

# Longitudinal HIV care outcomes by gender identity in the United States

Catherine R. Lesko<sup>a</sup>, Jessie K. Edwards<sup>b</sup>, David B. Hanna<sup>c</sup>,  
Angel M. Mayor<sup>d</sup>, Michael J. Silverberg<sup>e</sup>, Michael Horberg<sup>f</sup>,  
Peter F. Rebeiro<sup>g</sup>, Richard D. Moore<sup>h</sup>, Ashleigh J. Rich<sup>i</sup>,  
Kathleen A. McGinnis<sup>j</sup>, Kate Buchacz<sup>k</sup>, Heidi M. Crane<sup>l</sup>,  
Charles S. Rabkin<sup>m</sup>, Keri N. Althoff<sup>a</sup> and Tonia C. Poteat<sup>i</sup>

**Objective:** Describe engagement in HIV care over time after initial engagement in HIV care, by gender identity.

**Design:** Observational, clinical cohort study of people with HIV engaged in routine HIV care across the United States.

**Methods:** We followed people with HIV who linked to and engaged in clinical care (attending  $\geq 2$  visits in 12 months) in cohorts in the North American Transgender Cohort Collaboration, 2000–2018. Within strata of gender identity, we estimated the 7-year (84-month) restricted mean time spent: lost-to-clinic (stratified by pre/postantiretroviral therapy (ART) initiation); in care prior to ART initiation; on ART but not virally suppressed; virally suppressed ( $\leq 200$  copies/ml); or dead (pre/post-ART initiation).

**Results:** Transgender women ( $N = 482/101\ 841$ ) spent an average of 35.5 out of 84 months virally suppressed (this was 30.5 months for cisgender women and 34.4 months for cisgender men). After adjustment for age, race, ethnicity, history of injection drug use, cohort, and calendar year, transgender women were significantly less likely to die than cisgender people. Cisgender women spent more time in care not yet on ART, and less time on ART and virally suppressed, but were less likely to die compared with cisgender men. Other differences were not clinically meaningful.

**Conclusions:** In this sample, transgender women and cisgender people spent similar amounts of time in care and virally suppressed. Additional efforts to improve retention in care and viral suppression are needed for all people with HIV, regardless of gender identity.

*AIDS* 2022, **36**:1841–1849

**Keywords:** gender identity, HIV Care Continuum, survival, transgender women

<sup>a</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, <sup>b</sup>Department of Epidemiology, University of North Carolina School of Public Health, Chapel Hill, North Carolina, <sup>c</sup>Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York, <sup>d</sup>Department of Internal Medicine, Universidad Central del Caribe, Bayamón, Puerto Rico, <sup>e</sup>Division of Research, Kaiser Permanente Northern California, Oakland, California, <sup>f</sup>Kaiser Permanente Mid-Atlantic States, Mid-Atlantic Permanente Research Institute, Rockville, Maryland, <sup>g</sup>Division of Infectious Diseases and Epidemiology, Vanderbilt University Medical Center, Nashville, Tennessee, <sup>h</sup>Division of General Internal Medicine, Johns Hopkins School of Medicine, Baltimore, Maryland, <sup>i</sup>Department of Social Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina, <sup>j</sup>Veterans Aging Cohort Study Coordinating Center, VA Connecticut Healthcare System, West Haven, Connecticut, <sup>k</sup>HIV Research Branch, Division of HIV Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, <sup>l</sup>Department of Medicine, Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington, and <sup>m</sup>Infections and Immunoepidemiology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA.

Correspondence to Catherine R. Lesko, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe St., Baltimore, MD 21205, USA.

Tel: +1 410 614 6517; fax: +1 410 955 0863; e-mail: clesko2@jhu.edu

Received: 5 April 2022; revised: 30 June 2022; accepted: 11 July 2022.

DOI:10.1097/QAD.0000000000003339

## Introduction

Helping people with HIV achieve and maintain viral suppression is the second pillar of the United States (US)' strategic initiative to end the HIV epidemic in the US [1]. Durable viral suppression prevents HIV-related comorbidities and mortality in people with HIV, and effectively eliminates the risk of HIV transmission [2–4]. The HIV care continuum describes the stages through which people with HIV progress prior to attaining (and occasionally after losing) viral suppression [5,6].

One in five transgender women in the US are living with HIV [7,8]. Transgender women are a designated key population for HIV treatment [1] because stigma and discrimination related to their gender identity put them at high risk for poor HIV control [9]. Prior cross-sectional studies have suggested that, compared with cisgender people with HIV, transgender women have similar rates of retention in care, but are less likely to be virally suppressed [10–14]. However, the cross-sectional care continuum does not account for different risks of mortality between groups, different retention in care over time (typically restricting estimates of viral suppression to people who remain in care), or different patterns of viral suppression [15–18].

## Methods

We estimated the proportion of time spent across stages of HIV care by gender identity, focusing on the experience of transgender women, using a modified version of the longitudinal care continuum in a large sample of patients in routine care in the US [19].

### Study sample

The North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) is the North American region of the International epidemiology Databases to Evaluate AIDS (IeDEA) project [20]. Single- and multisite clinical and interval cohorts prospectively collect data on adults with HIV living in the US and Canada, which are then combined and harmonized. Data collection and analyses have been approved by local institutional review boards and the Johns Hopkins School of Medicine. Clinical cohorts include adults who attended two or more clinic visits in 12 months and consented to share their data. Patient demographics, HIV acquisition risk factor(s), prescribed medications, laboratory results, and dates of attended clinical visits were taken from patients' medical records. Fifteen cohorts contributed data on transgender patients; this subcohort comprises the North American Transgender Cohort Collaboration (NA-TRACC) [21]. Our study sample consisted of adults enrolled in a clinical cohort in the US in NA-TRACC who were in care ( $\geq 1$  HIV clinic visit,  $CD4^+$  cell count, or HIV-1 viral load measurement) between 2000 and 2018. We

excluded patients with a natal sex of female with an HIV acquisition risk factor of being a man who has sex with men ( $N=18$ ), and transgender men (too few to analyze separately,  $N=37$ ).

