to VS[1, 4, 13–16]. This approach ignores widely documented cyclical care patterns in which many PLWH engage, disengage and re-engage in care, often repeatedly[17–24], and thus provides an incomplete and likely inaccurate picture of program effectiveness. Indeed, overlooking transient or long-term treatment interruptions may overestimate patient retention in care and VS, ultimately contributing to inappropriate prioritization of interventions[18–20]. Additionally, as cohort studies assess individual-level outcomes they have not been used to date to estimate population-level progress towards the 95–95-95 targets, information that is critical to sound policy and funding decisions.

To address these limitations, we analyze routinely collected data from a large cohort of patients newly enrolling in HIV care in East Africa using multi-state models to estimate the probability of an individual being in 1 of 5 *states* within a dynamic HIV care cascade. As identifying populations requiring targeted interventions across the cascade is critical to curbing the HIV epidemic, we also compare these state-occupation probabilities among relevant sub-groups. In addition, as multi-state models in and of themselves do not measure the progress of an entire patient cohort towards the UNAIDS targets, we use novel methods to transform estimates of the probability that *an individual* occupies a state in the cascade to *population-level estimates* of the proportion of the cohort in each state at a given date.

Methods

Study design

We conducted a retrospective cohort analysis using routinely collected clinical data from patients enrolling in HIV care and treatment clinics in Kenya, Tanzania and Uganda that are affiliated with the East Africa region of the International epidemiology Databases to Evaluate AIDS (EA-IeDEA) Consortium[25]. The regulatory bodies affiliated with the sites, and the Institutional Review Boards at Indiana University and Columbia University have approved transfer and analysis of these data. As the data are routinely collected and de-identified prior to transfer to the regional data center, all regulatory bodies waived the requirement for patient informed consent.

Study sites and population

Sites participating in EA-IeDEA are predominately in public-sector outpatient facilities and provide secondary and tertiary levels of care in urban and semi-urban settings. We used data for PLWH who enrolled in HIV care at those sites between January 1, 2014 and May 30, 2020, were age 15 or older at enrollment and had at least one viral load (VL) measure. Clinical care was provided in accordance with local or national guidelines that were aligned with prevailing WHO guidelines. Data prior to 2014 were excluded as treatment protocols have changed markedly in this last decade compared to previous years, so patterns of care access prior to that time would be expected to not reflect current trends.

Data collection and management

As part of routine clinical care, patient sex, age, visit dates, longitudinal measures of WHO stage, CD4 count, ART status, VL, and information on transfers and deaths were captured on paper forms at enrolment and follow-up with subsequent transcription into local electronic medical records systems (EMR) or directly entered in the local EMR during the clinical visit. Data were collected according to national guidelines in the countries where each IeDEA-affiliated program belongs[26–28]. In particular, VL data were collected according to national guidelines but generally require a test six months after initiation of treatment and annually thereafter with some exceptions related to age or, after ART changes (Kenya) and based on prior VS (Tanzania). Data were de-identified by each site and transferred to the East Africa IeDEA Regional Data Center for cleaning, validation and merging. Database closure was on May 30, 2020.

Multi-state model of the HIV care cascade

As shown in Figure 1, we posit a multi-state model of the HIV care continuum that allows individuals to move *dynamically*, as opposed to sequentially, through 5 mutually exclusive states: (1) in HIV care; (2) on ART; (3) virally suppressed; (4) gap-in-care; and (5) deceased. The *HIV care* state includes patients enrolled in care who have not progressed to any of the other states, including ART initiation, and those re-engaging in care following a period of disengagement but prior to treatment re-initiation. The *gap-in-care* state reflects temporary or permanent disengagement from care regardless of whether the patient had initiated ART. Patients who had no interaction with the site for at least 60 days following a scheduled visit and who were not known to have died or transferred elsewhere were captured in this state. The *ART* state was defined as receiving ART *without* evidence of VS. The state of *viral suppression (VS)* was operationalized as being on ART and having a VL less than 1000 copies/ml. Transition from the virally suppressed state back to the ART state occurred when there was a subsequent VL measurement of 1000 copies/ml or greater. Patients in the VS state who did not have subsequent measurements remained in that state for 18 months and then were censored unless they had a gap-in-care or were known to have transferred to another clinic or died. The *death* state could be reached from any other state and is an "absorbing state" such that there is no possible transition from it to any other state. Patients known to have transferred to other sites were censored at the time of their documented transfer. Given the homogeneity of local treatment standards, we assume that patients remaining in care are representative of those transferring elsewhere.

Statistical analysis

We estimated time-dependent state-occupation probabilities across our dynamic cascade that account for varying follow-up durations across patients ("right censoring")[29, 30]. These models provide estimates of the probability of *each individual* being in 1 of the 5 states in our cascade. While some multi-state models simplify calculations by using the Markov assumption[31], which posits that the transition from 1 state to the next is impacted solely by the state of departure, this assumption is unlikely to hold in our setting where additional factors such as the duration of being within a state (e.g., length of time receiving ART) impacts the likelihood of transitioning to a new state (e.g., VS or death). To circumvent the Markov assumption and to account for potential within-clinic dependence, we used a moment-based nonparametric estimator of the marginal state-occupation probabilities for cluster-correlated data. We calculated the standard error of the estimates using 500 bootstrap replications. As patients without VL measurements were excluded from the analysis, we addressed the potentially important selection bias this introduced through inverse probability weighting (IPW). IPW estimated the probability of having a VL measurement based on relevant factors such as patient sex, age, point of entry into HIV care, and contextual characteristics reflecting differences in national HIV treatment guidelines (Supplementary Table 1).

To demonstrate how these methods allow for identification of sub-populations in need of targeted intervention, we further compared state-occupation probabilities between patient subgroups based on sex, age, CD4 count at enrollment and year of enrollment using a linear nonparametric test[32, 33]. Pairwise comparisons among more than 2 groups were adjusted by a Bonferroni procedure.

