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Ten-year trends in antiretroviral therapy persistence among US Medicaid beneficiaries

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Abstract

Objective—Whether the rate of HIV antiretroviral therapy (ART) persistence has improved over time in the United States is unknown. We examined ART persistence trends between 2001 and 2010, using non-HIV medications as a comparator.

Methods—We conducted a retrospective cohort study using Medicaid claims. We defined persistence as the duration of treatment from the first to the last fill date before a 90-day permissible gap and used Kaplan–Meier curves and Cox proportional hazard models to assess crude and adjusted nonpersistence. The secular trends of ART persistence in 43 598 HIV patients were compared with the secular trends of persistence with angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACEI/ARB), statins, and metformin in non-HIV-infected patients and subgroups of HIV patients who started these control medications while using ART.

Results—Median time to ART nonpersistence increased from 23.9 months in 2001–2003 to 35.4 months in 2004–2006 and was not reached for those starting ART in 2007–2010. In adjusted models, ART initiators in 2007–2010 had 11% decreased hazard of nonpersistence compared with those who initiated in 2001–2003 ($P < 0.001$). For non-HIV patients initiating angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ACEI/ARB), statins, and metformin, the hazard ratios for nonpersistence comparing 2007–2010 to 2001–2003 were 1.07, 0.94, and 1.02, respectively (all $P < 0.001$). For HIV patients initiating the three control

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Conflicts of interest

Authors not named here have disclosed no conflicts of interests.

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medications, the hazard ratios of nonpersistence comparing 2007–2010 to 2001–2003 were 0.71, 0.65, and 0.63, respectively (all $P < 0.001$).

Conclusion—Persistence with ART improved between 2001 and 2010. Persistence with control medications improved at a higher rate among HIV patients using ART than HIV-negative controls.

Keywords

antiretroviral therapy; Medicaid; medication adherence; medication persistence; United States

Introduction

Adherence to medications can be described as having three phases – initiation, implementation, and persistence – each of which is measured differently [1]. Persistence refers to continuous treatment with a prescribed medication, and it is measured by the duration of treatment before discontinuation [2]. Despite the known clinical benefits of long-term medication use for many chronic conditions, including HIV infection, a large proportion of patients who appropriately initiate medications do not persist with medication taking or experience gaps in treatment [3]. In previous studies, half of HIV patients using antiretroviral therapy (ART) had discontinued treatments by 2 years, and half of the patients with hypertension had discontinued treatments by 3 years [4–7]. Persistence with medications is especially challenging for asymptomatic chronic conditions for which treatment side effects and complications are typically experienced immediately, but for which health benefits are delayed, often for years [8].

Persistence with HIV ART has important clinical consequences. People who discontinue therapy experience viral rebound and the ongoing damaging effects of HIV on the immune system [2, 9]. In addition, treatment interruptions of ART increase the risk of viral resistance, reducing drug options for future therapy, and increase the risk of transmission to others. Because of these risks, approximately half of the HIV care sites in the United States have integrated ART adherence counseling into routine care, and one in five HIV-infected patients report using such programs [10, 11]. However, there are no population-based estimates of the rates of persistence with ART in the United States. How these rates have changed over the time period during which newer ART regimens became available, demographics of the HIV population changed, and many HIV clinics implemented adherence programs is also unknown [4, 12].

To fill this gap, we examined the trends in persistence with ART among Medicaid beneficiaries in the United States between 2001 and 2010. To understand the context of longitudinal ART persistence trends, we also examined the persistence trends in two control groups. First, to assess overall secular trends across chronic conditions, we compared trends in ART with trends in persistence with three other commonly used chronic medications in persons who do not have HIV: angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARBs), statins, and metformin. Second, to assess whether contextual factors specific to HIV care sites might have spillover effects on non-ART medications, we examined persistence with these same three non-HIV-related medications in HIV patients who were also on ART.