### Gender identity measurement

Transgender status was captured through various methods across the contributing cohorts including: presence of diagnosis codes for gender dysphoria; comparison of natal sex with reports of feminizing or masculinizing hormones from medication lists; gender identity queried at intake; and medical provider documentation in the clinical record [22]. Patients were categorized as transgender women, cisgender women, or cisgender men.

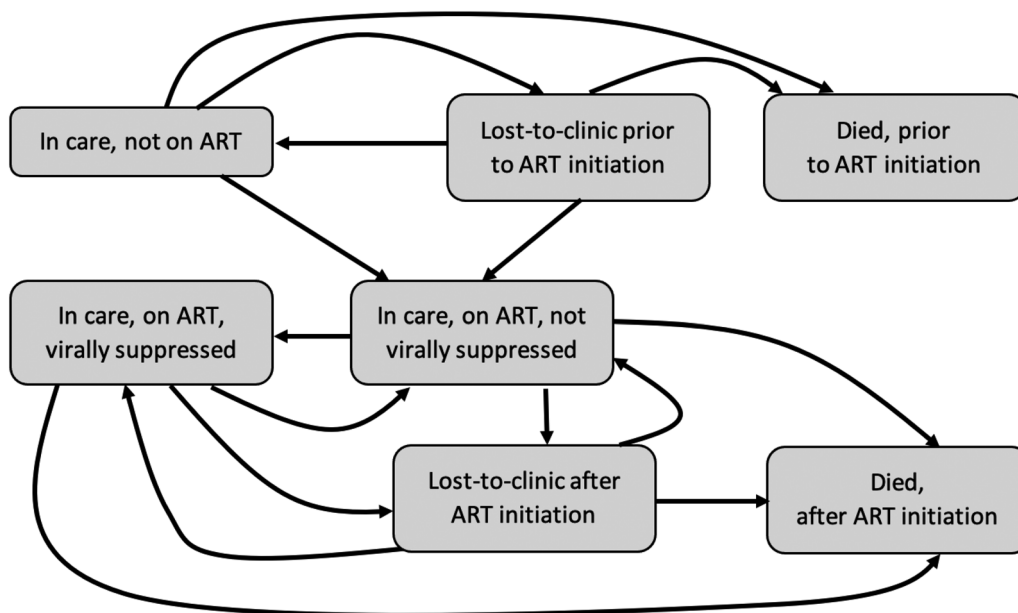
### Outcome definitions

Because our study sample was linked to care already, we focused on care continuum outcomes after linkage to care: loss-to-clinic/retention in care, ART initiation, viral suppression, and death. We stratified loss-to-clinic and death by whether they occurred before or after ART initiation, thus our framework includes seven stages (Fig. 1).

Participants were followed analytically from the earliest of enrollment into a participating cohort or the first HIV care encounter ( $CD4^+$  cell count, viral load measurement, or HIV clinic visit) after 1 January 2000 for people enrolled into a participating cohort prior to 2000. Time zero (time origin) for analyses was the first HIV care encounter after the administrative start of follow-up while ART-naive. The time origin was not observed for patients who enrolled into NA-ACCORD after initiating ART elsewhere; we assume their care history was approximated by people who enrolled into NA-ACCORD prior to ART initiation. ART initiation was defined as the first date on which a patient started three or more antiviral medications, at least one of which was a protease inhibitor, nonnucleoside reverse transcriptase inhibitor, or an integrase inhibitor. Viral suppression was defined as having the most recent viral load of 200 copies/ml or less. Loss-to-care was approximated by loss-to-clinic, defined as 12 months since the last HIV laboratory measurement or clinic visits. As described in the 'Statistical analysis' and Appendix A, viral suppression and loss-to-clinic were both reversible states (people who had a suppressed viral load were classified as unsuppressed as soon as they had a viral load of greater than 200 copies/ml, and people lost-to-clinic were re-entered into an 'in care' state when they had a new viral load,  $CD4^+$  cell count, or clinic visit). Death dates were obtained from clinic sources and regular matches against the Social Security Death Index or National Death Index and thus were available for all patients, regardless of whether or not they remained in care in the NA-ACCORD.

### Statistical analysis

Cross-sectional care continuums estimate the proportion of a population in a care continuum state at a point in



**Fig. 1. Conceptual framework for the HIV care continuum stages (boxes) and possible movement between them (arrows) employed in this analysis.**

time; in this study we estimate the average proportion of follow-up time spent in a care continuum state over the first 84 months (7 years) after baseline, where patients can move back and forth between states without restriction (except for ART initiation and death, which are absorbing states). Complete details of our approach are available in Appendix A. Briefly, we implemented and extended a previously published construction of the longitudinal care continuum [18] to accommodate late entries to the analysis (patients who transferred care having already initiated ART elsewhere) under the assumption that late entries are not informative [23,24]. We estimated the cumulative incidence of the following nine events (different from the seven stages) nonparametrically using the Aalen-Johansen estimator [25–27]. Events were not of interest in and of themselves, but represent transitions between the stages. We estimated curves based on all patients that were observed from the origin; origins for each event are listed in their definitions. Patients could experience multiple instances of events preceded by an asterisk (\*).

- (1) Death before ART initiation measured from enrollment among ART-naive patients; ART initiation is a competing event.
- (2) \*Loss-to-clinic before ART initiation measured from enrollment among ART-naive patients (or to subsequent instance of loss-to-clinic before ART initiation from date of prior re-entry to clinic); death before ART initiation and ART initiation are competing events.
- (3) \*No-longer-lost-to-clinic before ART initiation (death, ART initiation, or return to clinic) measured from most recent prior date lost-to-clinic.