While the multi-state models described above provide estimates of the probability of *an individual* being in a particular state in our HIV care cascade, they do not directly assess progress towards the UNAIDS targets at the *population level*. To determine what proportion of our cohort was on ART and virally suppressed as of the date of database closure in mid-2020 (the third "95" in the UNAIDS guideline), we summed state-occupation probabilities among all patients throughout their follow-up and up to database closure. This approach, herein referred to as the Aggregating State Occupation Probabilities (AeSOP) approach, provides a "snapshot" of the proportion of the entire population enrolled in care since 2014 that was on ART and virally suppressed as of mid-2020. Of note, these figures are akin to those typically assessed in population-based, cross-sectional surveys but are efficiently estimated using readily available clinical data from patients enrolled in HIV care. For more detail on these calculations, see Supplementary Material. All analyses were performed using the R environment[34].

Results

Patient characteristics

A total of 87,040 patients 15 years or older enrolled in HIV care at 91 sites participating in IeDEA during the study period. Of those, 35,649 patients at 78 sites had at least one VL measure and were eligible for inclusion in this analysis. The median age at enrollment in care across all patients was 32.3 years, and most patients were female (63.0%) and receiving care in Kenya (63.9%). Compared to PLWH not eligible for inclusion in the analysis, those included were older (34.6 vs 30.9 years) and had a lower CD4 count (297 vs 325 cells/μl) at enrollment. Also, a smaller proportion were pregnant at enrollment (12.5% vs 27.7%) and a greater proportion were receiving services in Kenya (66.5% vs 62.0%).

Multi-state cascade

Results from the IPW-adjusted multi-state model are presented in Figure 2. As patients move over time from the HIV care state into the on-ART state, the probability of being on ART without VS rises quickly but then drops as patients achieve VS, disengage from care or die. The proportion of patients who are virally suppressed increases rapidly and continues to increase, while the proportion of those in the gap-in-care state decreases as patients who are not engaged in care either re-engage or migrate to the death state.

Table 2 shows the estimated state-occupation probabilities1 year and 5 years following enrollment into care. At 1 year, only 2.8% of patients in our sample were in HIV care but not on ART, 86.7% were receiving ART but only 57.4% were virally suppressed. An additional 10.2% were currently disengaged from care and 0.3% were known to have died. Five years following enrollment, the proportion of patients on ART remained steady at 86.0% but the proportion virally suppressed increased substantially to 77.2%. Additionally, the proportion of patients experiencing a gap-in-care increased to 12.7% and 1.2% were known to have died.

Subgroup stratification

To demonstrate how state probabilities can be stratified to identify populations in need of targeted intervention, Figure 3 shows the probability of VS among those alive and in care by patient characteristics. While the probability of being virally suppressed increased dramatically after enrollment into care for the entire cohort, adolescents and young adults ≤25 years of age had a lower probability of VS over time compared to those over age 50 (overall age effect $p<0.001$), with no more than 60% of them achieving VS over time. In addition, enrollment in care after 2015, when treat-all guidelines were implemented, versus 2014–2015, was associated with a significantly higher probability of VS ($p<0.001$), likely a result of significantly more rapid treatment initiation after 2015 (Supplemental Figure 5). There were also significant sub-group differences in the probability of experiencing a gap-in-care (Figures 4). Notably, over 20% of those ≤25 years of age experienced a gap-in-care 5 years after enrollment.

By summing the individual state-occupation probabilities for the entire study cohort, we derived population-level estimates of progress towards the last two UNAIDS 95–95-95 targets as of May 30, 2020. As shown in Figure 5, this mid-2020 snapshot indicates that fully 90.1% of the population not known to have died was on ART, and, of those, 90.7% were virally suppressed.

Discussion

We used multi-state models to characterize the trajectories of over 35,000 ART-eligible patients enrolling in HIV care in East Africa from 2014 to 2020 across a dynamic HIV care cascade and presented a novel analytic approach—the Aggregating State-Occupation Probabilities or AeSOP approach—to estimate population-level progress towards the UNAIDS targets in mid-2020. By capturing patients' longitudinal but frequently non-linear movement along the HIV cascade, multi-state models better assess the effectiveness of HIV programs and identify subpopulations requiring targeted interventions than the oft-used unidirectional cascades assessed using survival analysis. By determining the proportion of the population on ART and virally suppressed at a point in time using readily available longitudinal medical record data from patients in HIV care, the AeSOP approach has the potential to routinely and efficiently assess efforts to end the HIV epidemic.

One year after enrollment, our multi-state models showed that 2.8% of patients in our sample were in HIV care but not on ART, 86.7% were on ART but only 57.4% of them were virally suppressed, 10.2% were out-of-care and 0.3% were known to have died. Recently, another multi-state analysis of adults enrolling in HIV care between 2014 and 2015 at 64 clinics in Zambia found that 75.2% of patients were on ART 1 year after enrollment, 15.7% were disengaged from care and 6.9% had died[35]. That study traced patients disengaged from care to determine whether they had re-engaged in care elsewhere or had died which likely explains the higher probability of death compared to our study. Nonetheless, both studies underscore the challenge of retaining patients in care. Our study, which additionally included outcomes 5 years after enrollment, showed only a small increase in the probability of being out of care (12.7%) or having died (0.012%) over time, suggesting that retention interventions are particularly important in the first year following enrollment into care. Further, our sub-group analyses indicated that PLWH age 15–24 had significantly worse outcomes across the cascade than their older counterparts: As many as 20% of them disengaged from care at least once during the 5 years following enrollment and less than 60% were virally suppressed during that period. In-depth interviews with adolescents experiencing a gap-in-care at two of the sites in this analysis suggest that trauma, social isolation and family-level factors are major contributors to their disengagement from care and ultimately uncontrolled HIV[36, 37]. Adolescent pregnancy has also been linked to care disengagement in our setting[38]. Individual-, clinic- and community-level interventions addressing these and other factors are emerging[39–41]. Rapid scale-up of interventions found to be effective will be needed to ensure efforts to end of the epidemic are not compromised. Our study also reinforces others which have documented a substantial decrease in time to ART initiation following launch of treat-all policies circa 2015 and a subsequent increase in viral suppression[42–45].