Methods

Data source

We conducted a retrospective cohort study of Medicaid fee-for-service patients who initiated ART, ACEI/ARB, statins, or metformin between 2001 and 2010. Medicaid, a public health insurance program with federal and state support, is the single largest source of care for HIV patients in the United States, covering approximately half of HIV-infected people in regular care [13]. We obtained Medicaid Analytic eXtract (MAX) Personal Summary Files and Prescription Drug Files from 14 states with the highest HIV prevalence in the United States: New York, California, Florida, Texas, Maryland, New Jersey, Pennsylvania, Illinois, Georgia, North Carolina, Virginia, Louisiana, Ohio, and Massachusetts. These 14 states account for 75% of HIV prevalence in the United States [14]. MAX Hospital Inpatient Files, Long-Term Care Files, and Other Services Files were also used to identify the HIV-infection status of each patient. The most recent year studied is 2010 because there is a delay of more than 3 years before MAX files can be requested.

Study sample

We identified patients who initiated ART, ACEI/ARB, statins, or metformin during our study period. We excluded those who were dually eligible for Medicare, were in Medicaid-managed care organizations, or possessed multiple-state eligibility at the time of treatment initiation because we may not have the complete claims of these patients. To identify patients who initiated treatment during our study period, we applied a 6-month preindex or 'clean' period; patients were included if they had no fill records for their respective medication during the 6 months prior to treatment initiation and were continuously eligible for Medicaid fee-for-service. Patients with at least 5 months of observation post-treatment initiation were included to allow sufficient time to accrue a permissible gap. Patients with a duration of medication use less than 1 month were excluded. The aforementioned selection criteria were applied to all medication groups. For ART users, we included only those using valid regimens, defined as those receiving a minimum of three different antiretroviral ingredients [5, 15, 16]. ACEI and ARB users were combined into one group.

We compared the persistence trends of HIV patients who initiated ART with two control groups. First, to assess broad secular trends in persistence, we examined persistence with three commonly used medications: ACEI/ARB, statins, and metformin among HIV-negative patients. Second, to explore whether there are contextual factors operating at HIV care sites, we examined persistence with these same three control medications in HIV patients who were on ART at the time of control medication initiation. HIV status of each patient was determined by two or more HIV diagnoses recorded on separate dates (International Classification of Diseases 9th Revision Code: 042, V08) or a minimum of two antiretroviral fill records between 2001 and 2010 (Supplementary Digital Content Fig. 1, <http://links.lww.com/QAD/B105>).

Assessment of persistence

Using days supplied and fill dates for medications within each therapeutic class, persistence was measured by the duration of treatment from the first fill date to the last fill date before a

‘permissible gap.’ A permissible gap is the maximum number of consecutive days that a patient can miss medications before being classified as nonpersistent [2, 17]. We defined the permissible gap as 90 days and half of the number of days of supply from the previous fill [5, 18]. For example, if a patient received a 30-day supply and had no subsequent refill within 105 days from the fill date, he or she was determined nonpersistent on the date of the last fill. A 90-day permissible gap is commonly used in medication persistence studies using pharmacy claims [18–23]. We applied the 90-day rule to ensure that each patient completely discontinued therapy before being classified as nonpersistent, considering the average 30-day supply among Medicaid patients. We accounted for medication accumulation if a patient possessed remaining medications from previous fills.

Certain patients with ART, ACEI/ARB, or statins switched some or all of their ingredients while on treatment (e.g. they switched ART ingredients or switched from ACEI to ARB). To account for switching, patients continued to accumulate days of medication use and were regarded as persistent as long as they continued to receive treatment from the respective therapeutic class (patient-level persistence) [2].

Patients’ medication exposure was censored at the earliest of the following events: end of study period, death, disenrollment from Medicaid coverage, enrollment in Medicare or Medicaid managed care, or if multistate Medicaid eligibility was noted. We included only the first persistent episode of each patient if they restarted treatment after the permissible gap.