- (4) ART initiation measured from first eligible care visit among ART-naive patients; death is a competing event.
- (5) \*Viral suppression measured from ART initiation (or time to viral re-suppression after prior loss of viral suppression); death is a competing event.
- (6) \*No-longer-virally-suppressed after viral suppression (death, loss-to-clinic, or unsuppressed viral load) from most recent date of viral suppression.
- (7) \*Loss-to-clinic after ART initiation measured from date of ART initiation (or time to subsequent loss-to-clinic after a return to clinic); death is a competing event.
- (8) \*No-longer-lost-to-clinic after ART initiation (death or return to clinic) measured from most recent date considered lost-to-clinic.
- (9) Time to death after ART initiation from date of ART initiation.

We multiplied the cumulative incidence estimates for the events above (conditional probabilities, conditional on experiencing the origin) by the probability of being at risk to experience each event (probability of having experienced the origin). This resulted in marginal estimates of the cumulative incidence of each of the events above, anchored to the time origin. Marginal cumulative incidence estimates of each of the nine events were added and subtracted to estimate the proportion of the study sample in each of the seven stages over time [18,28,29]. We plotted stacked proportions in each care continuum stage over time stratified by gender identity.

We summarized the 84-month restricted mean time spent in each stage. Restricted mean time is interpretable as the

average amount of time a patient spends in a given stage within a restricted (i.e. 84 months) time frame. We calculated restricted mean time differences for transgender women compared to cisgender women ( $RMTD_{TW-CW}$ ) and compared to cisgender men ( $RMTD_{TW-CM}$ ) to describe disparities in longitudinal HIV care continuum engagement by gender identity. For completeness, we also compared cisgender women to cisgender men.

To describe results independent of covariates known to be associated with engagement in care, we repeated the analysis in inverse probability weighted data [30–34]. Inverse probability (of gender identity) weights were estimated with multinomial logistic regression by regressing gender identity on age, race (white, Black, other nonwhite non-Black race, and unknown), ethnicity (Hispanic or non-Hispanic), injection drug use (IDU) as an HIV acquisition risk factor, calendar year of entry to the analysis, and cohort in which patients were enrolled. Weights were the inverse probability of having one's own gender identity, given their particular covariate values. Weights were stabilized by the marginal probability of having one's own gender identity.

We report 95% confidence intervals (CI) for estimates that were the 2.5th and 97.5th percentiles of the distribution of estimates from 500 nonparametric bootstrap resamples of the data [35].

### Role of the funding source

Funding for this study came from the National Institutes of Health. The funders had no role in the design, analysis, or interpretation of this study.

## Results

There were 101 841 adults in the study sample, of whom 0.5% ( $n=482$ ) were classified as transgender women. Transgender women were younger at the start of follow-up (median age = 35 years, compared to 40 years for cisgender women and 44 years for cisgender men), more likely to be Hispanic persons (24%, compared to 8% of

cisgender women and 11% of cisgender men), less likely to have IDU history (12%, compared to 16% of cisgender women and 19% of cisgender men), and newer to care in the NA-TRACC (median year of study entry = 2011, compared to 2007 among cisgender women and 2005 among cisgender men) (Table 1).

Transgender women spent an average of 22.1 out of 84 months of follow-up lost-to-clinic (cisgender women and cisgender men averaged 20.8 and 18.4 months lost-to-clinic, respectively); 10.5 months in care prior to ART initiation (14.7 and 12.2 months for cisgender women and cisgender men, respectively); 13.4 months on ART but not virally suppressed (13.1 and 12.5, respectively); and 35.5 out of 84 months virally suppressed (30.5 and 34.4, respectively). Transgender women lost 2.5 months to death (cisgender women and cisgender men lost 4.8 and 6.5 months, respectively) (Table 2; months lost to death was the sum of the 84-month restricted mean time spent in the 'dead' stage before and after ART initiation). Overall, transgender women spent approximately 59.4 months (71% of follow-up time) retained in clinic and 65.5 months (78% of follow-up time) having initiated ART. Transgender women were virally suppressed for 42% of total follow-up time and 73% of time in care after ART initiation.

After adjustment for age, race, ethnicity, history of IDU, calendar year, and cohort, transgender women spent similar time on ART and virally suppressed compared with cisgender women ( $RMTD_{TW-CW}$ : 3.1 months, 95% confidence interval (CI): -1.6, 8.7) and cisgender men ( $RMTD_{TW-CM}$ : 1.4 months, 95% CI: -3.2, 7.0). Transgender women spent 3.5 fewer months in care prior to ART initiation compared to cisgender women, although the difference was not statistically significant (95% CI: -7.1, 0.6;  $RMTD_{TW-CM}$ : -1.1 months, 95% CI: -4.8, 2.9). Additionally, transgender women had a lower cumulative incidence of death than cisgender women and cisgender men and thus the average time lost to death was lower ( $RMTD_{TW-CW}$ : -2 months;  $RMTD_{TW-CM}$ : -2.5 months). However, transgender women spent slightly more time lost-to-clinic after ART initiation than

**Table 1. Patient characteristics of 101 841 people with HIV engaged in clinical care in a collaborating cohort in the North American Transgender Cohort Collaboration, 2000–2018, stratified by gender identity.**

	Transgender women	Cisgender women	Cisgender men	Total
N	482	12 074	89 285	101 841
Age at study entry <sup>a</sup>	35 (27, 43)	40 (33, 48)	44 (35, 51)	43 (35, 51)
Race <sup>b</sup>				
White	155 (32)	3268 (27)	42 062 (47)	45 485 (45)
Black	220 (46)	7422 (61)	33 950 (38)	41 592 (41)
Other	59 (12)	679 (6)	4009 (4)	4747 (5)
Unknown	48 (10)	705 (6)	9264 (10)	10 017 (10)
Hispanic ethnicity <sup>b</sup>	117 (24)	1014 (8)	10 204 (11)	11 335 (11)
IDU history <sup>b</sup>	60 (12)	1922 (16)	17 334 (19)	19 316 (19)
Year of study entry <sup>a</sup>	2011 (2005, 2015)	2007 (2001, 2012)	2005 (2000, 2012)	2006 (2000, 2012)

<sup>a</sup>Median (Q1, Q3).

<sup>b</sup>N (%).

