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Rural Residence and Adoption of a Novel HIV Therapy in a National, Equal-Access Healthcare System

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Abstract

Rural persons with HIV face barriers to care that may influence adoption of advances in therapy. We performed a retrospective cohort study to determine rural–urban variation in adoption of raltegravir—the first HIV integrase inhibitor—in national Veterans Affairs (VA) healthcare. There were 1,222 veterans with clinical indication for raltegravir therapy at time of its FDA approval in October 2007, of whom 223 (19.1%) resided in rural areas. Urban persons were more likely than rural to initiate raltegravir within 180 days (17.3% vs. 11.2%, $P = 0.02$) and 360 days (27.5% vs. 19.7%, $P = 0.02$), but this gap narrowed slightly at 720 days (36.3% vs. 31.8%, $P = 0.19$). In multivariable analysis adjusting for patient characteristics, urban residence predicted raltegravir adoption within 180 days (odds ratio 1.72, 95% CI 1.09–2.70) and 360 days (OR 1.63, 95% CI 1.13–2.34), but not 720 days (OR 1.26, 95% CI 0.84–1.87). Efforts are needed to reduce geographic variation in adoption of advances in HIV therapy.

Abstract

Resumen Personas en zonas rurales con VIH enfrentan barreras medicas que pueden influir la adopción de avances de terapia. Realizamos un estudio de cohorte retrospectivo para determinar la variación en zonas rurales-urbanas y la adopción de raltegravir-el primer inhibidor de la integrasa del VIH-en hospitales nacionales de la Administración de Veteranos (VA). Había un total de 1,222 veteranos con indicación clínica para la terapia de raltegravir en el momento que fue aprobada por la FDA en Octubre del 2007, de los cuales 223 (19.1%) residían en zonas rurales. Personas en zonas urbanas eran más propensas que personas en zonas rurales en iniciar raltegravir dentro de 180 días (17.3% vs. 11.2%, $P = 0.02$) y 360 días (27.5% vs. 19.7%, $P = 0.02$), pero esta diferencia se redujo ligeramente a 720 días (36.3% vs. 31.8%, $P = 0.19$). Usando un análisis multivariable y ajustando las características del paciente, residencia urbana predijo la adopción de raltegravir dentro de 180 días (proporción de probabilidades 1.72, 95% de CI 1.09–2.70 y 360 días (proporción de probabilidades 1.63, 95% CI 1.13–2.34), pero no en 720 días (proporción de probabilidades 1.26, 95% CI 0.84–1.87). Mas esfuerzos son necesario para reducir la variación geograficos en los avances de terapia del VIH.

Keywords

HIV; Diffusion of innovation; Rural health

Introduction

Human immunodeficiency virus (HIV) therapy is arguably the most rapidly evolving field in medicine. In the mid 1990s, introduction of combination antiretroviral therapy (cART) improved survival and quality of life among persons with HIV who had access to care [1–3]. More recent advances—such as development of novel antiretroviral classes with activity against drug resistant virus—have further improved outcomes [4, 5].

The choice to adopt a newly approved HIV therapy is one of the most important decisions facing persons with HIV and their healthcare providers. Available evidence indicates that the choice to adopt a new HIV therapy is a shared decision made jointly by patients and healthcare providers, and that this decision is influenced by contextual characteristics of the care site and healthcare delivery system [6–9]. In the 1990's, studies in the United States found that early adoption of the first cART regimens was more common among whites, men, persons with private health insurance, and persons receiving care from experienced HIV providers working in clinics that specialize in HIV medicine [7, 9–11].

Rural persons with HIV face barriers to care at multiple levels. Person-level barriers include significant travel burdens when obtaining care, inadequate access to transportation, and risk for social isolation that may limit access to information about care options from peers living with HIV infection [12–15]. In addition, perception of greater stigma surrounding HIV infection may discourage rural persons with HIV from seeking healthcare [14]. Provider, care site, and healthcare system-level barriers include limited availability of providers and clinics with experience in HIV medicine and poor local access to critical health services, such as mental health and substance use treatment [12, 14, 15]. It is reasonable to hypothesize that these barriers to care may impact rural persons' adoption of important advances in HIV therapy, and that the rate of adoption of technological advances in HIV therapy may represent an important axis of rural–urban variation in HIV care. However, little is known about rural–urban variation in adoption of innovations in HIV therapy.