Study variables

Our main independent variable, treatment initiation year, was classified into the following three groups based on the availability of newer ART regimens and recommendation from clinicians: from 2001 to 2003, 2004 to 2006, and 2007 to 2010 [24, 25]. Demographic covariates included age at the time of treatment initiation, sex, race/ethnicity (non-Hispanic white, black, Hispanic, Asian/Pacific Islander/Native American, Multiracial/Unknown), and state. For patients using ART, we controlled for index regimen characteristics to account for regimen changes over time. First was the use of an index nucleoside reverse transcriptase inhibitor (NRTI) backbone classified into four groups using the criteria proposed by Willig *et al.* [26]: didanosine or stavudine containing regimens, zidovudine (ZDV) containing regimens, abacavir (ABC) or tenofovir (TDF) containing regimens, and others. Second, we noted the third drug composition of regimens: triple NRTI, non-NRTI-based, protease inhibitor-based, integrase inhibitor-based, and multiple classes. Finally, we controlled for ART daily pill burden. For patients using ACEI or ARBs, we controlled the type of index class used.

Statistical analysis

We provided descriptive statistics to evaluate patient and regimen characteristics by treatment initiation year among ART users. We used chi-square tests to evaluate the differences in baseline characteristics. We also compared the differences in baseline patient characteristics by different medication classes.

We used Kaplan–Meier plots and log-rank tests to examine the changes in time-to-treatment nonpersistence between 2001 and 2010. Median time-to-treatment nonpersistence indicated the time at which half of the patients initiating treatment became nonpersistent. For multivariable analyses, we used Cox proportional hazards models to evaluate the factors associated with nonpersistence adjusting for age, sex, race/ethnicity, state, and regimen characteristics (NRTI backbone, third-drug composition, and ART pill burden for ART users and the type of index class for ACEI/ARB users).

To determine whether censoring patients with changes in Medicaid eligibility status (e.g., a change from Medicaid alone to dual eligibility) had an effect on the results, we conducted a sensitivity analysis that excluded patients with eligibility changes. In a second sensitivity analysis, we tested whether our results were different when comorbid conditions were included in the ART model. We assessed statistical significance in all our models using two-sided tests at the 99% confidence level. We performed the analyses using SAS version 9.3 (SAS Institute, Cary, North Carolina, USA). The Brown University Institutional Review Board approved this study.

Results

Study patients

Patients and regimen characteristics are described for patients with ART by treatment year (Table 1). Among 397 836 HIV patients identified in the Medicaid dataset, our sample included 43 598 HIV patients who initiated ART between 2001 and 2010 and fulfilled the eligibility criteria for the study (Supplementary Digital Content Fig. 1, <http://links.lww.com/QAD/B105>). The majority of patients who initiated ART were aged between 35 and 54 years (65.7%), black (55.4%), male (56.3%), and living in New York (34.1%) and California (14.8%). The types of ART regimens used have markedly changed over time. Between 2001 and 2003, 56.1% of patients initiated ART with ZDV backbone, whereas from 2007 to 2010, 81.9% of patients initiated with TDF/ABC. Approximately half of the HIV patients in 2001–2003 took more than six ART pills per day; however, 34.3% of HIV patients in 2007–2010 used a single-tablet regimen.

The characteristics of HIV-negative patients who initiated control medications are shown in Table 2. The first control group included 674 105 HIV-negative patients who initiated an ACEI/ARB, 621 398 patients with a statin, and 326 877 patients with metformin. Compared with HIV patients using ART, HIV-negative patients who initiated ACEI/ARB, statins, or metformin between 2001 and 2010 were more likely to be older, women, and white (all $P < 0.001$).

The second control group, which is a subset of HIV patients who initiated control medications while on ART, included 3200 HIV patients with ACEI/ARB, 2647 patients with statin, and 867 patients with metformin (Supplementary Digital Content Table 1, <http://links.lww.com/QAD/B105>).

Time-to-treatment nonpersistence

Persistence with ART markedly improved over time (Fig. 1). The median time from ART initiation to nonpersistence increased from 23.9 months in 2001–2003 to 35.4 months in 2004–2006 and was not reached for those initiating in 2007–2010. Among HIV-negative control patients who initiated ACEI/ARB, the median times to nonpersistence were 25.6, 25.5, and 21.6 months for 2001–2003, 2004–2006, and 2007–2010, respectively. For statins and metformin, the numbers were 19.5, 20.4, and 20.7 months and 21.8, 21.9, and 20.6 months, respectively.

