Trends and Disparities in Antiretroviral Therapy Initiation and Virologic Suppression Among Newly Treatment-Eligible HIV-Infected Individuals in North America, 2001–2009

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Background. Since the mid-1990s, effective antiretroviral therapy (ART) regimens have improved in potency, tolerability, ease of use, and class diversity. We sought to examine trends in treatment initiation and resulting human immunodeficiency virus (HIV) virologic suppression in North America between 2001 and 2009, and demographic and geographic disparities in these outcomes.

Methods. We analyzed data on HIV-infected individuals newly clinically eligible for ART (ie, first reported CD4$^+$ count <350 cells/μL or AIDS-defining illness, based on treatment guidelines during the study period) from 17 North American AIDS Cohort Collaboration on Research and Design cohorts. Outcomes included timely ART initiation (within 6 months of eligibility) and virologic suppression (≤500 copies/mL, within 1 year). We examined time trends and considered differences by geographic location, age, sex, transmission risk, race/ethnicity, CD4$^+$ count, and viral load, and documented psychosocial barriers to ART initiation, including non–injection drug abuse, alcohol abuse, and mental illness.

Results. Among 10 692 HIV-infected individuals, the cumulative incidence of 6-month ART initiation increased from 51% in 2001 to 72% in 2009 (P_{trend} < .001). The cumulative incidence of 1-year virologic suppression increased from 55% to 81%, and among ART initiators, from 84% to 93% (both P_{trend} < .001). A greater number of psychosocial barriers were associated with decreased ART initiation, but not virologic suppression once ART was initiated. We found significant heterogeneity by state or province of residence (P < .001).

Conclusions. In the last decade, timely ART initiation and virologic suppression have greatly improved in North America concurrent with the development of better-tolerated and more potent regimens, but significant barriers to treatment uptake remain, both at the individual level and systemwide.

Keywords. antiretroviral therapy; healthcare disparities; HIV; time factors; viral load.

Since the mid-1990s, effective antiretroviral therapy (ART) regimens to treat human immunodeficiency virus (HIV) infection have improved in potency, tolerability, ease of use, and antiretroviral class diversity [1]. These have been linked to improvements in treatment adherence [2, 3] and clinical outcomes [4]. However, not all who are clinically eligible start treatment, a scenario sometimes associated with substance abuse and suboptimal insurance coverage, among other factors [5].

Monitoring trends in the successful initiation of ART is important, especially as population-based interventions such as expanded "test-and-treat" initiatives are introduced [6, 7] and as treatment guidelines recommend starting therapy at higher CD4$^+$ counts [8, 9]. Collectively, these changes increase the identification of previously undiagnosed individuals and, consequently, the pool of persons newly eligible for treatment. Owing to their size and heterogeneity, collaborative observational studies are particularly useful to monitor trends [10]. They can help identify disparities among subpopulations, including those defined by geography, which may be informative as many health policies are instituted at the state or province level. Reducing HIV-related health disparities in vulnerable populations is a priority of both the US National HIV/AIDS Strategy and the Federal Initiative to Address HIV/AIDS in Canada [11, 12].

We examined ART initiation and virologic suppression among newly treatment-eligible individuals between 2001 and 2009 in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). To assess changes over time in this large cohort, we estimated the annual cumulative incidence of ART initiation and virologic suppression following treatment eligibility. We also examined factors associated with these outcomes, and explored heterogeneity by geographic location.

METHODS

Data Source

The NA-ACCORD is a collaboration of single- and multisite prospective cohort studies that includes >100 000 HIV-infected individuals from >100 sites in the United States and Canada, and is a regional contributor to the International Epidemiological Databases to Evaluate AIDS [13–15]. Each participating cohort submits data regarding enrolled participants' demographic characteristics, prescribed medications, laboratory tests, clinical diagnoses, and vital status, which undergo quality control before being combined into standardized analysis files. Human subjects activities of the NA-ACCORD and each participating cohort are reviewed and approved by their respective institutional review boards.