Several factors make the Veterans Affairs (VA) health system a useful setting for the study of rural–urban variation in adoption of advances in HIV therapy. First, VA is the largest provider of HIV care in the United States, with more than 20,000 veterans in care for HIV in over 120 facilities in 2008 [16]. Approximately 18–19% of veterans in care for HIV reside in rural areas according to the census-based definition used by VA (Author, unpublished data). Second, VA has a national, integrated electronic health record and maintains rich data on patient clinical status, demographics, and medication use. This allows national studies of rural–urban variation in adoption of advances in HIV therapy that would be difficult outside VA. Third, VA is an equal-access healthcare system with minimal co-pays for visits or medications [17]. This removes confounding influences of insurance status from studies of adoption of advances in HIV therapy.

With exception of access barriers related to health insurance, rural veterans with HIV are likely to experience similar obstacles to obtaining newly-approved HIV therapies as rural non-veterans with HIV, including travel burdens and limited access to experienced HIV providers. Many rural veterans must travel long distances to obtain VA care [18]. Although VA facilities in large cities often include large HIV specialty clinics, smaller facilities serving predominantly rural areas often do not have HIV specialty clinics with experienced HIV providers [16].

Adoption of raltegravir, an important advance in anti-retroviral therapy, is an informative case-study in diffusion of innovation in HIV therapy. On October 12, 2007 the Food and Drug Administration (FDA) approved raltegravir—the first HIV integrase inhibitor—for use in treatment-experienced persons with HIV. Raltegravir has improved outcomes for persons with HIV infection resistant to previously available therapies [5, 19].

Thus, raltegravir adoption in VA provides a useful case study to examine rural–urban variation in adoption of advances in HIV therapy. We performed a retrospective cohort study among veterans with an indication for raltegravir therapy at the time of FDA approval, and hypothesized that urban-dwelling veterans would initiate raltegravir more rapidly than those residing in rural areas.

Methods

Data Sources

We analyzed data from VA's national Clinical Case Registry (CCR) of veterans in care for HIV infection [20]. Data were available from 1996 through December, 2009. In brief, veterans in care for HIV are included in the CCR using a case-finding algorithm that searches electronic health record data to identify patients with HIV-related diagnostic codes or laboratory tests. A registry coordinator at each VA facility reviews these records to confirm HIV infection. For each veteran the CCR compiles electronic health record data including demographics, care encounters with associated ICD-9CM codes, laboratory values, and medication fills.

We merged CCR data with VA Planning Systems and Support Group (PSSG) data including a measure of patient urban versus rural residence (see below). We also determined residence using Rural Urban Commuting Area (RUCA) codes [21]. RUCA codes are measures of rurality that incorporate population density as well as commuting patterns. The VA vital status file provided mortality data.

Identification of Raltegravir Eligible Cohort

Raltegravir was initially approved for treatment-experienced persons with HIV infection resistant to the three major classes of antiretrovirals in use at that time—nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs). We identified a cohort of veterans with clinical indication for raltegravir therapy at time of FDA approval. Criteria included: (1) at least one outpatient visit within VA (infectious disease or primary care clinic visit) in the year before raltegravir approval (October 1, 2006–October 12, 2007); (2) prior receipt of NRTIs, NNRTIs, and PIs

in VA; (3) persistent use of antiretroviral therapy in year before approval (the presence of at least two antiretroviral agents in the patient's regimen at both the beginning and end of the interval, with more than 90 days of medication dispensed during the year), and (4) detectable HIV viremia on therapy (viral load >400 copies/ml) on last measurement before raltegravir approval. Patients who died before October 12, 2007 were excluded.