Multivariable predictors of nonpersistence in adjusted model

Significant trends toward improved persistence with ART were observed after adjusting for patients and regimen characteristics (Table 3). Patients who initiated ART between 2007 and 2010 presented 11% decreased hazards of treatment nonpersistence compared with those who initiated treatment between 2001 and 2003 [hazard ratio, 0.89 (99% confidence interval (CI), 0.83–0.96)]. Younger age, female sex, black race, living in Texas and Louisiana, older ART regimens, and higher ART daily pill burden were also associated with higher hazards of ART nonpersistence.

Trends in HIV-negative control patients who initiated ACEI/ARB worsened over time (Table 3). Those who initiated ACEI/ARB in 2007–2010 presented 7% higher hazards of nonpersistence compared with those who initiated in 2001–2003 [hazard ratio, 1.07 (CI, 1.06–1.09)]. Persistence trends with statin and metformin were smaller than those seen for ART or remained the same. For statins and metformin, the hazard ratios for nonpersistence comparing 2007–2010 to 2001–2003 were 0.94 (CI, 0.92–0.95) and 1.02 (CI, 1.01–1.04), respectively.

To understand whether there are contextual factors operating to improve adherence at HIV care sites, we examined the subgroup of HIV patients who were concomitantly taking ART at the time of ACEI/ARB, statin, or metformin initiation (Fig. 2). Trends in improved persistence with these control medications were greater among HIV patients with ART than the HIV-negative group. Control group patients who were also using ART presented 29, 35, and 37% lower hazards of ACEI/ARB, statins, and metformin non-persistence in the 2007–2010 group compared with the 2001–2003 group.

Sensitivity analyses

We restricted the ART analysis to 24 452 HIV patients who were not censored due to eligibility changes. The adjusted hazards of ART nonpersistence were 22% lower among those who initiated ART in 2007–2010 compared with 2001–2003 [hazard ratio, 0.78 (CI, 0.72–0.84)]. Adding patient comorbid conditions (e.g., HIV-associated non-AIDS conditions or HIV-related conditions) to the adjusted model for ART did not change the results (results not shown but available upon requests).

Discussion

There are five main findings from this research. First, persistence with ART has improved over the 10-year time period that we examined, even after controlling for patient-level covariates and ART regimen characteristics. Second, because these improvements in persistence are greater than those seen for common chronic medicines used by HIV-negative control patients, these changes are not likely explained by secular trends alone. Third, the improvements in persistence were dramatically larger for control medicines when these patients were already on ART, suggesting that there could be something about using ART or about HIV care settings that improves persistence with other medications. Fourth, HIV patients who were taking less toxic ART regimens and fewer pills were more likely to persist with ART. Fifth, persistence for both ART and control medications was associated with race, sex, and state of residence.

To the best of our knowledge, this study is the first to demonstrate improvements in persistence with ART in a US population of HIV patients with Medicaid over a 10-year period. Most prior studies on ART persistence in the United States were based on subpopulations of HIV patients or cohorts from academic medical centers [5, 26–34]. In the University of Alabama cohort, the median duration of the initial ART regimen increased from 25.6 months in 2000–2004 to 34.3 months in 2004–2007 [26]. Slama *et al.* [27] reported significantly increased initial regimen duration in 2006–2009 compared with the 1996–2001 among 1009 HIV-infected MSM in the Multicenter AIDS Cohort Study. Compared with our study outcome of patient-level persistence, these studies defined regimen switches or persistence as the primary outcome [2].

Our use of two different control groups was aimed at understanding the mechanism of the observed improvement in ART persistence. The purpose of the first control group was to rule out the possibility that these improvements in ART persistence were part of a larger secular trend toward more effective medication taking. Although there was heterogeneity across these control medications, there was no consistent trend toward better medication persistence, making it less likely that our ART findings are explained by secular trends. We hypothesized further that if there were some contextual factor or factors operating at HIV care sites to improve ART persistence that there might be some spillover to non-HIV medications. The purpose of the second control group was to explore this hypothesis, and we found that persistence with control medications was dramatically improved in persons who were also on ART at the time of medication initiation.

