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Sociodemographic Factors Predict Early Discontinuation of HIV Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

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Abstract

Background/Objective—HIV infection has a devastating impact on individual and public health, and affects populations disproportionately. Treatment with antiretroviral therapy (ART) saves lives, but long-term adherence to ART is critical to its success. We performed an observational cohort study to determine the influence of race, sex and other sociodemographic factors on early ART discontinuations among HIV-infected persons.

Methods—TennCare-enrolled adults of black or white non-Hispanic race beginning ART with either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI) between 1996–2003 (N=3,654) were assessed for early discontinuation. A subgroup of discontinuations was validated using the primary medical record.

Results—Blacks were more likely than whites to discontinue NNRTIs (37 vs. 28%; P=0.003) and PIs (36 vs. 25%; P≤0.001). In multivariable models adjusting for race, sex, age, early HIV-related medical encounter, urban residence and TennCare enrollment category, black race, female sex and younger age were independent predictors of discontinuation among those starting PIs. Among persons starting NNRTIs, black race, younger age and a disability-based enrollment category predicted early drug discontinuation, but female sex did not.

Conclusions—Our results suggest that sociodemographic factors were associated with early NNRTI and PI discontinuation in this population, and some factors were ART class specific.

Keywords

HIV/AIDS; treatment; health insurance

INTRODUCTION

Improvements in human immunodeficiency virus (HIV) therapy have led to decreases in HIV morbidity and mortality.[1,2] Current treatment guidelines recommend that initial

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antiretroviral therapy (ART) for HIV infection include 2 nucleoside reverse transcriptase inhibitors (NRTIs) in combination with either a protease inhibitor (PI) or non-NRTI (NNRTI).[3,4] Successful long-term treatment of HIV requires meticulous adherence to ART drugs, but ART (and thus, successful treatment of HIV) can be limited by early adverse effects. For example, PIs can cause gastrointestinal symptoms such as nausea, vomiting and diarrhea early after treatment initiation, and NNRTIs are associated with rash and drug-induced hepatitis, which can also occur early in therapy.[5] The NNRTI efavirenz causes central nervous system symptoms, including insomnia, somnolence and intense dreams that are greatest early after initiation of therapy.[6] These and other early adverse effects can affect adherence, long-term tolerability, and ultimately, success of treatment.[7,8] Cohort studies have reported discontinuation rates of first ART regimens of 30–60% within the first year, with the majority of discontinuations due to toxicity.[8–10] Studies have also suggested that women have higher rates of adverse drug events[11,12] and drug discontinuation[9,13,14] than males.

Importantly, genetic differences may also influence the incidence and/or severity of side effects of ART and, thus, contribute to the observed variations in toxicity and discontinuation by race.[15] An example is a polymorphism in the hepatic cytochrome P450 2B6 enzyme (CYP2B6), the primary metabolic pathway of efavirenz. Increased plasma levels of efavirenz and central nervous system side effects have been reported shortly after treatment initiation in persons with a CYP2B6 polymorphism that is more common in African Americans than Caucasians.[16–19] Increased drug levels are associated with an increased risk of adverse effects,[6,20] which may contribute to poor adherence and drug discontinuation. Nevirapine is an NNRTI metabolized by both CYP2B6 and CYP3A4,[21] and increased plasma levels have been associated with a CYP2B6 polymorphism.[18] Data also suggest that variation in the multidrug resistance gene-1 (*MDR1* or *ABCB1*) is associated with an increased risk of nevirapine-associated hepatotoxicity.[22,23]

Population-based studies could be useful for developing strategies to predict drug toxicity, monitor adverse events and optimize treatment regimens in HIV-infected populations. Our hypothesis was that demographic factors that reflect the populations with the greatest recent increases in HIV infection rates and disparities in HIV outcomes (e.g., black race and female sex) would also be risk factors for early discontinuation of ART drugs. The objective of this study was to use data from a demographically diverse, statewide population to determine the influence of race, sex and other sociodemographic factors on discontinuation of NNRTI or PI early after treatment initiation, which could be an important surrogate for longer-term treatment success.