**Table 2. Crude and adjusted<sup>a</sup> restricted mean months over first 84 months following linkage to HIV care spent in each stage of the HIV care continuum stratified by gender identity, and difference in restricted mean months, North American Transgender Cohort Collaboration, 2000–2018.**

HIV care continuum stages	Transgender women RMM (95% CI)	Cisgender women RMM (95% CI)	Difference, TW – CW RMMD (95% CI)	Cisgender men RMM (95% CI)	Difference, TW – CM RMMD (95% CI)	Difference, CW – CM RMMD (95% CI)
<b>Crude</b>						
Months of life lost before ART initiation	0.5 (0, 1.4)	1.8 (1.5, 2.0)	–1.3 (–1.8, –0.4)	2.3 (2.2, 2.4)	–1.8 (–2.3, –0.9)	–0.5 (–0.7, –0.2)
Months lost-to-clinic before ART initiation	7.5 (5.7, 9.8)	7.8 (7.4, 8.3)	–0.3 (–2.3, 2.0)	6.3 (6.2, 6.5)	1.2 (–0.7, 3.5)	1.6 (1.1, 2.0)
Months in care, not ART initiated	10.5 (8.2, 12.2)	14.7 (14.2, 15.3)	–4.2 (–6.4, –2.5)	12.2 (12.1, 12.4)	–1.8 (–4.0, 0.0)	2.4 (1.8, 2.9)
Months on ART, not virally suppressed	13.4 (10.2, 15.9)	13.1 (12.5, 13.8)	0.2 (–3.0, 2.8)	12.5 (12.2, 12.8)	0.9 (–2.4, 3.4)	0.7 (–0.1, 1.4)
Months on ART, virally suppressed	35.5 (31.6, 39.3)	30.5 (29.6, 31.3)	5.0 (1.0, 9.1)	34.4 (34.0, 34.7)	1.1 (–2.7, 5.1)	–3.9 (–4.8, –3.1)
Months lost-to-clinic after ART initiation	14.6 (12.3, 18.2)	13.0 (12.5, 13.6)	1.6 (–0.8, 5.3)	12.1 (11.8, 12.3)	2.5 (0.3, 6.2)	0.9 (0.4, 1.5)
Months of life lost after ART initiation	2.0 (1.1, 3.1)	3.0 (2.8, 3.2)	–1.0 (–1.9, 0.2)	4.2 (4.1, 4.3)	–2.2 (–3.1, –1.1)	–1.2 (–1.4, –0.9)
<b>Adjusted<sup>a</sup></b>						
Months of life lost before ART initiation	RMM (95% CI) 0.5 (0, 1.2)	RMM (95% CI) 1.8 (1.5, 2.2)	RMMD (95% CI) –1.3 (–2.0, –0.5)	RMM (95% CI) 2.2 (2.1, 2.3)	RMMD (95% CI) –1.7 (–2.2, –1.0)	RMMD (95% CI) –0.4 (–0.8, 0.0)
Months lost-to-clinic before ART initiation	6.3 (4.4, 9)	7.1 (6.5, 7.7)	–0.9 (–2.8, 1.8)	6.5 (6.3, 6.7)	–0.3 (–2.1, 2.5)	0.7 (0.1, 1.3)
Months in care, not ART initiated	11.1 (7.4, 15.1)	14.6 (13.7, 15.4)	–3.5 (–7.1, 0.6)	12.3 (12.1, 12.4)	–1.1 (–4.8, 2.9)	2.2 (1.3, 3.1)
Months on ART, not virally suppressed	12.8 (7.2, 16.5)	12.7 (11.8, 13.7)	0.1 (–5.2, 3.9)	12.4 (12.1, 12.8)	0.4 (–5.1, 4.0)	0.3 (–0.8, 1.4)
Months on ART, virally suppressed	35.5 (30.8, 40.9)	32.3 (31, 33.4)	3.1 (–1.6, 8.7)	34.1 (33.7, 34.4)	1.4 (–3.2, 7.0)	–1.8 (–3.2, –0.6)
Months lost-to-clinic after ART initiation	15.5 (11.7, 19.7)	12.4 (11.8, 13.3)	3.1 (–0.8, 7.1)	12.4 (12.1, 12.6)	3.1 (–0.7, 7.5)	0.0 (–0.6, 0.9)
Months of life lost after ART initiation	2.3 (1.1, 4.4)	3.0 (2.7, 3.3)	–0.7 (–1.9, 1.4)	4.1 (4.0, 4.2)	–1.8 (–3.1, 0.2)	–1.1 (–1.4, –0.8)

CM, cisgender men; CW, cisgender women; RMM, restricted mean months; RMMD, restricted mean months difference; TW, transgender women.  
<sup>a</sup>Adjusted for: age, race, ethnicity, injection drug use as a risk factor for HIV acquisition, cohort, and year of study entry

cisgender women ( $RMTD_{TW-CW}$ : 3.1 months, 95% CI: –0.8, 7.1) and cisgender men ( $RMTD_{TW-CM}$ : 3.1 months, 95% CI: –0.7, 7.5). Transgender women spent similar time after ART initiation not virally suppressed and in care compared to cisgender women ( $RMTD_{TW-CW}$ : 0.1 months, 95% CI: –5.2, 3.9) and cisgender men ( $RMTD_{TW-CM}$ : 0.4 months, 95% CI: –5.1, 4.0) (Table 2). Patterns of longitudinal engagement in care according to gender are presented in Fig. 2.

After adjustment, compared to cisgender men, cisgender women spent 2.2 more months (95% CI: 1.3, 3.1) in care not yet having initiated ART and 1.8 fewer months (95% CI: –3.2, –0.6) on ART and virally suppressed. However, they also were less likely to die during follow-up; they lost 0.4 fewer months (95% CI: –0.8, 0.0) of life prior to ART initiation and 1.1 fewer months (95% CI: –1.4, –0.8) of life after ART initiation (Table 2).

## Discussion

In this sample of people with HIV in routine clinical care in multiple geographically diverse locations across the US,

we found similar or better HIV care continuum outcomes for transgender women compared with cisgender men and women. Transgender women in this sample were less likely to die than cisgender people.