We believe that there are at least three potential explanations for this effect. One is that patients with HIV who are on ART have come to understand the seriousness of the HIV infection, and of other health conditions they may have, and also to understand the positive health impact of engaging with care and properly using recommended medications [35]. Arguing against this individual patient-level theory as an explanation for our findings is the fact that it does not explain the changes in ART persistence that we observed over the 10-year period. If anything, the threat of HIV decreased over this time because of more effective and less toxic ART regimens. A second explanation is that as HIV patients experience increased success with ART adherence and viral suppression, they may have felt more

empowered to manage their other health conditions through medication adherence. Existing literature reports mixed evidence on the effects of multiple medications on medication taking behavior [36–38].

A third potential explanation is a more structural one. The adherence support activities that most HIV care settings have adopted as a routine part of care may be effective. Data from a meta-analysis by de Bruin *et al.* [39] found that adherence supports in the control arms of randomized trials were often quite effective, supporting the assertion that adherence supports in routine care can be effective. To directly support this explanation, we would like to be able to show either that adherence support activities were increasing over this time period or that patients were taking more effective advantage of them. Although we believe that both were likely true in the United States between 2001 and 2010, the claims data that we examined have no such information. Related to this, the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act supports a variety of adherence-related services at primary care sites in which approximately 500 000 patients with HIV receive care. These clinics provide extensive adherence counseling and health education services each year, and more than 30% of patients at these HIV care sites have Medicaid [11, 40]. Although we cannot determine which of the care sites used by the Medicaid patients that we studied received CARE Act funding, this is an additional structural factor that would have been operating during the study period. With the data that we have, we cannot distinguish between the individual and the structural explanations, and both may be operating. These findings suggest that more systematic efforts to prioritize and support medication adherence at the practice level could improve adherence with chronic medications more generally. Understanding the mechanism of improved medication persistence among HIV patients will have implications for other chronic conditions in future research.

Consistent with the findings of existing studies [5, 15, 26, 41], newer ART regimens with better tolerability and a lower ART pill burden were associated with substantial improvements in ART persistence. In this study, those who used single tablet regimens had 29% reduced hazards of nonpersistence compared with those who used more than six ART pills per day. Clinicians should consider these results when making prescription decisions.

Blacks, women, and residents in some states were less likely to persist with treatments. Blacks and women are reported to present lower levels of adherence possibly because of limited resources and restricted access to care [12, 30, 42]. Patients in southern states, such as Texas and Louisiana, also presented significantly higher hazards of treatment nonpersistence compared with patients in New York and California. These differences may explain the wide variation in viral suppression between different US states [43]. The generosity of state Medicaid programs varies in terms of eligibility criteria, medication drug payment caps, out-of-pocket payments, and access to providers, all of which are likely to affect medication-taking. The high levels of HIV-related stigma in culturally conservative Southern states may also affect poor adherence and negative health outcomes in HIV patients [44–46]. Of note, Texas has not yet decided to expand its Medicaid program under the Affordable Care Act, and Louisiana's Medicaid expansion took effect on 1 July 2016. Interventions that target these populations are needed to reduce sex, racial, and geographical disparities in HIV care.

This study has several limitations. First, the administrative data that we used do not include data on CD4⁺ cell counts and viral loads, so we cannot assess whether these improvements in persistence resulted in better viral and immunological outcomes. Although we lacked the dosing frequency for ART regimens, we controlled for ART daily pill burden, NRTI backbone, and third drug composition to account for changes in ART regimens and their complexity. Second, patients who initiated ART at different time periods may have differed in unmeasured characteristics, such as HIV transmission categories. Among US men newly diagnosed with HIV, the proportion of drug users slightly declined over time [14]. This would confound our findings if adherence differed between drug users and nondrug users, but data from a meta-analysis shows that the level of adherence among drug users is similar to nondrug users [47]. Third, our study may not be generalizable to the Medicare-insured, commercially insured, those in Medicaid managed-care organizations, and uninsured HIV patients in the United States. Fourth, we could not follow patients after disenrollment from Medicaid. For those who lost Medicaid coverage, many patients likely continued to use ART in a similar pattern supported by Ryan White CARE Act funds. Fifth, the removal of substance abuse claims in Medicaid data by the Centers for Medicare & Medicaid Services may have eliminated some of the encounters of HIV patients [48]. However, the rates of substance abuse claim redaction were similar from 2001 to 2010 (private communication from the CMS Research Data Assistance Center, 14 November 2014), and it is unlikely that these nondifferential redactions may have affected our trend estimates using pharmacy claims. Sixth, some of the patients with control medications may have discontinued for clinically appropriate reasons such as side effects or improved blood pressure control. Even still it is unlikely that the rates of these clinical decisions have changed over time to affect our trend estimates. Seventh, the follow-up time is necessarily shorter for the 2007–2010 cohort compared with the 2001–2003 cohort in all medication groups. Since we applied the same censoring rules for all patients in our study, it is unlikely that informative censoring would selectively explain our improvement findings in the ART group. Finally, the presence of a medication claim is not equivalent to medication consumption.