METHODS

TennCare Cohort Identification

This was an observational cohort study of persons in TennCare who initiated ART with an NNRTI or PI between January 1996 and June 2003. TennCare is Tennessee's managed care program for Medicaid enrollees and uninsured individuals. During the study period, all persons in Tennessee diagnosed with HIV infection were eligible for TennCare regardless of disease status. Data files, including enrollment, encounter and pharmacy information, were used to identify self-reported non-Hispanic white or black persons who initiated their first NNRTI or PI during the study period. Eligible persons were also required to have available data on urban or nonurban residence according to Standard Metropolitan Statistical Area (SMSA) and TennCare enrollment category (disability, aid to families of dependent children, uninsurable, qualified Medicare beneficiary or aged). The TennCare pharmacy file contains extensive data on outpatient prescriptions, including drug dose and days' supply dispensed.

Enrollment and Study Definitions

A schema of the overall study cohort is shown in Figure 1. Persons eligible for the cohort had to be enrolled in TennCare for ≥90 days prior to the entry date, have no other ART prescriptions during this 90-day period, have ≥1 additional medication refill and/or 1 HIV-related medical encounter claim during the 90-day period after the entry date, and have maintained continuous TennCare enrollment or died during the 270-day study period after entry. Other study definitions are listed below and also shown in Figure 1.

Entry date—Date of the first NNRTI or PI prescription was considered the date of cohort entry.

Qualifying drug—The study-qualifying drug was the NNRTI or PI prescribed at entry date. Persons prescribed a PI and NNRTI concomitantly, and those initiating the NNRTI delavirdine were excluded.

Early discontinuation—Early discontinuation was defined as a lapse in filled prescription days for the qualifying drug that exceeded the last dispensed prescription amount within 180 days after entry date, with no additional filled prescriptions for that drug during the remainder of the 270-day study period.

Validation Subgroup Identification

To validate the accuracy of the TennCare data files regarding drug exposure and discontinuation, a subgroup of persons from the cohort who received care at the Comprehensive Care Center (CCC) in Nashville, TN, were identified for detailed medical record review (Figure 2). The CCC is the largest HIV care provider in the middle Tennessee region and 1 of 8 designated AIDS Centers of Excellence in Tennessee. Persons included in this group had to have ≥1 TennCare medical claim from a CCC provider during their 270-day study period. Records for the subgroup of persons identified as early discontinuers underwent a standardized review by one of the authors (SA) to ascertain correct PI and NNRTI exposure and discontinuations, define the reason(s) for discontinuation, and to characterize any disagreement between the medical records and TennCare data files. Any uncertainty regarding these categories was resolved by consensus decision of a group of coauthors (TH, SPR, TRS). The State of Tennessee and Vanderbilt institutional review boards, and the Bureau of TennCare approved these studies.

Statistical Analyses

Demographic data and treatment and discontinuation categories are presented as proportions. Univariate comparisons were made using Fisher's exact, chi-squared or Wilcoxon rank-sum tests. In order to better examine early PI and NNRTI discontinuation among persons most likely to have good adherence to treatment and follow-up, a predetermined subgroup analysis included only persons meeting eligibility criteria who also had ≥1 outpatient medical claim that included an HIV-related diagnosis within 90 days of study entry. Multivariable logistic regression models were used to adjust for race, sex, age, TennCare enrollment category (disabled versus other), early medical encounters, qualifying drug (PI versus NNRTI) and residence (urban versus nonurban). Because reasons for discontinuing different ART classes may differ, separate models limited to persons initiating a PI or NNRTI were used as well. Analyses were performed using Stata SE (Stata Corp., College Station, TX).