Our findings suggest that transgender women who are effectively linked to and engaged in care have similar retention and viral suppression compared with cisgender people. However, our conclusions are limited to people who are linked to care and to transgender women who were identified as transgender in our data. In our sample, transgender women were younger and enrolled more recently, and despite the persistence of this survival benefit after adjusting for age and calendar time, it is possible that there were other dimensions such as socioeconomic position, mental health, or behavioral risk factors, along which transgender women enrolled in cohorts in NA-TRACC were healthier than cisgender people, for which we were unable to account (akin to residual ‘confounding’, although we are not interpreting these associations causally). However, enrollment in participating cohorts was based on enrollment in routine care and there is not a clear rationale for why transgender women seeking care at the same clinic as cisgender men

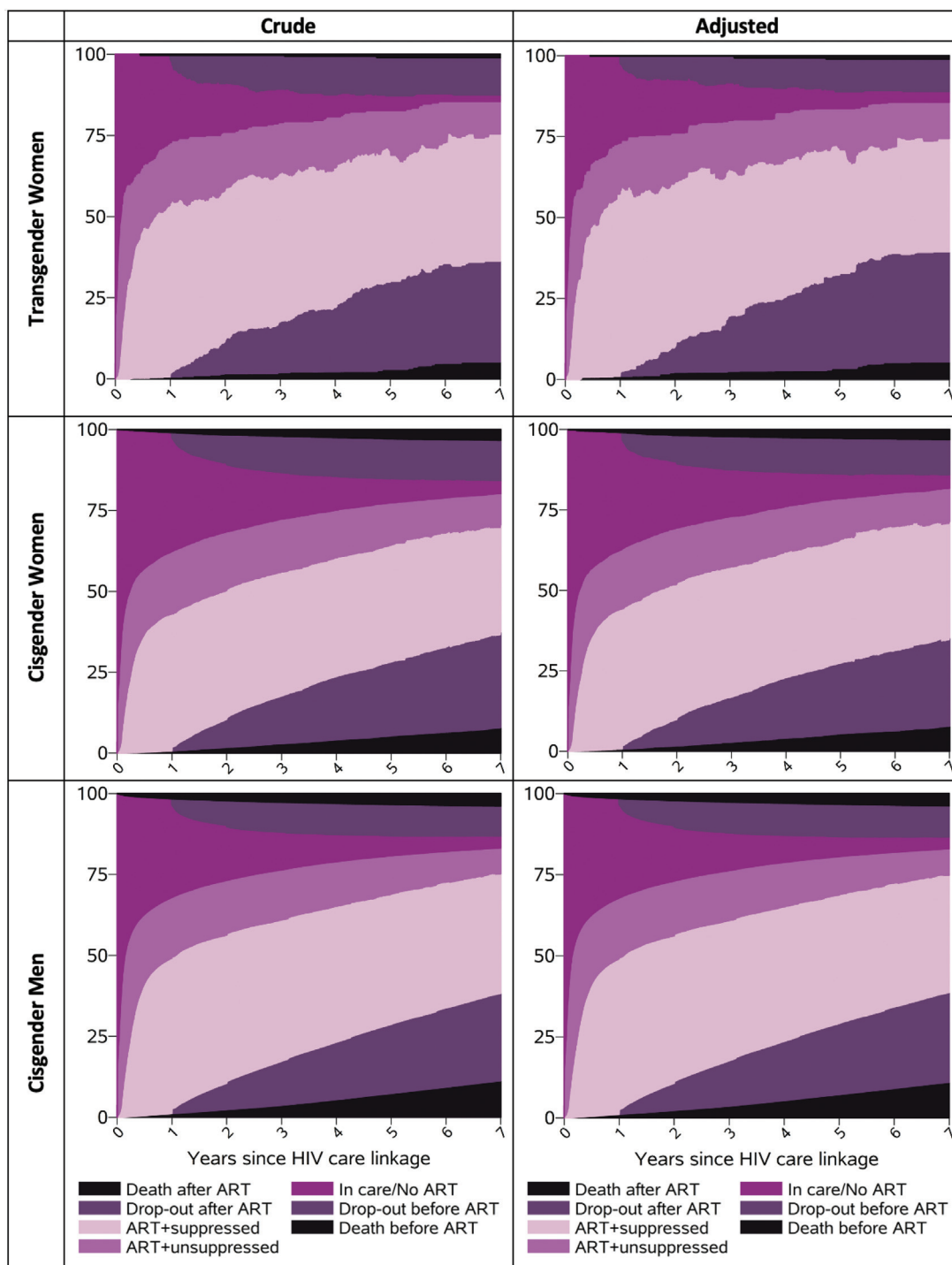


Fig. 2. Crude (left) and adjusted (right), stacked proportion of people in each care continuum stage over 84 months (7 years) following linkage to HIV care stratified by gender identity, ART-naïve people at enrollment into the North American Transgender Cohort Collaboration, 2000–2018.

or women would be healthier. Enrollment in NA-TRACC (and inclusion in this analysis) was based on having attended two or more clinic visits in 1 year, which is a rather stringent definition of linkage to care. Indeed, only 0.5% of our sample was classified as transgender, compared to 1.3% of patients in the Medical Monitoring

Project [12], potentially suggesting that transgender women were under-represented or transgender status was under-ascertained in our sample. Our results may not apply to transgender women who are less securely linked to care (a generalizability bias). Additionally, because some clinics compared the presence of feminizing or

masculinizing hormones to natal sex to identify transgender status, we may have under-ascertained transgender status, and patients classified as transgender in this analysis may represent a biased (towards people on hormone therapy) sample of transgender people in the cohort. That is, transgender women who have not been prescribed feminizing hormones and who would likely be at greater risk for poor HIV care outcomes [9,36] may have been misclassified in our analysis and therefore our results could overstate positive care continuum outcomes for transgender women (a misclassification bias). This potential for bias due to better ascertainment of gender identity among transgender women receiving more gender-affirming care is underscored by the observation that transgender women in our sample appear to have enrolled more recently than cisgender people.