In conclusion, whereas persistence with ART is improving, rates of nonpersistence with all of the highly effective chronic medications that we examined are still quite substantial, drawing attention to the need to improve this aspect of care quality. Our data suggest, but do not prove, that the ART-focused adherence support programs may have had a population-level impact, both in HIV and non-HIV medication taking. Given that the most recent Cochrane review of adherence interventions concluded that ‘even the most effective interventions did not lead to large improvements,’ further exploration of this possibility is urgently needed [49]. In addition, newer ART regimens requiring fewer pills were associated with improved ART persistence. Finally, in this Medicaid population there are substantial sex, racial, and geographic disparities in persistence. These disparities are substantial in size, did not improve over time in our data and were consistent across all of the medications examined, strengthening the case that disparities in medication adherence are an important driver of disparities in the health outcomes of persons with chronic conditions [50–53].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Time to treatment nonpersistence by treatment initiation year for HIV patients with (a) antiretroviral therapy and HIV-negative patients with (b) angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (c) statins and (d) metformin. *All log-rank tests $P < 0.001$. ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blockers.

Figure 2.

Adjusted hazards of treatment nonpersistence among those who initiated treatment between 2007 and 2010 compared with those who initiated treatment between 2001 and 2003. ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blockers; ART, antiretroviral therapy.

Table 1

Baseline characteristics of HIV patients who initiated antiretroviral therapy by treatment initiation year.

	All years	2001–2003	2004–2006	2007–2010
Total population, <i>n</i>	43 598	18334	13 301	11963
Age (year) (%)				
<25	8.4	8.0	8.5	9.1
25–34	17.2	18.2	16.7	16.2
35–44	36.7	41.1	36.7	29.9
45–54	29.0	26.4	29.4	32.7
55+	8.7	6.3	8.8	12.1
Sex (% male) *	56.3	54.5	56.5	58.9
Race/ethnicity (%)				
Black	55.4	53.9	55.3	57.8
White	18.8	18.3	19.5	18.7
Hispanic	18.0	19.5	17.9	15.9
Asian/Pacific Islander/Native American	1.1	1.1	1.0	1.2
Multiracial/unknown	6.7	7.3	6.3	6.4
State (%)				
New York	34.1	41.6	31.1	25.8
California	14.8	13.0	15.1	17.3
Florida	11.3	11.7	11.3	10.8
Illinois	6.8	5.9	6.8	8.1
North Carolina	6.1	4.3	6.9	7.9
Georgia	5.3	4.7	5.1	6.4
Massachusetts	4.7	4.2	5.1	5.1
Texas	4.4	3.8	4.7	4.7
Louisiana	4.1	3.0	3.9	6.1
New Jersey	3.8	3.9	4.3	3.3
Ohio	1.8	1.7	2.7	1.0
Maryland	1.5	1.1	2.0	1.8
Pennsylvania	0.7	0.5	0.5	1.2
Virginia	0.7	0.7	0.7	0.6
NRTI backbone (%)				
TDF/ABC	41.3	10.4	47.4	81.9
ZDV	39.7	56.1	39.8	14.5
DDI/D4T	17.4	31.9	11.4	2.1
Others	1.6	1.7	1.5	1.5
Regimen type (%)				
PI based	47.9	43.0	53.4	49.4
NNRTI based	37.8	35.1	37.3	42.7
Triple NRTI	9.5	17.3	5.3	2.0
Integrase inhibitor based	0.6	0.0	0.0	2.2