Dependent Variables

We created a series of dichotomous variables indicating raltegravir adoption within 180, 360, or 720 days of raltegravir approval on October 12, 2007. Adoption was defined as at least one raltegravir prescription fill, regardless of duration on therapy.

Independent Variables

We determined rural residence using two measures and compared results for consistency. The VA preferred rural measure uses census data and residential geocodes to categorize veterans as urban if residing in an urbanized area census tract, highly rural if in counties with fewer than seven residents per square mile, and rural in other areas [22]. We combined highly rural and rural persons to create a dichotomous urban–rural variable. We also applied RUCA codes linked to ZIP codes to categorize veterans as residing in urban or rural areas according to a standard algorithm [21].

Covariates included other patient characteristics that—based on published literature and clinical experience—were hypothesized to influence raltegravir adoption. Demographic variables were age, gender, and race/ethnicity categorized as (1) black, (2) white, non-Hispanic, (3) other, or (4) missing. Classification of race/ethnicity in VA administrative data is accurate for blacks and whites compared to self-report, but less accurate for other groups including Latinos, Native-Americans, and Asian-Americans [23]. We therefore combined these persons into a single “other” category for analysis.

Additional covariates included (1) the last available CD4 count and HIV viral load laboratory result in the year before raltegravir approval; (2) diagnosis of an AIDS defining illness in the year prior to approval; (3) alcohol or illicit substance use diagnosis in the year prior to approval; and (4) measures of antiretroviral experience and adherence prior to raltegravir approval. We used ICD-9CM codes to determine presence of an AIDS defining illness or substance use diagnosis (alcohol or illicit substance abuse or dependence) in the year prior to raltegravir approval using codes available on the Veterans Aging Cohort Study (VACS) website (www.vacohort.org). We required one inpatient or two outpatient codes for a diagnosis, as this improves accuracy of diagnoses compared to chart review [24]. This method for determining prevalent substance use diagnosis had sensitivity 79.2%, specificity 86.5%, and kappa 0.63 when compared to chart review in three VA clinics (unpublished data).

We also employed measures of antiretroviral experience and adherence prior to raltegravir approval. As detailed above, raltegravir eligibility was defined as prior exposure to the three previously-existing antiretroviral classes and persistent HIV viremia on therapy. In most cases, detectable HIV viremia while taking antiretroviral therapy results from either infection with drug-resistant virus or suboptimal antiretroviral adherence (a high frequency

of missed doses of antiretroviral medicines). Initiation of raltegravir made most sense for persons with detectable HIV viremia due to infection with drug-resistant HIV. Clinicians may have concluded that highly antiretroviral-experienced persons with detectable HIV viremia in the setting of suboptimal medication adherence may have benefitted more from interventions to improve consistency of antiretroviral use than from immediate initiation of a new agent such as raltegravir. This could bias associations between rural residence and raltegravir adoption if there were substantial differences in antiretroviral adherence at baseline among rural and urban veterans with detectable HIV viremia on therapy.

In order to control for possible differences between urban and rural patients in prior antiretroviral adherence, we used pharmacy data to estimate antiretroviral adherence during the year prior to raltegravir approval. Antiretroviral medication adherence during the year prior to raltegravir approval was estimated by MED-OUT, a validated index based on medication refill patterns [25]. This index uses the days supply dispensed and the time interval between individual refills to determine the proportion of days in which the patient was without medication. MED-OUT was first calculated separately for each antiretroviral drug, and then aggregated at the patient level as the time-weighted average across all drugs. For ease of interpretation, we express antiretroviral adherence as $(1 - \text{MED-OUT})$, which reflects the proportion of days with available medication.

To provide an additional measure of risk for drug resistant HIV infection due to extensive prior exposure to antiretroviral drugs, we also calculated the number of years each veteran had been receiving antiretroviral therapy in VA prior to raltegravir approval. Clinicians may have also used direct genotypic or phenotypic testing for HIV drug resistance in order to estimate a patient's need for raltegravir, but we did not have results for these tests for each patient.