Study Population

The study population included ART-naive HIV-infected adults (age ≥18 years) newly eligible to initiate ART between 2001 and 2009, from 17 NA-ACCORD cohorts. For consistency, clinical eligibility was based on US Department of Health and Human Services treatment guidelines during this period (ie, an incident AIDS-defining illness [ADI] or a recorded CD4$^+$ count of <350 cells/μL) [16, 17]. Inclusion criteria were a known state or province of residence, at least 2 CD4$^+$ counts in the study period (to ensure adequate follow-up), no prior CD4$^+$ counts <350 cells/μL or documented ADIs, and no documented history of ART use.

Outcomes of Interest

The outcomes of interest were time to ART initiation and time to virologic suppression, using date of ART eligibility (ie, the first date that an incident ADI or a CD4$^+$ count <350 cells/μL was recorded) as the time origin. Time to ART initiation was defined as the duration between the date of eligibility and the date ART was started. We used a standard definition for ART consistent with US guidelines [18]. On the basis of previous work using a 6-month window to capture successful initiation of treatment, [19] we censored time to ART initiation at 6 months after eligibility, focusing on timely initiation.

Virologic suppression was defined as any HIV type 1 viral load (VL) measurement ≤500 copies/mL within 1 year. This threshold was chosen to account for differences in detection limits of commercial assays over the study period [20, 21]. We censored suppression at 1 year after eligibility to focus on more timely virologic control. Seven percent of subjects did not have a second VL available by 1 year and were excluded from further analysis. A secondary outcome was time to virologic suppression, limited to those initiating ART within 6 months of eligibility. For this outcome, we used the date of ART initiation as the time origin instead of the date of ART eligibility.

Variables of Interest

Individual-level variables of interest, assessed at ART eligibility, included age; race/ethnicity; sex; transmission risk (ie, male sex with men, history of injection drug use [IDU], or other risk); CD4$^+$ count; VL; calendar year; jurisdiction of residence (ie, state or province); and psychosocial barriers to ART initiation, including documented histories of non–injection drug abuse, alcohol abuse, and mental illness. These barriers were dichotomized based on the presence of more specific diagnoses of drug or alcohol abuse/dependence or mental disorders as derived from electronic medical records and medical record reviews, and the variables were summed to form a single ordinal variable. State of residence was not available from 3 US cohorts, and for these the state of the clinic site was used

as a proxy. To assess potential misclassification due to this decision, we calculated the percentage of individuals living outside the state of the clinic site from the remaining US clinical cohorts; only 1% lived outside the state of the clinic site.

To account for potential differences in ART initiation influenced by characteristics of the cohorts or clinics themselves, we used information regarding employment (eg, unemployed, disabled, working) and insurance status (eg, uninsured, public, private) collected by a standardized questionnaire administered to all US NA-ACCORD clinical cohorts on their study populations, categorizing each as follows: higher socioeconomic status US clinical cohort, lower socioeconomic US clinical cohort, US interval cohort, and Canadian cohort. Interval cohorts differ from clinical cohorts in both timing and data collection; individuals are followed at specified intervals (eg, every 6 months) that are unrelated to healthcare visits, and data are collected according to defined protocols [22]. We also included variables representing mechanisms undertaken by individual clinics to assist patients in gaining access to ART, such as AIDS Drug Assistance Program (ADAP) enrollment, and distinguished between those performed by clinic staff and those requiring referral to entities outside the clinic. For cohorts not surveyed, we used the median of the answers from participating cohorts.

Statistical Methods

For each calendar year, we estimated the cumulative incidence of ART initiation (at 6 months of eligibility) and virologic suppression (at 1 year of eligibility; and among ART initiators, at 1 year of ART initiation), adjusting for the aforementioned covariates. We used a published method that determines the cumulative incidence for a given exposure (eg, calendar year) by averaging the individual predicted survival curves of people with that exposure, based on a Cox model stratified by year [23]. For time to virologic suppression, we excluded the small number of individuals who already had a VL <500 copies/mL at eligibility.