RESULTS

Overall TennCare Cohort Results

There were 3,654 HIV-infected TennCare enrollees who met eligibility criteria (Table 1). The median age of enrollees at entry date was 36 years, 1,070 (29%) were female and 1,948 (53%) were black. Most persons (75%) were prescribed a PI as part of their initial regimen. Cohort characteristics and differences in sociodemographic factors according to race and sex are also shown in Table 1.

Thirty-two percent of the cohort met criteria for early discontinuation. There was no overall difference in early discontinuations by drug class (33% of NNRTI group versus 31% of PI group; P=0.22), but blacks were more likely than whites to discontinue NNRTIs (37 vs. 28%; P=0.003) and PIs (36 vs. 25%; P<0.001), and females were more likely than males to discontinue NNRTIs (38% vs. 31%; P=0.03) and PIs (41 vs. 27%; P<0.001). These differences persisted when the analysis was limited to persons with an HIV-related outpatient medical claim (n=2,896; 79% of total; data not shown).

Results of a multivariable logistic regression model, including sociodemographic variables, presence of an early medical encounter (yes versus no) and qualifying drug class (PI versus NNRTI), are shown in Table 2. In the entire cohort, both black race (OR=1.54; 95% CI: 1.32–1.79; P<0.001) and female sex (1.45; 1.23–1.70; P<0.001) were independent predictors of early discontinuation. In addition, younger age (0.98; 0.97–0.99) per year increase; P<0.001) and having enrolled in TennCare due to disability (1.26; 1.08–1.46; P=0.003) were associated with early discontinuation in this model, but qualifying drug class was not (0.94; 0.80–1.11; P=0.45). In a separate model that was limited to persons initiating PI-based ART (n=2,757), black race (1.55; 1.30–1.85; P<0.001), female sex (1.54; 1.28–1.86; P<0.001) and younger age (0.98; 0.97–0.99; P<0.001) remained predictors of early discontinuation, but TennCare enrollment category (1.14; 0.96–1.35; P=0.14) was no longer statistically associated with early discontinuation. Among persons initiating NNRTI-based ART (n=897), black race (1.46; 1.08–1.99; P=0.015), younger age (0.97; 0.95–0.98; P<0.001) and disability as a TennCare enrollment category (1.73; 1.28–2.34; P<0.001) were associated with early discontinuation, but sex was not (1.20; 0.87–1.64; P=0.26).

Validation Subgroup Analysis

Of the 741 persons in the subgroup who received care at the CCC during the study period, 183 (25%) met the definition for discontinuation using the TennCare data files and went on to have medical record review for validation (Table 3). One-hundred-forty-seven (80%) of these persons entered the study with a PI prescription, and the remaining 36 (20%) initiated an NNRTI. The qualifying drug identified in TennCare data files agreed with the medical record 96% of the time. One-hundred-forty-four persons [79% (95% CI: 72–84%)] were found to have discontinued their PI or NNRTI at a time that agreed with the TennCare data files. Of these, 118 [82% (95% CI: 75–88%); 64% (57–71%) of total] also had entry date agreement. Of note, when only cases that were able to be validated with the medical record are included, the rate of complete agreement between TennCare and the medical record was >80%. Reasons for ART discontinuations, and—where applicable—reasons for disagreement between data sources, are shown in Table 4.

DISCUSSION

In this study, TennCare data files were used to identify a large, demographically diverse cohort of HIV-infected individuals who initiated ART containing a PI or NNRTI. Approximately one-third of this cohort discontinued therapy within 180 days of initiation.

Blacks were more likely than whites to discontinue drugs from either class. Females were more likely than males to discontinue PIs early, but not NNRTIs.