Importantly, to address progress towards the UNAIDS 95–95-95 goals, we developed the AeSOP approach to translate state-occupation probabilities representing the *probability* of *individual patients* being in 1 of the 5 cascade states into estimates of the *proportion of our entire population* on ART and virally suppressed. We found that substantial progress has been made towards the second and third of these targets: by the date of database closure in mid-2020, 90.1% of the population was on ART, and, of those, 90.7% were virally suppressed. Using cross-sectional surveys, the PHIA have also provided snapshots of progress towards the UNAIDS targets in the three countries included in our analysis between 2017 and 2021. Those surveys found that 96.0% of PLWH reported being on ART in Kenya (2018), 93.6% in Tanzania (2017–2018) and 96.1% in Uganda (2020–21)[7, 10, 11]. Additionally, of those on ART, 96.0%, 93.6% and 96.1% had achieved VS in Kenya, Tanzania, and Uganda, respectively. While these surveys provide important nationally representative estimates of all three UNAIDS targets and rich data on associated factors, with 5500 to nearly 17,000 household interviews and 11,000 to 41,000 blood draws per survey, their high cost prohibits routine and widespread implementation[12]. Additionally, most population-based surveys do not have sufficient statistical power to provide reliable subnational estimates which are needed to guide targeted funding decisions. Indeed, in the Kenyan PHIA, the proportion of PLWH on ART for Uasin Gishu county was estimated from a sample of 24 PLWH diagnosed with HIV[11], while our analysis, used routinely collected data from 7,771 PLWH enrolled in care at 11 HIV care clinics in that same county.

The findings in this paper highlight two key advantages of multi-state methods over other analytic approaches that have traditionally been used to examine HIV care cascade outcomes among patients observed over time, namely survival analysis and competing risks analysis. First, multi-state models directly quantify the dynamic nature of care engagement in which patients often experience multiple transitions between different but interlinked states of care over time. In contrast, survival analysis typically examines the time to a single event in the HIV care cascade, for example, a gap in care or death. Complications arise in that case when the time in the previous state needs to be accounted for, where left-truncation of the survival time may need to be considered. While competing and semi-competing risk analysis extends this approach (and is a special case of multi-state models), using multistate models we can explicitly model cyclical patterns of engagement in care (i.e., engagement and re-engagement in care), as is the case in a realistic HIV CoC. As we have shown in this paper, this setup can be used to simulate a population survey, by summing backwards the probabilities that each member of a cohort is in a certain state, in order to obtain estimates of the proportion of the population being in a certain state at a certain calendar time. This is similar in spirit to previous work by Jose and colleagues [1] who estimated person-years at one of several states in the HIV care cascade but without the explicit accounting for access to care. Our approach is particularly useful when evaluating programmatic or policy changes, such as the introduction of treat-all guidelines. Rather than simply comparing time to treatment initiation before and after such a policy [46], using this approach we can identify shifts in the distribution of the population across all states over time. This facilitates a more nuanced understanding of the downstream impacts or unintended consequences of a policy change.

Limitations of our study should also be noted. First and foremost, our study, and cohort studies in general, can only inform the latter two “95” components in the 95–95-95 UNAIDS targets, since they capture PLWH only after they have been linked to care. Linkage to care among all individuals living with HIV can only be addressed through proxy measures of disease progression at entry or national or subnational estimates of HIV prevalence in the ambient catchment area of each cohort. Within our data, limitations include the fact that outcomes of patients who disengaged from care were ascertained passively and thus the state-occupation probability of death in our cascade is most certainly underestimated. Indeed, the proportion of individuals known to have died 1 year after enrollment in care was 0.03%, far lower than the 6.9% reported by the sole other study examining a dynamic cascade in Africa using multi-state models[35] and our own adjusted estimates of mortality in this setting[47]. However, as our population-level estimates of the proportion of PLWH enrolling in care since 2014 who were on ART and virally suppressed as of mid-2020 only considered individuals not known to have died, it is possible that progress towards the latter 2 UNAIDS targets may be even greater than we estimated. Additionally, our assumption that patients who transfer from one HIV clinic to another have similar clinical outcomes to those remaining in care at their original site does not account for situations where a transfer results in fragmented care and viral suppression is compromised, even if temporarily. If this is common, our estimate of VS would be overstated. Another limitation, common to all longitudinal studies, is the lack of data on VS when patients are experiencing a gap-in-care. Only knowing that a patient was virally suppressed prior to their disengagement from care and was not suppressed upon their return to care results in “interval censoring”[48]. Finally, while most HIV clinics collect the data necessary to estimate a dynamic HIV cascade and the last 2 UNAIDS targets using the AeSOP approach, scale-up of these methods will require ready access to high-quality data from many HIV clinics, particularly if subnational estimates are desired.

Conclusion

Our multi-state analysis of readily available data from PLWH receiving care in HIV clinics in Kenya, Tanzania and Uganda provided robust estimates of the dynamic nature of patient movement through the HIV care cascade and indicated that targeted interventions are needed to address poor outcomes among adolescents and young adults. The AeSOP approach extended that multi-state analysis and demonstrated significant population-level progress towards the UNAIDS 95-95-95 targets. Our approach should be considered for widespread and routine use as efforts to end the HIV epidemic are monitored.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

Funding for this work was provided by the National Institutes of Health contract AI069911 (East Africa IeDEA Consortium). In addition, GB was funded by the aforementioned program and by R21 grant AI145662.