We constructed multivariable Cox regression models to determine hazard ratios for factors associated with time to ART initiation and time to virologic suppression. We explored potential interactions between these factors and calendar time (ie, 2001–2005 and 2006–2009) in subgroup analyses by time period, based on observed time trends. Because not all cohorts could provide information on each of the psychosocial barriers examined, we performed sensitivity analysis among the 11 cohorts contributing data on all 3 (n = 9370). To account for potential selection bias in the analysis of virologic suppression among those who initiated treatment, we performed a sensitivity analysis using inverse probability of selection weighting as an alternative to simply limiting the analysis to ART initiators

(Supplementary Appendix). We also replaced time-to-event outcomes with dichotomous outcomes as a further sensitivity analysis. Overall inferences did not change using these alternate approaches.

We tested for geographic heterogeneity in each outcome using likelihood ratio testing, with jurisdiction of residence modeled as a random effect. Because representativeness of estimates in NA-ACCORD to the general HIV-infected population may vary within each jurisdiction, we limited estimates to those with ≥100 eligible individuals and ≥1000 participants in the overall NA-ACCORD, and reported estimates by geographic region instead of the jurisdictions themselves.

Analyses were conducted using SAS software version 9.2 and the R package version 2.15.0. A *P* value < .05 guided statistical interpretation.

RESULTS

From 115 882 living HIV-infected individuals in NA-ACCORD between 2001 and 2009, 10 692 were ART-naive and became newly eligible for ART initiation during the study period. There were 9186 (86%) participants eligible for analyses of virologic suppression because they were not suppressed at eligibility and had at least 1 VL recorded within 1 year. Participant characteristics are listed in Table 1. Thirty-four percent were eligible for ART because of a CD4$^+$ count < 200 cells/μL, and an additional 63% had a CD4$^+$ count between 200 cells/μL and 350 cells/μL. Only 3.6% were eligible for ART based solely on an incident ADI. Among the participants, 0.3% had both a CD4$^+$ count < 350 cells/μL and an incident ADI.

The study population comprised 9619 individuals from 33 US states (plus the District of Columbia) and 1073 from 5 Canadian provinces. Fourteen states and 3 provinces had sufficient representation to estimate cumulative incidence at the jurisdictional level (Supplementary Appendix Table 1). The 3 most highly represented jurisdictions were California (19%), New York (18%), and Texas (11%).

Trends in ART Initiation and Virologic Suppression, 2001–2009
Figure 1 shows time trends in ART initiation and virologic suppression. The adjusted 6-month cumulative incidence of ART initiation was 57% overall, increasing from 51% in 2001 to 72% in 2009. The adjusted cumulative incidence of virologic suppression after 1 year of ART eligibility was 62%, increasing from 55% in 2001 to 81% in 2009. Among ART initiators, the cumulative incidence of virologic suppression after 1 year was 87%, increasing from 84% in 2001 to 93% in 2009. All trends were statistically significant (P_{trend} < .001), and generally persisted within individual cohorts (data not shown).

Table 1. Characteristics of Newly Treatment-Eligible HIV-Infected Individuals, North American AIDS Cohort Collaboration on Research and Design, 2001–2009 (N = 10 692)

Characteristic	No.	%
Age at eligibility, y, median (interquartile range)	40	(33–46)
18–29	1848	17
30–39	3434	32
40–49	3618	34
50–59	1460	14
≥60	332	3
Race/ethnicity		
Black	4414	41
Hispanic, any race	1804	17
White	3505	33
Asian/Pacific Islander	159	1.5
Other race/ethnicity[a]	810	8
Sex and transmission risk		
Men who have sex with men	4586	43
Male injection drug user	1151	11
Male, other risk	2125	20
Female injection drug user	464	4
Female, other risk	2366	22
Antiretroviral therapy eligibility criteria		
CD4+ count 0–199 cells/μL	3631	34
CD4+ count 200–349 cells/μL	6679	62
Incident AIDS-defining illness	382	4
Viral load at eligibility		
Undetectable	774	7
501–9999 copies/mL	1677	16
10 000–99 999 copies/mL	4210	39
≥100 000 copies/mL	2837	27
Missing	1194	11
Documented history of psychosocial barriers[b]		
Alcohol abuse	684	7
Non–injection drug abuse	1303	14
Mental illness	2315	22
Number of psychosocial barriers[c]		
0	7649	72
1	2033	19
2	757	7
3	253	2
Calendar year of eligibility		
2001–2005	6035	56
2006–2009	4657	44