A further limitation of this analysis that is not specific to results for transgender women is our inability to distinguish between loss-to-clinic and loss-to-care. Participants classified as lost-to-clinic may have enrolled in care elsewhere, in which case our estimates of time spent lost-to-clinic would overestimate time spent lost-to-care. This is a limitation of almost all clinical cohorts that do not undertake extra tracing efforts [37,38].

Transgender women face considerable barriers to ART adherence, at least some of which can be attributable to a lack of gender-affirming care [9]. Yet in this analysis, we did not observe those same disparities in HIV care outcomes. While our results do not apply to all transgender women living with HIV, they can be thought to indicate what is possible under certain conditions. Several NA-TRACC clinics have been proactively providing gender-affirming care in the context of HIV care, which may partially explain the lack of disparities in ART use or viral suppression among transgender women in our sample. We did not specifically study the impact of gender-related care in this analysis.

Prior estimates of the cross-sectional HIV care continuum for transgender women have been imprecise, but suggest that, of transgender women diagnosed with HIV, 76–98% were retained in care, 54–75% were on ART, and 21–67% were virally suppressed [10,11,39,40]. Of transgender women in care for HIV, 80–98% were retained in care, 76–93% were on ART, and 68–82% were virally suppressed [12–14,40,41]. In our analysis, we estimated that of transgender women engaged in HIV care, 74% of their time was spent retained in the clinic; almost certainly, this is an underestimate of the time spent retained in care anywhere. We estimated that 82% of time in care was spent on ART, which includes calendar time where universal ART was not standard practice. And we estimated that 60% of time in care was spent virally suppressed; 73% of time on ART was spent virally suppressed. In cross-sectional analyses, compared with cisgender patients, transgender women were as likely to be retained in care [11,13,41] and to receive ART

[12,41]. However, in most [12–14] but not all studies [21,41], transgender women were less likely than cisgender people to have a suppressed viral load. In national surveillance data, transgender women with HIV were less likely than cisgender people to have a suppressed viral load, but transgender women who were in care were more likely to have a suppressed viral load than cisgender people who were in care [40].

Although cross-sectional and longitudinal care continuum estimates are fundamentally different [16], our results tell a story consistent with these prior studies. Transgender women engaged in care had similar outcomes when compared to cisgender people engaged in care. Cross-sectional estimates of retention are commonly based on attending two or more clinic visits in a calendar year [21,42] while loss-to-care in this study was defined as 12 or more months without a clinic visit, viral load, or CD4<sup>+</sup> cell count, which might be a less specific measure of retention [43]. Additionally, cross-sectional estimates of viral suppression are commonly based on the last viral load value in a calendar year, whereas in this longitudinal study, people were classified according to their most recent viral load value and our method was therefore more sensitive to capturing transient viral nonsuppression [44].

When stratified by race, prior studies found gender disparities were concentrated among Black people [14], pointing to the intersectional nature of vulnerabilities, stigma, and othering faced by Black transgender women living with HIV. It was beyond the scope of this analysis to examine intersectionality, but it is an important area for future research.

Although not the primary focus of our investigation, we also found cisgender women spent marginally less time on ART or virally suppressed than cisgender men. This is in line with limited prior traditional care continuum analyses that found women were less likely than men to be retained in care, prescribed ART, or virally suppressed (it is unclear whether sex or gender was captured in this analysis) [45].

Our approach assumed that people who transferred care having initiated ART elsewhere were similar to people who were ART-naïve when they enrolled in NA-TRACC. Estimates using the new approach and the old approach (that did not rely on this assumption) [18] were similar, increasing our confidence that this assumption was plausible (data not shown). A strength of our new approach was that it allowed us to include substantially more participants than we would have had we been restricted to those who were ART-naïve; particularly given the high rate of transfers between clinics, patients who transfer in during their course of care are an important group to study.

Both cross-sectional estimates of the proportion of people retained or virally suppressed, and our longitudinal

estimates of the proportion of time spent retained or with viral suppression, are lower than would be optimal for individuals' health and population transmission of HIV [1]. In contrast to cross-sectional care continuum analyses, we found transgender women and cisgender patients spent similar amounts of time virally suppressed on ART after engagement in care. Cross-sectional care continuum metrics typically exclude people who were lost to care or who died in the prior year, thus 'better' HIV care continuum outcomes might be observed for subgroups with a high proportion of vulnerable members who drop out of the study sample. Additionally, compared to cross-sectional care continuum metrics that summarize people's experience with care across an entire year, longitudinal metrics may under-capture poor engagement in care, but be more sensitive for unstable viral suppression. For all people with HIV, but particularly transgender women, we need to increase time spent durably virally suppressed. Further studies that evaluate the quality of engagement in care and both barriers to and resiliencies enabling durable viral suppression among transgender women are needed to better understand the HIV clinical course in this population.

## Acknowledgements

C.R.L. conceived of the concept, conducted statistical analyses, and drafted the paper. J.K.E. checked all statistical notation and methods. T.C.P. provided subject-matter expertise and guided framing of the problem and interpretation of results. All other authors guided data collection and harmonization and provided expert insight into interpretation of results using these data. All authors read the manuscript, provided substantive comments, and have approved of the manuscript as submitted.