References

1. Jose S, et al. , A continuum of HIV care describing mortality and loss to follow-up: a longitudinal cohort study. Lancet HIV, 2018. 5(6): p. e301–e308. [PubMed: 29893243]
2. Gardner EM, et al. , The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. Clin Infect Dis, 2011. 52(6): p. 793–800. [PubMed: 21367734]
3. Centers for Disease Control and Prevention, Understanding the HIV care continuum. 2014: Atlanta, USA.
4. Touloumi G, et al. , HIV continuum of care: bridging cross-sectional and longitudinal analyses. AIDS, 2022. 36(4): p. 583–591. [PubMed: 34772850]
5. Gonsalves GS, et al. , A Flow-Based Model of the HIV Care Continuum in the United States. J Acquir Immune Defic Syndr, 2017. 75(5): p. 548–553. [PubMed: 28471841]
6. Joint United Nations Programme on HIV/AIDS (UNAIDS), 90-90-90: An ambitious treatment target to help end the AIDS epidemic. 2014: Geneva, Switzerland.
7. Tanzania Commission for AIDS (TACAIDS), Zanzibar AIDS Commission (ZAC),, Tanzania HIV Impact Survey (THIS) 2016–2017: Final Report. 2022: Dar es Salaam, Tanzania.
8. Porter L, et al. , HIV General Population Surveys: Shedding Light on the Status of HIV Epidemics and Informing Future Actions. J Acquir Immune Defic Syndr, 2021. 87(Suppl 1): p. S2–S5. [PubMed: 34166307]
9. Justman JE, Mugurungi O, and El-Sadr WM, HIV Population Surveys - Bringing Precision to the Global Response. N Engl J Med, 2018. 378(20): p. 1859–1861. [PubMed: 29768142]
10. PHIA Project, Uganda Summary Sheet 2020-2021.
11. National AIDS and STI Control Programme (NASCOP), Kenya Population-based HIV Impact Assessment (KENPHIA) 2018: Final Report. 2022, NASCOP: Nairobi, Kenya.
12. Morrison CS, et al. , Assays for estimating HIV incidence: updated global market assessment and estimated economic value. J Int AIDS Soc, 2017. 20(3).
13. Kay ES, Batey DS, and Mugavero MJ, The HIV treatment cascade and care continuum: updates, goals, and recommendations for the future. AIDS Res Ther, 2016. 13: p. 35. [PubMed: 27826353]
14. Fox MP, et al. , Estimating retention in HIV care accounting for patient transfers: A national laboratory cohort study in South Africa. PLoS Med, 2018. 15(6): p. e1002589. [PubMed: 29889844]
15. Kaplan SR, et al. , Contemporary disengagement from antiretroviral therapy in Khayelitsha, South Africa: A cohort study. PLoS Med, 2017. 14(11): p. e1002407. [PubMed: 29112692]
16. Mee P, et al. , Changes in patterns of retention in HIV care and antiretroviral treatment in Tanzania between 2008 and 2016: an analysis of routinely collected national programme data. J Glob Health, 2019. 9(1): p. 010424. [PubMed: 30992984]
17. Eaton EF, Saag MS, and Mugavero M, Engagement in human immunodeficiency virus care: linkage, retention, and antiretroviral therapy adherence. Infect Dis Clin North Am, 2014. 28(3): p. 355–69. [PubMed: 25151561]

18. Hallett TB and Eaton JW, A side door into care cascade for HIV-infected patients? J Acquir Immune Defic Syndr, 2013. 63 Suppl 2: p. S228–32. [PubMed: 23764640]
19. Krentz HB and Gill MJ, The effect of churn on “community viral load” in a well-defined regional population. J Acquir Immune Defic Syndr, 2013. 64(2): p. 190–6. [PubMed: 24047969]
20. Krentz HB, Vu Q, and Gill MJ, The Impact of “Churn” on Plasma HIV Burden Within a Population Under Care. Open Forum Infect Dis, 2019. 6(6): p. ofz203.
21. Lee H, et al. , Beyond binary retention in HIV care: predictors of the dynamic processes of patient engagement, disengagement, and re-entry into care in a US clinical cohort. AIDS, 2018. 32(15): p. 2217–2225. [PubMed: 30005018]
22. Mugavero MJ, et al. , The state of engagement in HIV care in the United States: from cascade to continuum to control. Clin Infect Dis, 2013. 57(8): p. 1164–71. [PubMed: 23797289]
23. Nachega JB, et al. , Addressing the Achilles’ heel in the HIV care continuum for the success of a test-and-treat strategy to achieve an AIDS-free generation. Clin Infect Dis, 2014. 59 Suppl 1: p. S21–7. [PubMed: 24926028]
24. Sikombe K, et al. , Understanding patient transfers across multiple clinics in Zambia among HIV infected adults. PLoS One, 2020. 15(11): p. e0241477. [PubMed: 33147250]
25. Chammartin F, et al. , International epidemiology databases to evaluate AIDS (IeDEA) in sub-Saharan Africa, 2012–2019. BMJ Open, 2020. 10(5): p. e035246.
26. National AIDS Control Programme, United Republic of Tanzania. National Guidelines for the Management of HIV and AIDS in Tanzania.. 2019.
27. National AIDS & STI Control Program, Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infection in Kenya. 2018, NASCOP: Nairobi, Kenya.
28. Uganda Ministry of Health, Consolidated guidelines for the prevention and treatment of HIV in Uganda, second edition. 2018.
29. Keiding N, Klein JP, and Horowitz MM, Multi-state models and outcome prediction in bone marrow transplantation. Stat Med, 2001. 20(12): p. 1871–85. [PubMed: 11406847]
30. Meira-Machado L, et al. , Multi-state models for the analysis of time-to-event data. Stat Methods Med Res, 2009. 18(2): p. 195–222. [PubMed: 18562394]
31. Kay R, A Markov model for analysing cancer markers and disease states in survival studies. Biometrics, 1986. 42(4): p. 855–65. [PubMed: 2434150]
32. Bakoyannis G, Nonparametric tests for transition probabilities in nonhomogeneous Markov processes. J Nonparametr Stat, 2020. 32(1): p. 131–156. [PubMed: 32317843]
33. Bakoyannis G, Nonparametric analysis of nonhomogeneous multistate processes with clustered observations. Biometrics, 2021. 77(2): p. 533–546. [PubMed: 32640037]
34. R Core Team, R: A Language and Environment for Statistical Computing. 2020, Foundation for Statistical Computing: Vienna, Austria.
35. Mody A, et al. , Longitudinal Care Cascade Outcomes Among People Eligible for Antiretroviral Therapy Who Are Newly Linking to Care in Zambia: A Multistate Analysis. Clin Infect Dis, 2020. 71(10): p. e561–e570. [PubMed: 32173743]
36. Enane LA, et al. , “I just keep quiet about it and act as if everything is alright” - The cascade from trauma to disengagement among adolescents living with HIV in western Kenya. J Int AIDS Soc, 2021. 24(4): p. e25695. [PubMed: 33838007]
37. Myers C, et al. , “Who am I going to stay with? Who will accept me?”: family-level domains influencing HIV care engagement among disengaged adolescents in Kenya. J Int AIDS Soc, 2022. 25(2): p. e25890. [PubMed: 35192747]
38. Nuwagaba-Biribonwoha H, et al. , Adolescent pregnancy at antiretroviral therapy (ART) initiation: a critical barrier to retention on ART. J Int AIDS Soc, 2018. 21(9): p. e25178. [PubMed: 30225908]
39. Amstutz A, et al. , VIBRA trial - Effect of village-based refill of ART following home-based same-day ART initiation vs clinic-based ART refill on viral suppression among individuals living with HIV: protocol of a cluster-randomized clinical trial in rural Lesotho. Trials, 2019. 20(1): p. 522. [PubMed: 31439004]