[a] Includes Native Americans, Aboriginal Canadians, and persons of other or unknown race/ethnicity.

[b] Among participants with data available, 9865, 9515, and 10 648 had data on alcohol abuse, non–injection drug abuse, and mental illness, respectively.

[c] Includes a documented history of alcohol abuse, non–injection drug abuse, and mental illness.
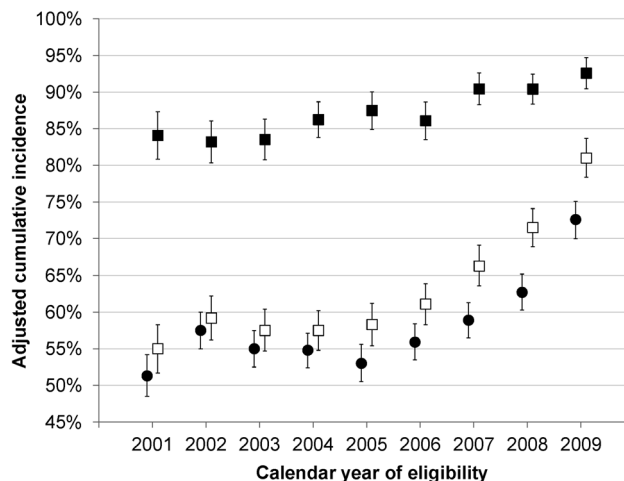

Figure 1. Trends in antiretroviral therapy (ART) initiation and virologic suppression among newly treatment-eligible individuals in North America, NA-ACCORD, 2001–2009. Solid circles: ART initiation 6 months after eligibility; hollow squares: virologic suppression 1 year after eligibility; solid squares: virologic suppression 1 year after ART initiation. Error bars represent 95% confidence intervals. Estimates were adjusted for age; race/ethnicity; sex; transmission risk; documented history of non–injection drug abuse, alcohol abuse, and mental illness; CD4+ count and viral load at eligibility; jurisdiction of residence; type of cohort; and clinic-specific mechanisms undertaken to assist with access to ART. Unadjusted trends (not shown) were similar.

Factors Associated With ART Initiation and Virologic Suppression

Table 2 shows factors associated with ART initiation and virologic suppression. Increasing age was associated with both more timely ART initiation and virologic suppression, among both the full study population ($P_{trend} < .001$) and the subset who initiated ART ($P_{trend} = .001$). Regarding race/ethnicity, those in the "other" category (comprising mostly Native Americans and Canadian aboriginals) were less likely to have timely ART initiation than those of white race (adjusted hazard ratio [HR], 0.84 [95% confidence interval {CI}, .72–.98]), but this association disappeared when examining virologic suppression.

Compared to those with a CD4+ count 200–349 cells/μL, those with a CD4+ count <200 cells/μL were more likely to have timely ART initiation (HR, 2.29 [95% CI, 2.16–2.42]) and virologic control (HR, 1.75 [95% CI, 1.64–1.85]) after eligibility. However, among ART initiators, those with a CD4+ count <200 cells/μL were no more or less likely to become suppressed (HR, 0.99 [95% CI, .93–1.05]). Individuals clinically eligible for treatment solely due to an ADI were less likely to initiate ART (HR, 0.66 [95% CI, .55–.79]) or achieve suppression (HR, 0.85 [95% CI, .71–1.01]) than those with a CD4+ count 200–349 cells/μL, but once initiating ART, they also reached similar suppression (HR, 0.93 [95% CI, .76–1.15]).