Our findings are consistent with previous studies reporting racial differences in efavirenz adherence and efficacy. A study from the Johns Hopkins HIV Cohort found that African Americans were more likely to discontinue efavirenz at 1 year than non-Hispanic whites.[24] Similarly, a study of more than 400 U.S. military health care beneficiaries found significantly shorter time to failure among African Americans receiving efavirenz compared to Caucasians.[25] In contrast, data from a multinational trial found no significant differences in time to treatment failure between blacks and Caucasians on an efavirenz-based regimen.[26] A randomized, controlled trial of dual- or triple-NRTI therapy in combination with efavirenz in treatment-naïve subjects, AIDS Clinical Trials Group Study A5095, did not find a difference in outcomes between efavirenz-based treatment arms but did identify an increased risk of virologic failure and grade-3 or -4 adverse events among blacks compared to whites.[27] Additional analyses of this clinical trial population have found a greater effect of nonadherence on risk of virologic failure in blacks on efavirenz-based regimens compared to whites.[28] These results merit further study.

The relationship between sex and early discontinuation was studied in drug-class-specific multivariable models and was only seen with PI use, a finding consistent with prior reports of increased adverse drug events and toxicities in females.[11,12] This phenomenon may be due to sex differences in plasma concentration of some PIs.[29–31] A single small study reported higher nevirapine plasma concentrations in HIV-infected women versus men,[32] but a correlation between plasma nevirapine levels and hepatotoxicity has not been established.[33,34] Together with the results of our study, this finding would suggest that drug-class-specific factors that are not directly related to adherence, toxicity or access to care can influence early discontinuations. Interestingly, females in our study were not significantly more likely than males to discontinue NNRTIs when controlling for race and other sociodemographic factors. The sex difference seen in the PI model could be due in part to pharmacodynamic factors (body weight and composition, effects of sex hormones, etc.), the effects of which on more subtle clinical toxicities such as gastrointestinal adverse effects have not yet been well characterized.

The findings that disability enrollment status and younger age predicted a higher likelihood of early discontinuation are intriguing. Disability status may reflect more advanced HIV disease, less capacity to tolerate mild-to-moderate adverse effects (e.g., nausea, diarrhea) or an increased risk for more severe adverse effects during the early stages of ART. One might predict that older age would be associated with increased risk of drug toxicity and discontinuation due to decreases in drug metabolism with aging. We found the opposite association; one that was also reported in another cohort study of treatment discontinuation.[35] This could reflect other unknown and/or unmeasured sociodemographic or clinical factors that contributed to early drug discontinuation. We cannot exclude the possibility that older age was associated with better adherence to drugs despite subtle early side effects that may have caused younger patients to discontinue their therapy.

Although pharmacy databases are considered relatively accurate[36,37] and compare favorably to self-report,[38] they cannot fully account for medication adherence. We were unable to include additional measures of adherence. We were also unable to control for other factors known to influence ART discontinuation (such as substance abuse/injection drug use and hepatitis C coinfection),[39] or measures of HIV disease status and treatment efficacy (such as immunologic status, AIDS-defining illnesses or HIV suppression), nor did we characterize the role of specific ART combinations beyond the PI/ NNRTI used. Our data cannot yield information on why individual persons discontinued their therapy. This study was restricted

to the highly active ART era (post-1996), but temporal changes in therapy have also impacted drug tolerability. Due to programmatic changes in TennCare that affected enrollment status of many HIV-infected persons in July 2003, we ended our study period at that time. As a result, the majority of PI use in this study was early-generation therapy (e.g., nelfinavir and indinavir) that did not include pharmacologic boosting with low-dose ritonavir. These regimens tended to have greater pill burdens than newer PIs (e.g., atazanavir, lopinavir/ ritonavir), which may have influenced early drug discontinuations to an extent that our data could not determine. Nonetheless, the fundamental relationships between sociodemographic factors and early discontinuation would not be expected to vary substantially between early- or later-generation therapies. Use of NNRTIs in this population was less frequent than PIs throughout the study period, limiting our ability to compare discontinuations in smaller subpopulations (e.g., black versus white females initiating efavirenz) and decreasing the sample size in drug-class-specific multivariable models.