Funding/Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Centers for Disease Control and Prevention. This work was supported by National Institutes of Health grants K01AA028193, K01AI125087, U01AI069918, F31AI-124794, F31DA037788, G12MD007583, K01AI093197, K01AI131895, K23EY013707, K24AI065298, K24AI-118591, K24DA000432, KL2TR000421, N01CP01004, N02CP055504, N02CP91027, P30AI027757, P30AI-027763, P30AI027767, P30AI036219, P30AI050409, P30AI050410, P30AI094189, P30AI110527, P30MH-62246, R01AA016893, R01DA011602, R01DA012568, R01AG053100, R24AI067039, R34DA045592, U01A-A013566, U01AA020790, U01AI038855, U01AI-038858, U01AI068634, U01AI068636, U01AI069432, U01AI069434, U01DA036297, U01DA036935, U10E-Y008057, U10EY008052, U10EY008067, U01HL146-192, U01HL146193, U01HL146194, U01HL146201, U01HL146202, U01HL146203, U01HL146204, U01-

HL146205, U01HL146208, U01HL146240, U01HL14-6241, U01HL146242, U01HL146245, U01HL146333, U24AA020794, U54GM133807, UL1RR024131, UL-1TR000004, UL1TR000083, UL1TR002378, Z01CP-010214 and Z01CP010176; contracts CDC-200-2006-18797 and CDC-200-2015-63931 from the Centers for Disease Control and Prevention, USA; contract 90047713 from the Agency for Healthcare Research and Quality, USA; contract 90051652 from the Health Resources and Services Administration, USA; the Grady Health System; grants CBR-86906, CBR-94036, HCP-97105 and TGF-96118 from the Canadian Institutes of Health Research, Canada; Ontario Ministry of Health and Long Term Care, and the Government of Alberta, Canada. Additional support was provided by the National Institute Of Allergy And Infectious Diseases (NIAID), National Cancer Institute (NCI), National Heart, Lung, and Blood Institute (NHLBI), Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD), National Human Genome Research Institute (NHGRI), National Institute for Mental Health (NIMH) and National Institute on Drug Abuse (NIDA), National Institute on Aging (NIA), National Institute of Dental & Craniofacial Research (NIDCR), National Institute of Neurological Disorders and Stroke (NINDS), National Institute of Nursing Research (NINR), National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Deafness and Other Communication Disorders (NIDCD), and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

## Conflicts of interest

P.F.R. received funding from Gilead and Johnson & Johnson for consulting work unrelated to this research in the prior 36 months. K.N.A. serves as a consultant to the All of Us Research Program, National Institutes of Health (funds paid to her), and TrioHealth (funds paid to her). H. M.C. has received grant funding from ViiV to her institution not related to this project.

## References

1. Fauci AS, Redfield RR, Sigounas G, Weahkee MD, Giroir BP. **Ending the HIV epidemic: a plan for the United States.** *JAMA* 2019; **321**:844–845.
2. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, *et al.* **Prevention of HIV-1 infection with early antiretroviral therapy.** *N Engl J Med* 2011; **365**:493–505.
3. Insight Start Study Group, Lundgren JD, Babiker AG, Gordin F, Emery S, Grund B, *et al.* **Initiation of antiretroviral therapy in early asymptomatic HIV infection.** *N Engl J Med* 2015; **373**:795–807.
4. Eisinger RW, Dieffenbach CW, Fauci AS. **HIV viral load and transmissibility of HIV infection: undetectable equals untransmittable.** *JAMA* 2019; **321**:451–452.
5. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. **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**:793–800.