Table 2. Factors Associated With Antiretroviral Therapy Initiation and Virologic Suppression Among Newly Treatment-Eligible HIV-Infected Individuals (CD4+ Count <350 Cells/µL or AIDS-Defining Illness), 2001–2009

	ART Initiation (at 6 mo of Eligibility)		Viral Load Suppression (at 1 y of Eligibility)[a]		Viral Load Suppression (1 y After ART Initiation)[b]	
	No.	Adjusted HR (95% CI)	No.	Adjusted HR (95% CI)	No.	Adjusted HR (95% CI)
Total	10 692		9186		5329	
Age at eligibility						
18–29	1848	Ref.	1639	Ref.	910	Ref.
30–39	3434	1.10 (1.02, 1.19)	2987	1.06 (.97, 1.14)	1728	1.08 (.99, 1.19)
40–49	3618	1.14 (1.06, 1.24)	3056	1.11 (1.02, 1.21)	1777	1.11 (1.01, 1.21)
50–59	1460	1.23 (1.12, 1.36)	1236	1.28 (1.16, 1.42)	750	1.24 (1.11, 1.38)
≥60	332	1.13 (.97, 1.33)	268	1.29 (1.10, 1.52)	164	1.12 (.94, 1.34)
Race/ethnicity						
White	3505	Ref.	3074	Ref.	1764	Ref.
Asian/Pacific Islander	159	1.18 (.95, 1.47)	140	1.17 (.94, 1.46)	74	1.24 (.97, 1.58)
Black	4414	0.93 (.87, 1.00)	3720	0.95 (.88, 1.02)	2139	0.98 (.90, 1.06)
Hispanic (any race)	1804	1.01 (.93, 1.10)	1529	1.04 (.96, 1.14)	944	0.99 (.90, 1.09)
Other race/ethnicity[c]	810	0.84 (.72, 0.98)	723	0.99 (.85, 1.15)	408	1.01 (.85, 1.19)
Sex and transmission risk						
Men who have sex with men	4586	Ref.	4036	Ref.	2411	Ref.
Female injection drug user	464	0.64 (.54, .75)	365	0.73 (.62, .86)	135	0.85 (.69, 1.04)
Female, other risk	2366	0.87 (.81, .94)	2028	0.99 (.92, 1.06)	1139	0.99 (.91, 1.08)
Male injection drug user	1151	0.81 (.74, .90)	924	0.80 (.73, .89)	462	0.85 (.76, .96)
Male, other risk	2125	1.00 (.93, 1.08)	1833	0.94 (.87, 1.02)	1182	0.91 (.84, .99)
ART eligibility criteria						
CD4+ count 0–199 cells/µL	3631	2.29 (2.16, 2.42)	3257	1.75 (1.64, 1.85)	2597	0.99 (.93, 1.05)
CD4+ count 200–349 cells/µL	6679	Ref.	5641	Ref.	2623	Ref.
Incident AIDS-defining illness	382	0.66 (.55, .79)	288	0.85 (.71, 1.01)	109	0.93 (.76, 1.15)
Viral load at eligibility						
Undetectable	774	Ref.	N/A	N/A	N/A	N/A
501–9999 copies/mL	1677	0.51 (.45, .58)	1539	Ref.	580	Ref.
10 000–99 999 copies/mL	4210	0.79 (.71, .88)	3888	1.24 (1.14, 1.35)	2130	0.77 (.70, .85)
≥100 000 copies/mL	2837	1.04 (.94, 1.16)	2675	1.33 (1.21, 1.45)	2002	0.58 (.52, .64)
Missing	1194	0.69 (.61, .78)	1084	1.35 (1.21, 1.50)	617	0.65 (.57, .74)
No. of psychosocial barriers[d]						
0	7649	Ref.	6573	Ref.	4042	Ref.
1	2033	0.83 (.77, .89)	1757	0.89 (.83, .96)	916	0.99 (.91, 1.07)
2	757	0.70 (.62, .79)	642	0.84 (.75, .94)	289	1.02 (.90, 1.17)
3	253	0.58 (.47, .72)	214	0.66 (.54, .82)	82	0.85 (.66, 1.08)
Calendar year of eligibility		1.05 (1.04, 1.06)		1.07 (1.06, 1.09)		1.03 (1.02, 1.04)

Cox regression, adjusted for all other factors, plus state or province of residence, type of cohort.