The TennCare administrative data files have been used to answer important pharmacoepidemiologic questions for several years,[40–42] but until recently no studies assessing ART utilization had been published.[43] Our results are strengthened by the fact that TennCare enrollees made up a substantial proportion of HIV-infected persons in Tennessee during the study period, with >45% of HIV-infected persons in Tennessee enrolled in TennCare programs for ≥1 day.[44,45] We performed a limited validation of drug exposure and discontinuation through a detailed medical record review of a subgroup of the TennCare cohort. Where records were complete, the accuracy of the TennCare data files was good.

Acknowledging the limitations of this study, we conclude that black TennCare enrollees were more likely than whites to discontinue their first NNRTI or PI within 180 days of starting therapy, and females were more likely than males to discontinue their first PI—after adjustment for other potentially important sociodemographic factors. Although our results cannot be used to determine the specific reasons for these differences, careful analysis of TennCare and other administrative databases could potentially be used to monitor drug discontinuation at the population level and could enhance our understanding of disparities in responses to treatment of HIV infection.

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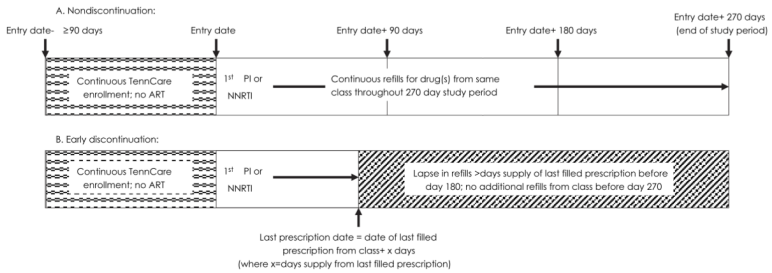

Figure 1. Schematic representation of study definitions for qualifying drug initiation and discontinuation using the TennCare pharmacy data file

To qualify for the overall study cohort, an individual was required to have been non-Hispanic white or black and have ≥1 additional prescription medication refill (of any type) and/or 1 HIV-related medical encounter during the first 90 days after entry. Entry date could have been from January 1, 1996 to June 30, 2003. Schema A represents a nondiscontinuer; Schema B represents an individual defined as an early discontinuer, including the subgroup included in the validation analysis.

ART: Antiretroviral therapy; PI: Protease inhibitor; NNRTI: Non-nucleoside reverse transcriptase inhibitor