40. Denison JA, et al. , Family Connections randomized controlled trial: assessing the feasibility and acceptability of an intervention with adolescents living with HIV and their caregivers in Ndola, Zambia. AIDS Care, 2022. 34(4): p. 459–468. [PubMed: 33764845]
41. Mogoba P, et al. , The CombinADO study to assess the impact of a combination intervention strategy on viral suppression, antiretroviral therapy adherence, and retention in HIV care among adolescents and young people living with HIV: protocol for a cluster-randomized controlled trial. Trials, 2021. 22(1): p. 956. [PubMed: 34961567]
42. Dah TTE, et al. , Rapid antiretroviral therapy initiation and its effect on treatment response in MSM in West Africa. AIDS, 2021. 35(13): p. 2201–2210. [PubMed: 34352834]
43. Gomillia CES, et al. , Rapid Antiretroviral Therapy (ART) Initiation at a Community-Based Clinic in Jackson, MS. AIDS Res Ther, 2020. 17(1): p. 60. [PubMed: 33032617]
44. Pilcher CD, et al. , The Effect of Same-Day Observed Initiation of Antiretroviral Therapy on HIV Viral Load and Treatment Outcomes in a US Public Health Setting. J Acquir Immune Defic Syndr, 2017. 74(1): p. 44–51. [PubMed: 27434707]
45. Ford N, et al. , Benefits and risks of rapid initiation of antiretroviral therapy. AIDS, 2018. 32(1): p. 17–23. [PubMed: 29112073]
46. Tymejczyk O, et al. , Changes in rapid HIV treatment initiation after national “treat all” policy adoption in 6 sub-Saharan African countries: Regression discontinuity analysis. PLoS Med, 2019. 16(6): p. e1002822. [PubMed: 31181056]
47. Geng EH, et al. , Estimation of mortality among HIV-infected people on antiretroviral treatment in East Africa: a sampling based approach in an observational, multisite, cohort study. Lancet HIV, 2015. 2(3): p. e107–16. [PubMed: 26424542]
48. Bakoyannis G, Yu M, and Yiannoutsos CT, Semiparametric regression on cumulative incidence function with interval-censored competing risks data. Stat Med, 2017. 36(23): p. 3683–3707. [PubMed: 28608412]

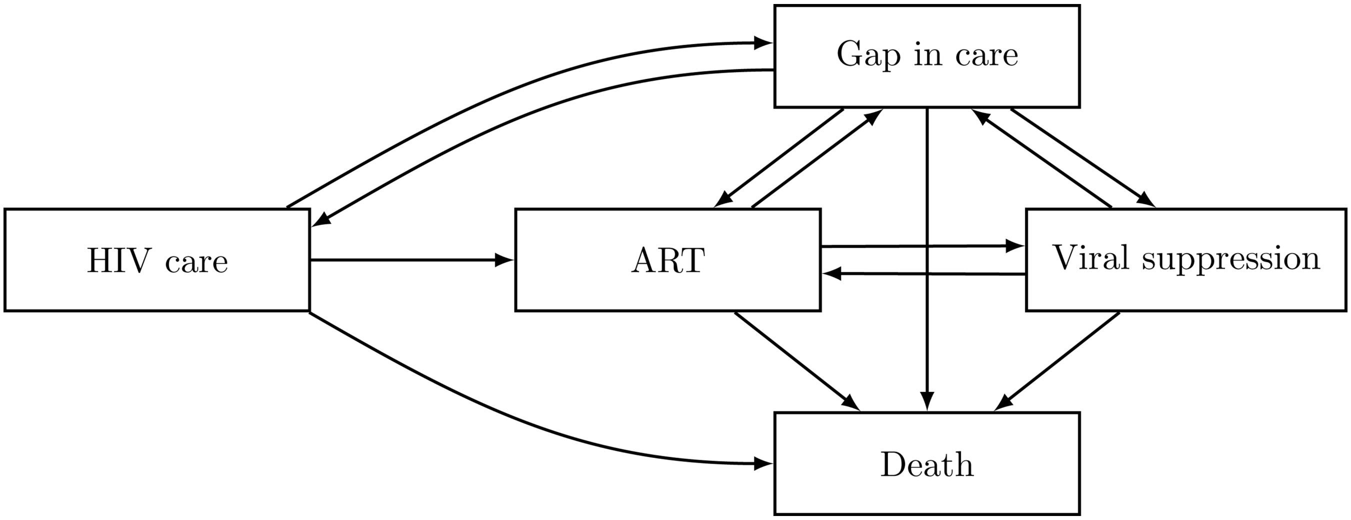

Figure 1.
Multi-state model of the HIV care cascade.