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; HIV, human immunodeficiency virus; HR, hazard ratio; N/A, not applicable.

[a] Excludes those with undetectable viral load at eligibility and those with no viral load within 1 year.

[b] Also excludes those who did not initiate ART within 6 months.

[c] Includes Native Americans, Aboriginal Canadians, and persons of other or unknown race/ethnicity.

[d] Includes a documented history of alcohol abuse, non–injection drug abuse, and mental illness.

A history of IDU was associated with less timely ART initiation and virologic suppression, particularly in female users, but after taking into account ART initiation, the association with virologic suppression was diminished (Table 2). We identified a significant dose–response effect on the basis of an increasing number of psychosocial barriers (including history of non–injection drug use, alcohol abuse, and mental illness) when assessing the hazard of ART initiation (HR decreased

from 0.83 for 1 barrier to 0.58 for 3 barriers, $P_{trend} < .001$) and suppression (HR decreased from 0.89 to 0.66, $P_{trend} < .001$). However, limiting the analysis to those who initiated ART mitigated this association ($P_{trend} = .53$).

Consistent with the aforementioned time trends, there was a statistically significant increase in ART initiation and virologic suppression with each successive calendar year: 5% and 7% per year, respectively. We explored interactions between all factors and calendar period (2001–2005, and 2006–2009), but did not observe any substantial differences in effect estimates for these factors except for calendar year itself (ie, no annual change between 2001–2005 for ART initiation [$P_{trend} = .11$], but a significant increase between 2006–2009 [$P_{trend} < .001$]).

Estimation of Treatment Outcome Rates, by Jurisdiction of Residence

Among the 14 states and 3 provinces examined, the cumulative incidence of ART initiation after 6 months ranged from 35% to 94% after adjusting for individual- and cohort-level characteristics (Figure 2A), a 2.7-fold relative difference. We found a statistically significant effect of jurisdiction of residence on ART initiation ($P < .001$), suggesting heterogeneity exceeding what would be expected by chance.

The adjusted 1-year virologic suppression incidence by jurisdiction ranged from 45% to 78% (Figure 2B), with a similarly significant, though smaller, jurisdiction effect ($P < .001$). The effect remained statistically significant ($P < .001$) among those who initiated ART (Figure 2C). Among states and provinces, the cumulative incidence of ART initiation was only weakly correlated with virologic suppression ($r = 0.14$).