Analyses

We first compared characteristics of urban and rural persons (by VA definition) in the raltegravir eligible cohort using χ^2 tests for categorical and rank sum tests for continuous measures. We generated Kaplan–Meier curves for raltegravir adoption among rural and urban persons with censoring at end of data availability on December 31, 2009 (day 811) or time of death among persons not initiating raltegravir. Censoring due to death was rare and occurred at identical rates for rural and urban persons (2% by day 180 and 5% at 720 days).

We determined the cumulative proportion of persons who had initiated raltegravir before pre-determined time points (day 180, 360, and 720 days) and compared adoption by urban versus rural residence as well as other independent variables. As censoring due to death was rare, we included all raltegravir eligible persons in the denominator when calculating proportions of persons initiating raltegravir, even if these persons died before starting raltegravir.

We next fitted multivariable logistic regression models to determine associations between urban residence and raltegravir adoption within 180, 360, and 720 days, adjusting for patient-level covariates. Models included an urban residence indicator, age, gender, race/ethnicity, CD4 count, HIV viral load, AIDS defining illnesses or substance use diagnosis in

year prior to raltegravir approval, and years prior antiretroviral exposure in VA categorized as <10 or ≥10 (the approximate median years prior antiretroviral use for both urban and rural veterans). Standard errors were adjusted for clustering of patients within care sites (VA facilities) using generalized estimating equations with an independent working correlation matrix, implemented within PROC GENMOD in SAS v. 9.2 (Cary, NC).

Model fitting involved multiple steps. Initial bivariable analyses evaluated for co-linearity between patient-level variables (correlation coefficient >0.5). Significant predictor variables in the multivariate model were determined by backwards elimination, using a P-value <0.05 for inclusion. We tested for significant interactions between urban–rural residence and other predictor variables. The final model also included non-significant predictors, as they were hypothesized a priori to predict adoption. We repeated these analyses with adjustment for antiretroviral adherence in the year prior to raltegravir approval and evaluated for meaningful change in the coefficient linking urban residence to raltegravir adoption (>10% change).

Finally, we tested for sensitivity of results to varying methods for identification of urban residence using RUCA codes. We also evaluated sensitivity of results to use of more or less stringent criteria for raltegravir eligibility. The less-stringent cohort included all persons in VA care for HIV at time of raltegravir approval regardless of antiretroviral treatment experience or laboratory values. More stringent definitions included three-class experienced persons with viral loads greater than 1,000 or 10,000 on therapy.

Results

We identified 21,570 persons (3,925 rural, 18.2%) receiving HIV care in 128 VA facilities in the year prior to raltegravir approval. Limitation to persons with prior three-class antiretroviral exposure in VA, persistent antiretroviral use in year prior to raltegravir approval, and a detectable viral load (>400 copies/ml) on therapy left 1,222 persons in 111 facilities in the raltegravir eligible cohort (233 rural, 19.1%).

Raltegravir eligible veterans had extensive prior antiretroviral treatment in VA (the median years of prior ART was 11 for both urban and rural veterans) and high rates of advanced immune deficiency, as reflected by high proportions with very low CD4 counts (Table 1). Nearly half of raltegravir eligible veterans had CD4 counts less than 50 (40.2% of urban vs. 46.8% of rural, $\chi^2 = 24.5$, $df = 5$, $P < 0.001$ for overall CD4 comparison). Rural persons were more likely than urban to be white (48.5% vs. 32.8%, $\chi^2 = 24.3$, $DF = 3$, $P < 0.001$ for overall race/ethnicity comparison) and less likely to have a substance use diagnosis (19.3% vs. 25.2%, $\chi^2 = 3.55$, $df = 1$, $P = 0.06$). Median antiretroviral adherence in the year prior to raltegravir approval was similar for rural and urban persons 0.74 vs. 0.73, Wilcoxon rank sum $Z = -1.39$, $P = 0.17$), indicating that the relative contribution of non-adherence to detectable viral load on therapy was similar in the two groups.