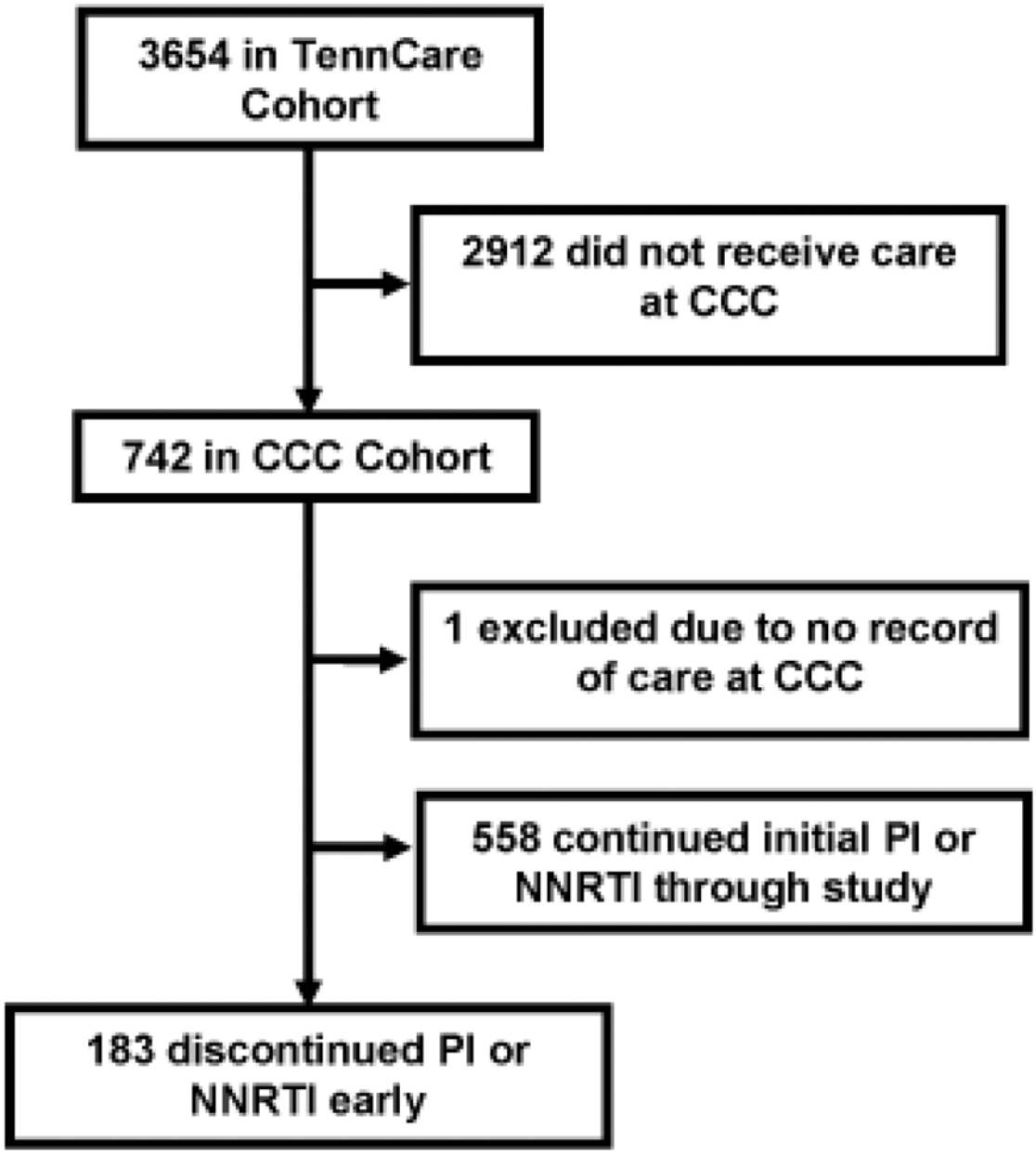

Figure 2. Flow diagram of disposition of individuals included in the overall TennCare cohort and validation analyses

CCC: Comprehensive care center; PI: Protease inhibitor; NNRTI: Non-nucleoside reverse transcriptase inhibitor