	All years	2001–2003	2004–2006	2007–2010
Multiple classes	4.2	4.6	4.1	3.8
ART pill burden (%) [*]				
1	10.2	0	2.7	34.3
2–3	30.0	24.6	36.1	31.3
4–5	24.4	22.9	29.7	20.7
6+	35.5	52.5	31.5	13.7

ABC, abacavir; ART, antiretroviral therapy; D4T, stavudine; DDI, didanosine; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; TDF, tenofovir; ZDV, zidovudine. All *P* values from chi-square tests were <0.001. Percentage may not sum to 100 because of rounding.

^{*} Missing values accounted for 0.29% of sex and 0.10% of pill burden.

Table 2

Baseline characteristics of HIV-negative patients who initiated angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, statins, and metformin.

	ACEI/ARB	Statins	Metformin
Total population, <i>n</i>	674 105	621 398	326 877
Calendar year of treatment initiation (%)			
2001–2003	32.1	30.0	30.2
2004–2006	33.4	35.4	33.3
2007–2010	34.6	34.7	36.6
Age (year) (%)			
<25	5.7	2.7	9.4
25–34	9.5	7.0	10.3
35–44	19.8	18.8	19.1
45–54	31.3	33.4	29.1
55+	33.8	38.2	32.2
Sex (% male)*	39.3	37.6	33.4
Race/ethnicity (%)			
Black	31.1	23.2	26.4
White	40.8	46.0	39.6
Hispanic	16.4	17.4	22.0
Asian/Pacific Islander/Native American	4.1	5.1	4.5
Multiracial/unknown	7.6	8.3	7.5
State (%)			
New York	12.1	13.4	12.8
California	21.4	22.2	22.8
Florida	7.0	7.5	6.4
Illinois	12.2	11.8	12.0
North Carolina	9.0	8.0	8.3
Georgia	6.2	5.3	5.4
Massachusetts	4.8	5.9	4.9
Texas	8.6	7.4	9.1
Louisiana	6.1	4.8	5.1
New Jersey	1.8	1.8	1.8
Ohio	6.4	7.0	6.5
Maryland	0.5	0.4	0.6
Pennsylvania	2.4	2.9	2.7
Virginia	1.6	1.6	1.7
Index regimen type (%)			
ACEI	75.2	–	–
ARB	24.4	–	–
ACEI + ARB	0.4	–	–

ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blockers. All *P* values from chi-square tests were <0.001. Percentage may not sum to 100 because of rounding.

* Missing values in sex accounted for 0.17% of ACEI/ARB, 0.13% of statins and 0.17% of metformin initiators.

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Multivariable predictors of the hazards of treatment nonpersistence in HIV patients with antiretroviral therapy and HIV-negative patients with control medications.