Raltegravir adoption curves indicated that urban veterans were more likely than rural to initiate raltegravir within 180 or 360 days of FDA approval, but that the absolute difference in adoption had slightly narrowed at 720 days (Fig. 1; Table 2). Cumulative adoption

frequencies for urban compared to rural persons were 17.3% versus 11.2% at 180 days ($\chi^2 = 5.24$, $df = 1$, $P = 0.02$), 27.5% vs. 19.7% at 360 days ($\chi^2 = 5.90$, $df = 1$, $P = 0.02$), and 36.6% vs. 31.8% at 720 days ($\chi^2 = 1.70$, $df = 1$, $P = 0.19$). In contrast to prior studies of antiretroviral adoption, black and white persons initiated raltegravir at similar frequencies at all time points. In general, early raltegravir adoption (within 180 days of approval) was more common with increasing age, CD4 count under 350, increasing viral load, absence of a substance use diagnosis, and greater than ten years antiretroviral experience in VA. Although there was an apparent tendency toward greater adoption among men than women, the small number of women initiating raltegravir in this VA cohort makes it difficult to interpret this finding.

In multivariate models adjusting for patient characteristics, urban persons were more likely than rural to initiate raltegravir within 180 days (odds ratio 1.72, 95% confidence interval 1.09–2.70) and 360 days (OR 1.63, 95% CI 1.13–2.34). Complete multivariate results are shown for early adoption, defined as within 180 days (Table 3). Results were similar at 360 days. This relative difference in adoption between urban and rural veterans had decreased by 720 days and was no longer statistically significant (OR 1.26, 95% CI 0.84–1.87). There were no significant interactions between urban residence and other independent variables.

Further adjustment for antiretroviral adherence in the year prior to raltegravir approval did not substantively change the association between urban residence and early adoption of raltegravir (OR 1.74, 95% CI 1.10–2.75). In addition, the association between substance use diagnoses and raltegravir adoption was not sensitive to antiretroviral adherence in the year prior to raltegravir approval.

Results were not sensitive to method of measuring rural residence or raltegravir eligibility. Using RUCA codes to measure residence, 154 (12.6%) resided in rural areas and the odds ratio for adoption within 180 days for urban compared to rural veterans was 1.90, 95% CI 1.08–3.44. Repeating analyses using the less and then more stringent criteria for raltegravir eligibility produced similar urban–rural odds ratios for early adoption, ranging from 1.70 to 1.80.

Discussion

Urban veterans were more likely than rural to be early adopters of raltegravir, although absolute differences in adoption had slightly narrowed by two years after raltegravir approval. The rate of adoption of newly-approved HIV therapies represents a potentially important axis of rural–urban variation in HIV care.

A central question is whether our findings generalize outside VA care. Does delayed adoption of raltegravir among rural veterans reflect the experience of the broader rural population of persons with HIV in the United States? VA healthcare differs from non-VA care in significant ways. Important differences include minimal insurance-related barriers to accessing healthcare, service to a mostly-male population of adult veterans, and reliance on a nationally-integrated delivery system. However, rural veterans are otherwise likely to face many of the same barriers to HIV care as rural non-veterans, including travel burdens and

limited access to experienced HIV providers and specialty clinics. Therefore, we believe that our finding of delayed adoption of raltegravir among rural veterans may reflect barriers to care that are common to the larger population of rural persons with HIV in the United States.

Other characteristics of VA care may actually decrease rural–urban variation in adoption of novel HIV therapies. For example, VA has centralized programs to deliver guidance to providers on use of new HIV therapies. When new antiretrovirals such as raltegravir become available, VA disseminates criteria for their use among providers and pharmacists providing care for veterans with HIV [26]. This may reduce rural–urban variation in adoption of new therapies in VA, in comparison to non-VA care.