DISCUSSION

In this heterogeneous population of HIV-infected individuals newly eligible to begin ART, we documented between 2001 and 2009 a substantial improvement in timely ART initiation and resulting virologic suppression, with sustained increases since 2006. Several temporal changes occurred during this period, including the use of better tolerated and more convenient formulations, [4] and increasing evidence that starting therapy earlier results in better outcomes [19, 24–26]. Documenting treatment patterns in this large subset of the North American HIV-infected population is important as newer interventions are developed to further improve clinical outcomes, both at the individual level (eg, newer formulations) and at the
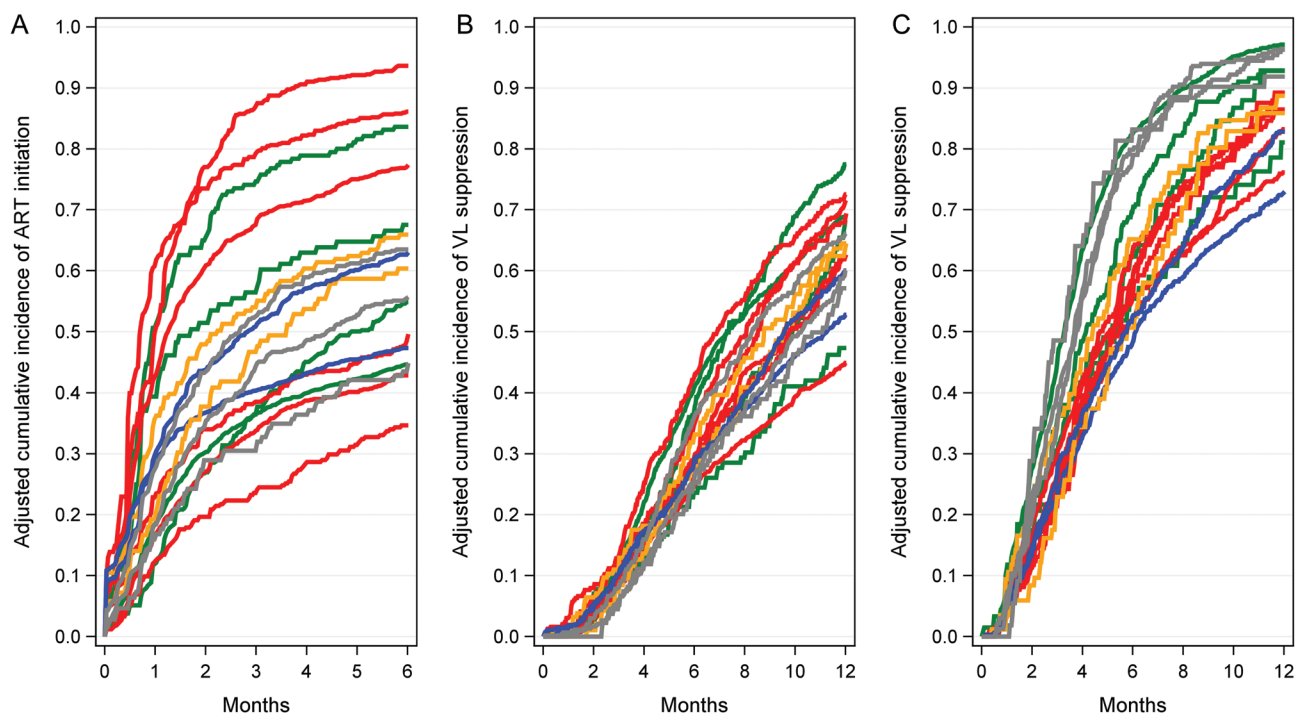
Figure 2. Adjusted cumulative incidence of antiretroviral therapy (ART) initiation and virologic suppression, by jurisdiction, 2001–2009. *A*, ART initiation, through 6 months after eligibility. *B*, Virologic suppression, through 1 year after eligibility. *C*, Virologic suppression among ART initiators, through 1 year after initiation. Estimates were adjusted for age; race/ethnicity; sex; transmission risk; documented history of non–injection drug abuse, alcohol abuse, and mental illness; CD4$^+$ count and viral load at eligibility; calendar year; type of cohort; and clinic-specific mechanisms undertaken to assist with access to ART. Colors used to identify geographic regions: blue = Northeast United States; green = Western United States; gray = Canada; orange = Midwest United States; red = Southern United States. Abbreviations: ART, antiretroviral therapy; VL, viral load.

population level (eg, "test and treat" strategies). As US guidelines now recommend starting ART regardless of CD4$^+$ cell count, [9] it will be even more important to understand temporal trends in ART initiation and resulting clinical outcomes.

We confirmed previously noted barriers to timely initiation of ART, such as younger age and higher CD4$^+$ counts [27, 28]. Less timely ART initiation among those solely eligible due to an incident ADI may have been a consequence of concerns about immune reconstitution inflammatory syndrome, as data supporting the safety of initiating ART in such individuals were not available until recently, [29] or of physicians wanting patients to demonstrate adherence to opportunistic infection treatment before prescribing ART [30].