Table 1

Characteristics of TennCare Study cohort, total and by race and sex

	Total Cohort	Black, Non-Hispanic	White, Non-Hispanic		Female	Male	
	N=3,654	N=1,948	N=1,706	P value[b]	N=1,070	N=2,584	P value[b]
Age at Entry Date in Years, Median (Range)	36 (18–98)	36 (18–87)	36 (18–98)	0.01	33 (18–87)	37 (18–98)	<0.001
Female Sex	1,070 (29)	776 (40)	294 (17)	<0.001	–	–	
Race							
Non-Hispanic, black	1,948 (53)	–	–		776 (73)	1,172 (45)	<0.001
Non-Hispanic, white	1,706 (46)	–	–		294 (27)	1,412 (55)	
Urban Residence[a]	3,178 (87)	1835 (94)	1343 (79)	<0.001	944 (88)	2,234 (87)	0.16
Enrollment Category				<0.001			<0.001
Disabled	1,976 (54)	1,007 (52)	969 (57)		416 (39)	1,560 (60)	
Uninsured	1,280 (35)	637 (33)	643 (38)		333 (31)	947 (37)	
Aid to families of dependent children	355 (10)	284 (15)	71 (4)		317 (30)	38 (1)	
Qualified Medicare beneficiary	37 (1)	14 (<1)	23 (1)		2 (<1)	35 (1)	
Aged	6 (<1)	6 (<1)	–		2 (<1)	4 (<1)	
Cohort qualifying Medication							
Protease inhibitor	2,757 (75)	1,427 (73)	1,330 (78)	0.001	753 (70)	2,004 (78)	<0.001
Nelfinavir	1,293 (47)	800 (56)	493 (37)		430 (57)	863 (43)	
Indinavir	1,105 (40)	482 (34)	623 (47)		245 (33)	860 (43)	
Saquinavir	155 (6)	53 (4)	102 (8)		32 (4)	123 (6)	
Lopinavir/ritonavir	142 (5)	69 (5)	73 (5)		36 (5)	106 (5)	
Ritonavir	39 (<1)	12 (<1)	27 (2)		7 (<1)	32 (2)	
Amprenavir	23 (<1)	11 (<1)	12 (<1)		3 (<1)	20 (1)	
Non-nucleoside reverse transcriptase inhibitor	897 (25)	521 (27)	376 (22)		317 (30)	580 (22)	
Efavirenz	407 (45)	245 (47)	162 (43)		126 (40)	281 (48)	
Nevirapine	490 (55)	276 (53)	214 (57)		191 (60)	299 (52)	
Early HIV-Related Medical Encounters	2,896 (79)	1,469 (75)	1,427 (84)	<0.001	825 (77)	2,071 (80)	0.04
Early Drug Discontinuations	1,153 (32)	713 (37)	440 (26)	<0.001	425 (40)	728 (28)	<0.001

Data shown are n (%) except where noted otherwise.

[a]Urban residence defined as primary residence in a county classified as a standard metropolitan statistical area;

[b] P values for race and sex comparisons obtained from chi-squared, Fisher's exact, and Wilcoxon rank-sum tests, as appropriate

Table 2

Multivariable logistic regression model results for the total study cohort and by qualifying drug

	Total Cohort Model (n=3,654)	PI Model (n=2,757)	NNRTI Model (n=897)
Covariate	**OR (95% CI); P value**	**OR (95% CI); P value**	**OR (95% CI); P value**
Race (Black vs. White)	1.54 (1.32–1.79); <0.001	1.55 (1.30–1.85); <0.001	1.46 (1.08–1.99); 0.015
Sex (Female vs. Male)	1.45 (1.23–1.70); <0.001	1.54 (1.28–1.86); <0.001	1.20 (0.87–1.64); 0.26
Age (Per Year Increase)	0.98 (0.97–0.99); <0.001	0.98 (0.97–0.99); <0.001	0.97 (0.95–0.98); <0.001
TennCare Enrollment Criteria (Disabled vs. Other[a])	1.26 (1.08–1.46); 0.003	1.14 (0.96–1.35); 0.14	1.73 (1.28–2.34); <0.001
Early Medical Encounter[b] (Yes vs. No)	1.05 (0.88–1.25); 0.59	0.97 (0.79–1.19); 0.78	1.32 (0.94–1.86); 0.11
Qualifying Drug (PI vs. NNRTI)	0.94 (0.80–1.11); 0.45	–	–
Urban Residence[c] (Yes vs. No)	0.97 (0.78–1.22); 0.82	0.95 (0.73–1.23); 0.68	1.06 (0.70–1.60); 0.80

OR: Odds ratio; CI: Confidence interval; PI: Protease inhibitor; NNRTI: Non-nucleoside reverse transcriptase inhibitor;

[a]Other includes uninsured status, aid to families of dependent children, qualified Medicare beneficiary and aged;

[b]Defined as an outpatient visit with an HIV-related billing code within 90 days of qualifying drug prescription.