6. Greenberg AE, Hader SL, Masur H, Young AT, Skillicorn J, Dieffenbach CW. **Fighting HIV/AIDS in Washington, DC.** *Health Aff* 2009; **28**:1677–1687.
7. Becasen JS, Denard CL, Mullins MM, Higa DH, Sipe TA. **Estimating the prevalence of HIV and sexual behaviors among the US transgender population: a systematic review and meta-analysis, 2006–2017.** *Am J Public Health* 2019; **109**:e1–e8.
8. Baral SD, Poteat T, Strömdahl S, Wirtz AL, Guadamuz TE, Beyrer C. **Worldwide burden of HIV in transgender women: a systematic review and meta-analysis.** *Lancet Infect Dis* 2013; **13**:214–222.
9. Rosen JG, Malik M, Cooney EE, Wirtz AL, Yamanis T, Lujan M, et al. **Antiretroviral treatment interruptions among Black and Latina transgender women living with HIV: characterizing co-occurring, multilevel factors using the gender affirmation framework.** *AIDS Behav* 2019; **23**:2588–2599.
10. Santos G-M, Wilson EC, Rapues J, Macias O, Packer T, Raymond HF. **HIV treatment cascade among transgender women in a San Francisco respondent driven sampling study.** *Sex Transm Infect* 2014; **90**:430–433.
11. Doshi RK, Milberg J, Isenberg D, Matthews T, Malitz F, Matosky M, et al. **High rates of retention and viral suppression in the US HIV Safety Net System: HIV Care Continuum in the Ryan White HIV/AIDS Program, 2011.** *Clin Infect Dis* 2014; **60**:117–125.
12. Mizuno Y, Frazier EL, Huang P, Skarbinski J. **Characteristics of transgender women living with HIV receiving medical care in the United States.** *LGBT Health* 2015; **2**:228–234.
13. Thomas JA, Irvine MK, Xia Q, Harriman GA. **Service utilization and HIV outcomes among transgender women receiving Ryan White Part A services in New York City.** *PLoS One* 2021; **16**: e0253444.
14. Klein PW, Psihopaidas D, Xavier J, Cohen SM. **HIV-related outcome disparities between transgender women living with HIV and cisgender people living with HIV served by the Health Resources and Services Administration's Ryan White HIV/AIDS Program: a retrospective study.** *PLoS Med* 2020; **17**: e1003125.
15. Colasanti J, Kelly J, Pennisi E, Hu YJ, Root C, Hughes D, et al. **Continuous retention and viral suppression provide further insights into the HIV care continuum compared to the cross-sectional HIV care cascade.** *Clin Infect Dis* 2016; **62**:648–654.
16. Haber N, Barnighausen T, Lesko CR, Edwards JK, Fox M, Bor J, et al. **Longitudinal cascades more accurately assess health systems performance than cross-sectional cascades such as UNAIDS 90-90-90 targets: a simulation-based demonstration.** Mexico City, Mexico: ; 2019.
17. Haber N, Naidu K, Pillay D, Barnighausen T. **HIV system assessment with longitudinal treatment cascade in Kwazulu-Natal, South Africa.** San Diego, CA; 2015. Available at: <http://paa2015.princeton.edu/abstracts/152645> [accessed 11 February 2016].
18. Lesko CR, Edwards JK, Moore RD, Lau B. **A longitudinal, HIV care continuum: 10-year restricted mean time in each care continuum stage after enrollment in care, by history of injection drug use.** *AIDS* 2016; **30**:2227–2234.
19. Althoff KN, Buchacz K, Hall HI, Zhang J, Hanna DB, Rebeiro P, et al. **US trends in antiretroviral therapy use, HIV RNA plasma viral loads, and CD4 T-lymphocyte cell counts among HIV-infected persons, 2000 to 2008.** *Ann Intern Med* 2012; **157**:325–335.
20. Gange SJ, Kitahata MM, Saag MS, Bangsberg DR, Bosch RJ, Brooks JT, et al. **Cohort profile: the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD).** *Int J Epidemiol* 2007; **36**:294–301.
21. Poteat T, Hanna DB, Rebeiro PF, Klein M, Silverberg MJ, Eron JJ, et al. **Characterizing the human immunodeficiency virus care continuum among transgender women and cisgender women and men in clinical care: a retrospective time-series analysis.** *Clin Infect Dis* 2020; **70**:1131–1138.
22. Poteat TC, Hanna DB, Althoff KN. **Feasibility and acceptability of developing a multisite clinical cohort of transgender people with HIV infection.** *AIDS Res Hum Retroviruses* 2015; **31**:870–872.
23. Cox DR. **Regression models and life tables.** *J R Stat Soc B, Stat Methodol* 1972; **34**:187–220.
24. Allison PD, Institute SAS. *Survival analysis using the SAS system: a practical guide.* 2nd ed. Cary, NC: SAS Institute; 2010.
25. Borgan O. **Aalen-Johansen estimator.** *Encyclop Biostat* 1998; **1**:5–10.
26. Cole SR, Hudgens MG, Brookhart MA, Westreich D. **Risk.** *Am J Epidemiol* 2015; **181**:246–250.
27. Cole SR, Lau B, Eron JJ, Brookhart MA, Kitahata MM, Martin JN, et al. **Estimation of the standardized risk difference and ratio in a competing risks framework: application to injection drug use and progression to AIDS after initiation of antiretroviral therapy.** *Am J Epidemiol* 2015; **181**:238–245.
28. Edwards JK, Cole SR, Adimora A, Fine J, Martin J, Eron J. **Illustration of a measure to combine viral suppression and viral rebound in studies of HIV therapy.** *J Acquir Immune Defic Syndr* 2015; **68**:241–244.
29. Goukova NA, Cole SR, Eron JJ, Fine JP. **Viral suppression in HIV studies: combining times to suppression and rebound.** *Biometrics* 2014; **70**:441–448.
30. Cole SR, Hernan MA. **Adjusted survival curves with inverse probability weights.** *Comput Methods Progr Biomed* 2004; **75**:45–49.
31. Cole SR, Hernan MA. **Constructing inverse probability weights for marginal structural models.** *Am J Epidemiol* 2008; **168**:656–664.
32. Xie J, Liu C. *Adjusted Kaplan–Meier estimator and log-rank test with inverse probability of treatment weighting for survival data.*
33. Sato T, Matsuyama Y. **Marginal structural models as a tool for standardization.** *Epidemiology* 2003; **14**:680–686.
34. Robins JM, Hernan MA, Brumback B. **Marginal structural models and causal inference in epidemiology.** *Epidemiology* 2000; **11**:550–560.
35. Efron B, Tibshirani R. *An introduction to the bootstrap.* New York: Chapman & Hall; 1993. Available at: <http://www.loc.gov/catdir/enhancements/fy0730/93004489-d.html>.
36. Summers NA, Huynh TT, Dunn RC, Cross SL, Fuchs CJ. **Effects of gender-affirming hormone therapy on progression along the HIV Care Continuum in Transgender Women.** *Open Forum Infect Dis* 2021; **8**:ofab404.
37. Edwards JK, Lesko CR, Hecce ME, Murenzi G, Twizere C, Lelo P, et al. **Gone but not lost: implications for estimating HIV care outcomes when loss to clinic is not loss to care.** *Epidemiology* 2020; **31**:570–577.
38. Edwards JK, Cole SR, Westreich D, Moore R, Mathews C, Geng E, et al. **Loss to clinic and five-year mortality among HIV-infected antiretroviral therapy initiators.** *PLoS One* 2014; **9**:e102305.
39. Bukowski LA, Chandler CJ, Creasy SL, Matthews DD, Friedman MR, Stall RD. **Characterizing the HIV Care Continuum and Identifying Barriers and Facilitators to HIV diagnosis and viral suppression among Black transgender women in the United States.** *J Acquir Immune Defic Syndr* 2018; **79**:413–420.
40. Centers for Disease Control and Prevention. **Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2019; 2021.** Available at: <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-vol-26-no-2.pdf> [accessed 29 November 2021].
41. Yehia BR, Fleishman JA, Moore RD, Gebo KA. **Retention in care and health outcomes of transgender persons living with HIV.** *Clin Infect Dis* 2013; **57**:774–776.
42. Rebeiro PF, Horberg MA, Gange SJ, Gebo KA, Yehia BR, Brooks JT, et al. **Strong agreement of nationally recommended retention measures from the Institute of Medicine and Department of Health and Human Services.** *PLoS One* 2014; **9**:e111772.
43. Lesko CR, Mugavero MJ, Shen NM, Fojo AT, Moore RD, Keruly JC, et al. **Exploring definitions of retention in care for people living with HIV in the United States in the modern treatment era.** *AIDS* 2022.
44. Lesko CR, Chander G, Moore RD, Lau B. **Variation in estimated viral suppression associated with the definition of viral suppression used.** *AIDS* 2020; **34**:1519–1526.
45. Matson TE, McGinnis KA, Rubinsky AD, Frost MC, Czarnogorski M, Bryant KJ, et al. **Gender and alcohol use: influences on HIV care continuum in a national cohort of patients with HIV.** *AIDS* 2018; **32**:2247–2253.