A qualitative study of decision making regarding antiretroviral treatment found that the choice to start a new therapy was a joint decision shared by the patient and provider [6]. Patients were active participants in the decision and incorporated information from a variety of sources, including peers, family members, healthcare professionals, and the media. In addition to travel burdens that may prevent or postpone treatment discussions with providers, rural persons with HIV are at risk for social isolation and may have less access to information about new therapies from peers living with HIV [13]. Providers caring for rural persons with HIV are often less experienced in HIV medicine [27]. This may make them less likely to be aware of or recommend a new therapy [11, 27]. Moreover, rural persons with HIV have poor access to large, HIV specialty clinics, where adoption of advances in HIV therapy is more rapid [9]. Viewed in this multilevel context, slower adoption of newly-approved HIV therapies among rural compared to urban persons may result from person-level barriers to care, from differences in the medication prescribing behaviors of the healthcare providers serving rural areas, or from characteristics of the healthcare sites where encounters between providers and rural patients occur.

Alternatively, slower adoption of advances in HIV therapy among rural persons may be viewed in the context of the literature on diffusion of innovations. Rogers defined diffusion of innovation as “the process by which an innovation is communicated through certain channels over time among the members of a social system” [28]. The choice to adopt a new HIV therapy is shared between patient and provider; important channels for communication about innovations in HIV therapy may include interactions between persons with HIV and their peers in the community, between persons with HIV and their healthcare providers, and between providers and other healthcare professionals in the HIV care community. The patient, provider, and healthcare system level barriers facing rural persons with HIV may influence social networks and impede communication about therapeutic innovations through all of these channels. Rural persons with HIV may interact less frequently with peers and providers, and providers caring for small numbers of persons with HIV in clinics that serve rural settings may be less likely to interact with other healthcare professionals in the broader HIV care community.

Regardless of whether delayed adoption of raltegravir among rural persons resulted from patient, provider, or care site characteristics, the implications for rural patients were the same—delayed use of a potentially life-saving advance in therapy. Future studies should work to determine the specific patient, provider, and care site-level mechanisms contributing

to delayed adoption of novel HIV therapies among rural persons. This is necessary to target interventions to reduce rural disparities in adoption of advances in HIV therapy. Detailed understanding of these mechanisms will require rich data on characteristics of rural persons HIV and their healthcare providers, including their social networks and communication channels for learning about new therapies.

We found that differences in raltegravir adoption between rural and urban veterans narrowed somewhat by 720 days. This is a common finding in studies evaluating the diffusion of technological innovations: as innovations enter the mainstream, later-adopting groups eventually catch up with early-adopting groups [28]. Indeed, studies in the 1990s found that racial and socioeconomic disparities in early adoption of cART had evened out by 2 years after cART became available [7, 8, 10].

We also found that raltegravir adoption was less common among persons with a substance use diagnosis, even after adjusting for differences in antiretroviral adherence prior to raltegravir availability. This is consistent with prior studies showing that substance use influences antiretroviral prescribing and may result in part from provider attitudes regarding the relative utility of antiretroviral therapy among substance users [7, 29, 30]. In contrast to studies of cART adoption in the 1990s that did not include VA patients we did not observe substantial racial variation in raltegravir adoption in VA [7, 10]. Racial disparities in access to novel HIV therapies may be less pronounced in equal access healthcare systems lacking insurance and financial barriers to care.

This study has strengths, most notably the analysis of a national dataset with a significant number of raltegravir-eligible persons living in rural areas, and rich data on important clinical covariates such as CD4 counts and comorbidities. It also has important limitations, notably the reliance on retrospective data extracted from an electronic health record and compiled in an electronic patient registry. We lacked important measures of patient socioeconomic status and educational attainment that are often significant determinants of healthcare use. Unmeasured differences in these factors may have contributed to differences in raltegravir adoption among rural and urban veterans.

We did not have access to results for viral resistance testing. The raltegravir eligible cohort no-doubt included treatment-experienced persons with detectable viral load due to non-adherence, but without clear multi-class resistance. It is possible that urban veterans had greater indication for raltegravir therapy reflected by greater viral resistance identified through genotypic or phenotypic testing. This is however made less likely by the observation that rural and urban veterans had similar degrees of prior antiretroviral experience and adherence, although the pharmacy-refill based adherence measure in this study may have overestimated actual medication-taking behavior [31]. We were also not able to evaluate antiretroviral treatment experience that occurred prior to entering VA care. Also, this study did not evaluate adherence and persistence with raltegravir therapy after initiation.