Table 3

Characteristics of the CCC cohort and validation subgroup

	CCC Cohort		
	Total	**Nondiscontinuers**	**Discontinuers (validation Group)**
Characteristic	**N=741**	**N=558**	**N=183**
Age at Entry in Years, Median (Range)	36 (18–72)	36 (19–72)	36 (18–56)
Female Sex	168 (23) *	109 (20)	59 (32)#
Race			
Black, non-Hispanic	277 (37) *	196 (35)	81 (44)#
White, non-Hispanic	464 (63)	362 (65)	102 (56)
Urban Residence[a]	662 (89)	496 (89)	166 (91)
Enrollment Category			
Disabled	384 (52)	293 (53)	91 (50)
Uninsured	305 (41)	232 (42)	73 (40)
Aid to families of dependent children	52 (7)	33 (6)	19 (10)
Aged	–	–	–
Cohort qualifying Medication			
Protease Inhibitor	592 (80) *	445 (80)	147 (80)
Nelfinavir	315 (53) **	214 (48)	101 (69)##
Indinavir	217 (37)	186 (42)	31 (21)
Saquinavir	11 (2)	9 (2)	2 (1)
Lopinavir/rito navir	33 (6)	23 (5)	10 (7)
Ritonavir	8 (1)	7 (2)	1 (1)
Amprenavir	8 (1)	6 (1)	2 (1)
Non-nucleoside reverse transcriptase inhibitor	149 (20) *	113 (20)	36 (20)
Efavirenz	58 (39)	51 (45)	7 (19)##
Nevirapine	91 (61)	62 (55)	29 (81)

Data shown are n (%) except where noted otherwise.

[a]Urban residence defined as primary residence in a county classified as a standard metropolitan statistical area;

*p<0.01 for comparison of TennCare cohort versu.total CCC cohort (Fisher's exact test);

**p<0.01 for comparison of nelfinavir versus all other protease inhibitors among the protease inhibitor qualifying drug group;

#p<0.01 for comparison of CCC discontinuers versus nondiscontinuers;

##p<0.01 for comparisons of nelfinavir versus all other protease inhibitors among protease inhibitor qualifying drug group, and nevirapine versus efavirenz among non-nucleoside reverse transcriptase inhibitor qualifying drug group.

Table 4

Results of limited validation medical record review (total n=183)

Validation Category	n (%)[a]
Reasons for Disagreement of qualifying Drug Discontinuation	
Unable to Validate	13 (7)
No qualifying drug documented	11 (6)
Medical record not available for review	1 (<1)
Person did not receive care at the CCC	1 (<1)
Lost to follow-up	11 (6)
Continued use of drug after last TennCare prescription date	7 (4)
Subtotal (n, % of total discontinuation group)	31 (17)
Reasons for Exclusion	
Concomitant use of PI/NNRTI	7 (4)
Race incorrectly recorded	1 (<1)
Subtotal	8 (4)
Reasons for Disagreement in qualifying Drug Initiation	
Initial ART not documented in medical record	12 (7)
AIDS drug assistance program	5 (3)
Living in another state	3 (2)
Clinical trial	3 (2)
Incarcerated	2 (1)
Private Insurance plan	1 (<1)
Subtotal	26 (14)
Reasons for Discontinuation among the Group with Agreement in Both qualifying Drug Initiation and Discontinuation, N (% of Group)	
Undocumented	40 (34)
Toxicity	34 (29)
Gastrointestinal intolerance	15 (44)
Unspecified	8 (24)
Rash	4 (12)
Central nervous system/psychiatric toxicity	4 (12)
Hepatitis	3 (9)
Nonadherence	29 (25)
Death[b]	11 (9)
Virologic failure[c]	4 (3)
Subotal	118 (65)

[a]Data are presented as mutually exclusive categories for the purposes of the table. Individuals with disagreement in both qualifying drug initiation/entry date and discontinuation are included in the latter category;

[b]No deaths were believed to be due to ART or a direct result of ART discontinuation;

[c]Virologic failure defined as an increase in plasma HIV-RNA to or above the pretreatment level on ≥1 measure prior to documented discontinuation; CCC: Comprehensive Care Center; ART: Antiretroviral therapy; PI: Protease inhibitor; NNRTI: Non-nucleoside reverse transcriptase inhibitor