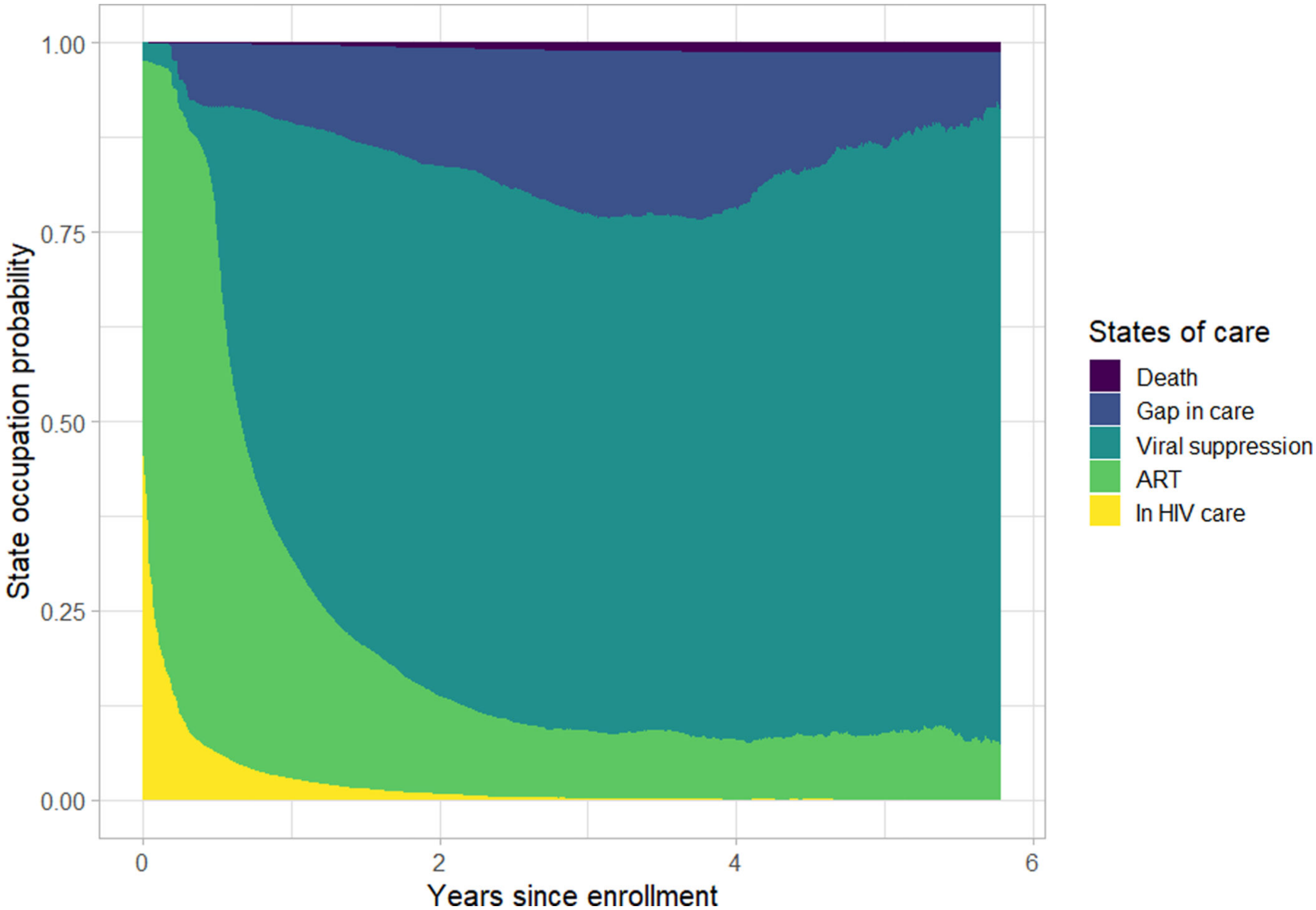

Figure 2.
State-occupation probabilities for a dynamic HIV care cascade, n=35,649