As discussed above, our results may not generalize outside VA, where cost and insurance factors are often paramount determinants of healthcare use. The small number of women in this study prevented examination of gender disparities in raltegravir adoption.

Conclusion

We found that urban veterans were more likely than rural to be early adopters of raltegravir. Advances in antiretroviral therapy continue to improve outcomes for persons with HIV, but not all persons are equally likely to adopt these advances. Future studies should explore patient, provider, and care site characteristics that are associated with rapid adoption of ongoing innovations in HIV therapy and that may explain rural–urban disparities in access to new therapies. This will inform interventions to reduce geographic disparities in access to advances in HIV therapy.

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Fig. 1.
Adoption of raltegravir among urban and rural veterans

Table 1

Characteristics of 1,222 raltegravir eligible patients, by residence

Characteristic	Urban N = 989 (80.9%)	Rural N = 233 (19.1%)	χ^2 (df)*	P
Age				
0–40	100 (10.1)	19 (8.1)	0.84 (3)	0.84
41–50	349 (35.3)	84 (36.1)		
51–60	412 (41.7)	100 (42.9)		
61 plus	128 (12.9)	30 (12.9)		
Gender				
Male	963 (97.4)	227 (97.4)	0.002 (1)	0.96
Female	26 (2.6)	6 (2.6)		
Race/ethnicity				
Black	576 (58.2)	96 (41.2)	24.3 (1)	< 0.001
White, non-hispanic	324 (32.8)	113 (48.5)		
Other	71 (7.2)	17 (7.3)		
Missing	18 (1.8)	7 (3.0)		
CD4 count				
0–50	398 (40.2)	109 (46.8)	24.5 (5)	<0.001
51–200	173 (17.5)	35 (15.0)		
201–350	176 (17.8)	29 (12.4)		
351–500	98 (9.9)	18 (7.7)		
>500	132 (13.4)	29 (12.5)		
Missing	12 (1.2)	13 (5.6)		
AIDS defining illness				
Yes	197 (19.9)	43 (18.5)	0.26 (1)	0.61
No	792 (80.1)	190 (81.5)		
Substance abuse				
Yes	249 (25.2)	45 (19.3)	3.55 (1)	0.06
No	749 (74.8)	188 (80.7)		
HIV viral load				
401–999	224 (22.6)	66 (28.4)	5.6 (3)	0.13
1,000–9,999	323 (32.7)	80 (34.3)		
10,000–99,999	303 (30.6)	56 (24.0)		
100,000 plus	139 (14.1)	31 (13.3)		
Years on ART				
Median (IQR)	11 (8–12)	11 (7–12)	−0.05 [†]	0.96
ART adherence				
Median (IQR)	0.73 (0.52–0.90)	0.74 (0.54–0.92)	−1.39 [†]	0.17

* Chi-square value (degrees of freedom)

[†] Wilcoxon rank sum Z statistic is given for continuous measures, years on ART and ART adherence