Table 3

	ART			ACEI/ARB			Statins			Metformin		
	HR	99%	CI	HR	99%	CI	HR	99%	CI	HR	99%	CI
Year of initiation (ref = 2001–2003)												
2004–2006	1.00	0.95	1.05	1.01	1.00	1.02	0.96	0.95	0.97	0.99	0.98	1.01
2007–2010	0.89	0.83	0.96	1.07	1.06	1.09	0.94	0.92	0.95	1.02	1.01	1.04
Age, years (ref = 55+)												
<25	1.80	1.63	2.00	1.84	1.81	1.88	1.77	1.73	1.82	2.30	2.25	2.35
25–34	1.74	1.59	1.91	1.64	1.61	1.67	1.58	1.55	1.61	1.86	1.82	1.90
35–44	1.42	1.30	1.54	1.34	1.32	1.36	1.38	1.36	1.39	1.35	1.33	1.38
45–54	1.22	1.12	1.33	1.13	1.12	1.14	1.15	1.14	1.17	1.13	1.11	1.15
Sex (ref = female)												
Male	0.90	0.86	0.94	0.96	0.95	0.97	0.90	0.89	0.91	0.91	0.90	0.92
Race/ethnicity (ref = white)												
Black	1.28	1.21	1.35	1.27	1.25	1.28	1.27	1.25	1.29	1.22	1.20	1.24
Hispanic	1.09	1.02	1.17	1.21	1.19	1.23	1.43	1.41	1.45	1.21	1.19	1.24
Asian/Pacific Islander /Native American	1.01	0.81	1.25	1.03	1.00	1.06	1.17	1.14	1.20	0.96	0.92	0.99
Multiracial/unknown	1.02	0.93	1.12	1.06	1.03	1.08	1.11	1.09	1.13	1.04	1.01	1.07
State (ref = New York)												
California	0.82	0.77	0.88	0.99	0.97	1.00	1.00	0.98	1.01	1.04	1.02	1.07
Florida	0.95	0.88	1.02	0.93	0.91	0.95	1.08	1.06	1.11	1.01	0.98	1.04
Illinois	0.94	0.87	1.02	0.99	0.97	1.01	1.01	0.99	1.03	1.19	1.16	1.22
North Carolina	0.91	0.83	0.99	0.91	0.89	0.93	0.88	0.86	0.90	0.96	0.93	0.99
Georgia	1.03	0.94	1.12	0.95	0.92	0.97	0.98	0.95	1.00	1.02	0.98	1.05
Massachusetts	1.02	0.93	1.13	0.99	0.96	1.01	0.97	0.95	1.00	1.01	0.98	1.05
Texas	1.20	1.08	1.33	1.02	1.00	1.04	0.99	0.97	1.01	1.10	1.06	1.13
Louisiana	1.22	1.11	1.34	1.03	1.01	1.06	1.04	1.02	1.07	1.13	1.09	1.17
New Jersey	0.69	0.61	0.78	0.83	0.79	0.87	0.87	0.83	0.91	0.90	0.85	0.96
Ohio	0.82	0.69	0.97	0.82	0.80	0.84	0.77	0.75	0.79	0.89	0.86	0.92

	ART			ACEI/ARB			Statins			Metformin		
	HR	99%	CI	HR	99%	CI	HR	99%	CI	HR	99%	CI
Maryland	0.68	0.53	0.86	0.88	0.81	0.97	0.85	0.77	0.94	0.99	0.89	1.10
Pennsylvania	0.76	0.56	1.02	0.83	0.80	0.86	0.82	0.79	0.84	0.90	0.86	0.95
Virginia	0.75	0.55	1.02	0.83	0.79	0.86	0.82	0.79	0.86	0.89	0.84	0.95
NRTI backbone (ref = TDF/ABC)												
ZDV	1.32	1.24	1.40	-	-	-	-	-	-	-	-	-
DDI/D4T	1.09	1.01	1.17	-	-	-	-	-	-	-	-	-
Others	0.92	0.77	1.09	-	-	-	-	-	-	-	-	-
Regimen type (ref = PI based)												
NNRTI based	1.01	0.95	1.08	-	-	-	-	-	-	-	-	-
Triple NRTI	1.38	1.26	1.50	-	-	-	-	-	-	-	-	-
Integrase inhibitor based	0.81	0.50	1.31	-	-	-	-	-	-	-	-	-
Multiple classes	1.29	1.17	1.42	-	-	-	-	-	-	-	-	-
ART pill burden (ref = 6+)												
1	0.71	0.62	0.82	-	-	-	-	-	-	-	-	-
2-3	0.77	0.71	0.83	-	-	-	-	-	-	-	-	-
4-5	0.89	0.84	0.95	-	-	-	-	-	-	-	-	-
ACEI/ARB (ref = ACEI)												
ARB	-	-	-	0.92	0.91	0.93	-	-	-	-	-	-
ACEI and ARB	-	-	-	0.79	0.73	0.87	-	-	-	-	-	-

ABC, abacavir; ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blockers; ART, antiretroviral therapy; CI, confidence interval; D4T, stavudine; DDI, didanosine; HR, hazard ratio; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; ref, reference category; TDF, tenofovir; ZDV, zidovudine.