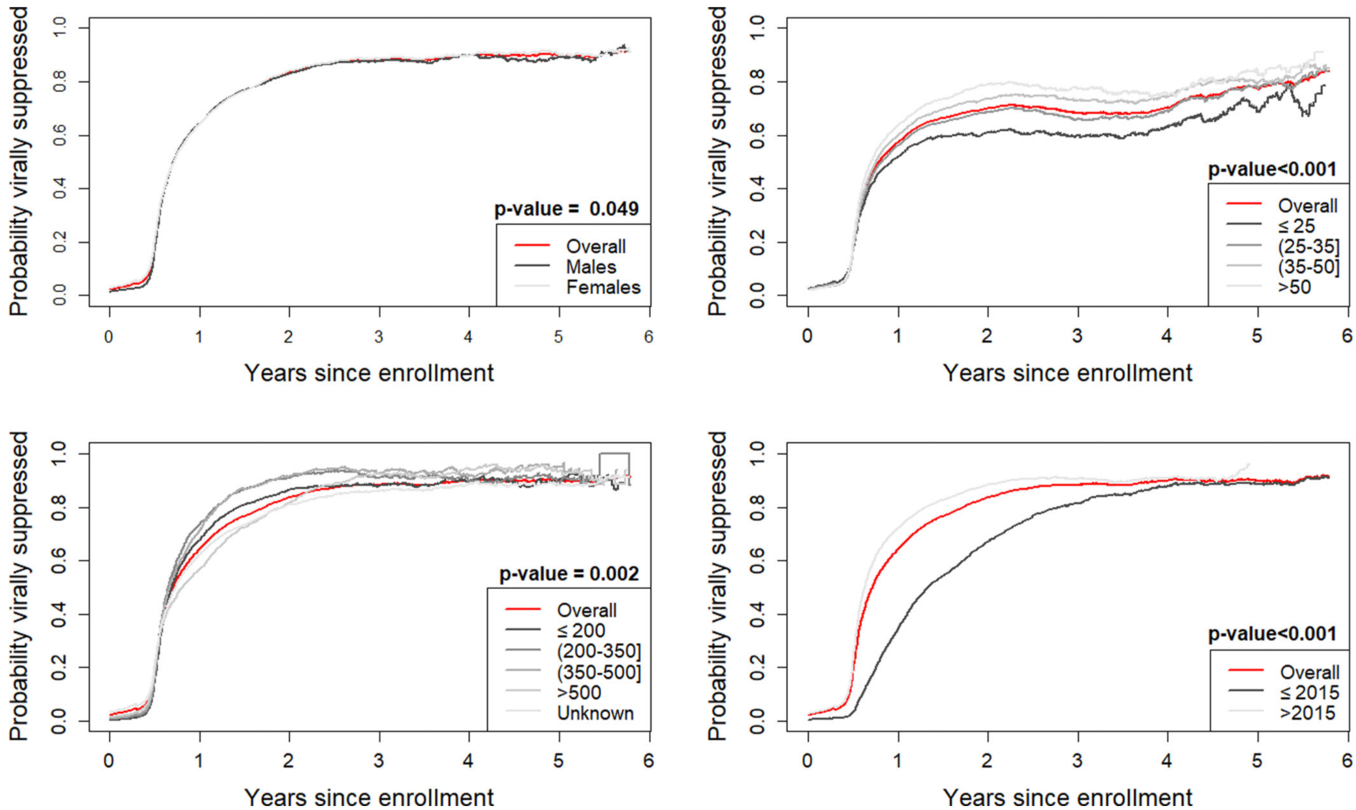

Figure 3.

Probability of being virally suppressed over time since enrollment, among those alive and in care, by sex (top left), age (top right), CD4 count at enrollment (bottom left), and year of enrollment (bottom right).

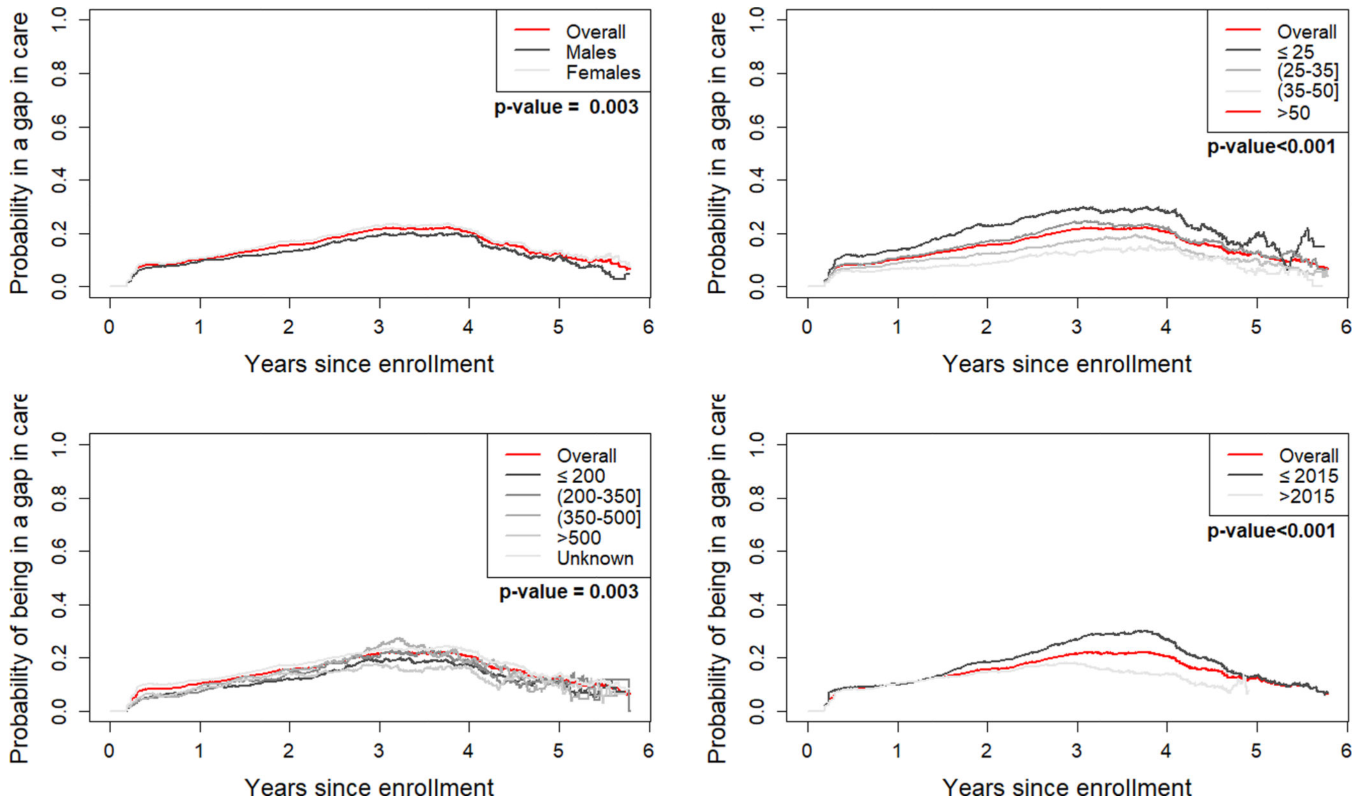

Figure 4.

Probability of being in a gap-in-care over time since enrollment by sex (top left), age (top right), CD4 at enrollment (bottom left), and year of enrollment (bottom right).