We also identified potential barriers to ART initiation that, once overcome, may play less of a role in achieving virologic suppression, which is an immediate goal of ART. Persons with a history of IDU were less likely to initiate ART or achieve virologic suppression compared to other risk groups, but these differences were moderated when suppression was considered among injection drug users who initiated ART. The effects of other factors often considered stumbling blocks for patients—such as a history of mental illness, abuse of other drugs and alcohol, and the co-occurrence of these [31]—were also mitigated when examining their impact on achieving virologic suppression. These findings are consistent with some studies that have found that if people have adequate support systems when they initiate treatment, they can greatly improve their chances of virologic success [32–34]. Additional studies that account for duration, severity, and specific diagnoses of mental illness and substance use are warranted, to better understand the nuances of their influences on treatment goals.

After we controlled for individual-level factors, disparities in the timely initiation of therapy by state or province of residence remained, suggesting that system-level factors likely contribute to differential ART access. Disparities by state or province are relevant because there may be policy-related factors that could be modified to reduce these differences. For example, an estimated two-thirds of HIV-infected Americans obtain ART through public programs like Medicaid and the Ryan White Part B ADAP, [35] where state-specific differences in funding and eligibility may play a role in observed disparities [36]. Other recent studies have identified geographic disparities in HIV-related outcomes in the United States [37, 38] and even in Canada, despite universal healthcare [39]. We are conducting further studies in NA-ACCORD to assess how differences in US state-specific ADAP benefits may factor into geographic disparities.

Our analysis has several limitations. First, we cannot determine the extent to which psychosocial barriers delay treatment, either due to a patient's inability to remain engaged in care or a provider being less likely to initiate treatment in patients with disrupted lives [40]. However, our findings suggest that once individuals do initiate ART, many achieve virologic suppression despite these barriers. Furthermore, assessment of psychosocial factors was broad in that we did not distinguish between recent and past history or level of severity, which may influence the timeliness of treatment initiation and positive outcomes in different ways. Other potential psychosocial or structural barriers that we did not have information on include lack of social support, perceived stigma, incarceration, or unstable housing [41–45] In addition, 1 cohort could not supply data on mental illness, and 5 did not supply data on alcohol abuse or non–injection drug abuse. Excluding these cohorts did not change our findings appreciably (data not shown), but more complete measurement of these factors will be valuable in future studies.

Although treatment guidelines aim for successful initiation of ART and virologic suppression, our study cannot distinguish nonuse of ART owing to barriers to treatment vs by choice, and similarly, virologic failure due to nonadherence versus metabolic effects. Nonetheless, our analysis adjusts for many patient- and system-level factors, including mechanisms that clinics have to assist patients in obtaining medications.

Our jurisdiction-level inferences may not be generalizable to all HIV-infected persons living in a particular state or province, because of the variable extent to which patients attending individual clinics represent the underlying HIV population. Therefore, we did not rank states and provinces in terms of treatment outcomes. However, NA-ACCORD is the largest longitudinal cohort of HIV-infected individuals with detailed histories in North America, and its size and diversity play a major role in being able to monitor the larger population [18].

We followed people through 6 months of eligibility to assess "timely" ART initiation. However, other HIV-care quality measures are being developed as performance standards, such as being prescribed potent ART within a 1-year period [46]. Other relevant outcomes that could be examined include longer-term virologic control and retention in care, both of which are important to fully realize the benefits of ART [47, 48].

The importance of timely ART initiation is now well established [9]. Unfortunately many barriers, both at the individual level and systemwide, complicate access to and successful use of treatment for people with HIV infection, even in resource-rich countries. Continued monitoring will be crucial in addressing these disparities, including those related to geography, especially as HIV testing practices change, and, in the United States, as the Affordable Care Act is implemented [49].

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org/). Supplementary materials consist of data

provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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