Table 2

Frequency of raltegravir adoption over time, by patient characteristic

Characteristic	Number of raltegravir adoptors at each time point								
	180 Days			360 Days			720 Days		
	N (%)	χ^2 (df)*	P	N (%)	χ^2 (df)*	P	N (%)	χ^2 (df)*	P
Overall	197 (16.1)			318 (26.0)			433 (35.4)		
Residence									
Urban	171 (17.3)	5.24 (1)	0.02	272 (27.5)	5.90 (1)	0.02	359 (36.3)	1.70 (1)	0.19
Rural	26 (11.2)			46 (19.7)			74 (31.8)		
Age									
0–40	10 (8.4)	11.0 (3)	0.01	23 (19.3)	4.93 (3)	0.18	34 (28.6)	6.12 (3)	0.11
41–50	84 (19.4)			115 (26.6)			156 (36.0)		
51–60	73 (14.3)			131 (25.6)			176 (34.4)		
61 plus	30 (19.0)			49 (31.0)			67 (42.4)		
Gender									
Male	196 (16.5)	4.10 (1)	0.04	314 (26.4)	3.12 (1)	0.08	425 (35.7)	1.56 (1)	0.21
Female	1 (3.1)			4 (12.5)			8 (25.0)		
Race/ethnicity									
Black	98 (14.6)	3.33 (3)	0.34	166 (24.7)	2.31 (3)	0.51	230 (34.2)	2.19 (3)	0.53
White, non-hispanic	77 (17.6)			123 (28.2)			165 (37.8)		
Other	16 (18.2)			21 (23.9)			28 (31.8)		
Missing	6 (24.0)			8 (32.0)			10 (40.0)		
CD4 count									
0–50	90 (17.8)	10.5 (5)	0.06	149 (29.4)	19.8 (5)	0.001	200 (39.5)	24.6 (5)	<0.001
51–200	39 (18.8)			66 (31.7)			89 (42.8)		
201–350	36 (17.6)			52 (25.4)			70 (34.2)		
351–500	15 (12.9)			21 (18.1)			30 (25.9)		
>500	16 (9.9)			26 (16.2)			38 (23.6)		
Missing	1 (4.0)			4 (16.0)			6 (24.0)		
AIDS defining illness									
Yes	42 (17.5)	0.42 (1)	0.52	67 (27.9)	0.56 (1)	0.46	90 (37.5)	0.56 (1)	0.46
No	155 (15.8)			251 (25.6)			343 (34.9)		
Substance abuse									
Yes	22(7.5)	21.4 (1)	<0.001	48 (16.3)	18.9 (1)	<0.001	69 (23.5)	24.2 (1)	<0.001
No	175 (18.9)			270 (29.1)			364 (39.2)		
HIV viral load									
401–999	26 (9.0)	24.4 (3)	<0.001	51 (17.6)	22.8 (3)	<0.001	75 (25.9)	26.2 (3)	0.01
1,000–9,999	57 (14.1)			96 (23.8)			131 (32.5)		
10,000–99,999	74 (20.6)			114 (31.8)			156 (43.5)		
100,000 plus	40 (23.5)			57 (33.5)			71 (41.8)		
Years on ART									
<10	76 (13.1)	7.57 (1)	0.006	119 (20.5)	17.7 (1)	<0.001	165 (28.4)	24.0 (1)	<0.001

Characteristic	Number of raltegravir adoptors at each time point								
	180 Days			360 Days			720 Days		
	N (%)	χ^2 (df)*	P	N (%)	χ^2 (df)*	P	N (%)	χ^2 (df)*	P
10	121 (18.9)			199 (31.1)			268 (41.8)		

* Chi-square value (degrees of freedom)

Table 3

Association of patient characteristics with raltegravir adoption by 180 days, multivariate model

Characteristic	Odds ratio (95% CI)*
Residence	
Urban	1.72 (1.09–2.70)
Rural	Ref
Age	
0–40	Ref
41–50	3.25 (1.42–7.44)
51–60	2.42 (1.10–5.33)
61 plus	2.95 (1.13–7.71)
Gender	
Male	5.51 (0.68–44.9)
Female	Ref
Race/ethnicity	
Black	0.85 (0.58–1.24)
White, non-hispanic	Ref
Other	1.23 (0.59–2.53)
Missing	1.64 (0.44–6.13)
CD4 count	
0–50	2.04 (1.06–3.91)
51–200	2.04 (1.11–3.75)
201–350	1.96 (1.05–3.64)
351–500	1.45 (0.73–2.85)
>500	Ref
Missing	0.43 (0.03–6.76)
AIDS defining illness	
Yes	1.27 (0.90–1.79)
No	Ref
Substance abuse	
Yes	0.32 (0.18–0.56)
No	Ref
HIV viral load	
401–999	Ref
1,000–9,999	1.75 (1.15–2.65)
10,000–99,999	2.92 (1.90–4.48)
100,000 plus	3.71 (2.06–6.67)
Years on ART	
<10	Ref
≥10	1.71 (1.19–2.46)

Ref referent category