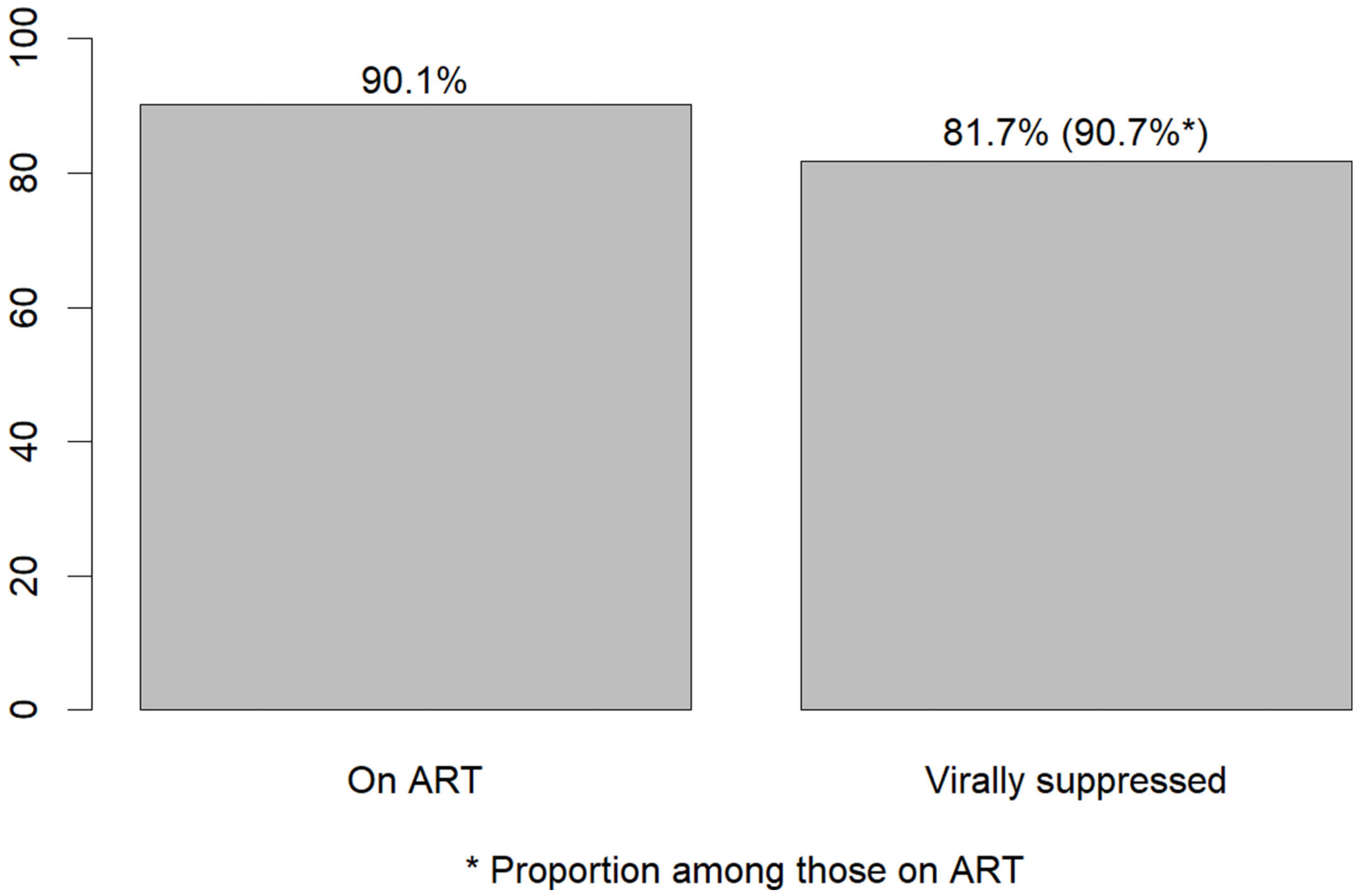

Figure 5.
Proportion of patients not known to have died who were on ART and virally suppressed as of May 30, 2020.

Table 1.

Characteristics of patients at enrollment in HIV care by availability of viral load measurement before May 30, 2020.

	Overall N (%)	Had at least 1 viral load N (%)	Did not have any viral load N (%)	p-value
N	87,040 (100)	35,649 (41.0)	51,391 (59.0)	
Gender				0.200
Female	54864 (63.0)	22371 (62.8)	32493 (63.3)	
Male	32176 (37.0)	13278 (37.2)	18898 (36.7)	
Pregnant at enrollment				<0.001
No	30453 (78.9)	14502 (87.5)	15951 (72.3)	
Yes	8166 (21.1)	2066 (12.5)	6100 (27.7)	
Country				<0.001
Kenya	55587 (63.8)	23722 (66.5)	31865 (62.0)	
Uganda	26772 (30.8)	10211 (28.6)	16561 (32.2)	
Tanzania	4681 (5.4)	1716 (4.8)	2965 (5.8)	
Median age in years (IQR)	32.3 (26.1, 40.7)	34.6 (28.0, 42.8)	30.9 (25.1, 39.1)	<0.001
Median CD4 in cells/μl (IQR)	312 (137, 519)	297 (134, 493)	325 (141, 540)	<0.001
Median calendar year of enrollment (IQR)	2016 (2015, 2018)	2016 (2015, 2017)	2016 (2015, 2018)	<0.001

Multi-state cascade

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

State-occupation probabilities at 1 year and 5 years from enrollment in HIV care, n=35,649.

State	State-occupation probability	95% confidence interval	
At 1 year from enrollment			
In HIV care	0.028	0.022	0.033
On ART without viral suppression	0.293	0.254	0.333
On ART with viral suppression	0.574	0.535	0.612
Gap-in-care	0.102	0.082	0.122
Death	0.003	0.002	0.004
At 5 years from enrollment			
In HIV care	0.000	0.000	0.001
On ART without suppression	0.088	0.063	0.113
On ART with viral suppression	0.772	0.737	0.807
Gap-in-care	0.127	0.101	0.154
Death	0.012	0.009	0.015

Subgroup stratification