Patterns and Correlates of Discontinuation of the Initial HAART Regimen in an Urban Outpatient Cohort

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Objectives: To describe the patterns and correlates of discontinuation of the initial highly active antiretroviral therapy (HAART) regimen in an urban, outpatient cohort of antiretroviral-naive patients.

Design: Retrospective cohort of 345 randomly selected antiretroviral-naive patients who initiated HAART on 6 selected regimens between January 1997 and May 2001 in New Orleans, LA.

Methods: An investigator reviewed medical records to collect information on concurrent medications, symptoms/diagnoses, staging indicators, and reasons for HAART discontinuation. Proportional hazards regression methods were used to identify predictors of discontinuation.

Results: After a median follow-up of 8.1 months, 61% of patients changed or discontinued their initial HAART regimen; 24% did so because of an adverse event. The events most commonly cited as the cause for discontinuation were nausea, vomiting, and diarrhea. A detectable viral load was associated with discontinuation at any time, while reporting nausea/vomiting or dizziness at the previous visit were associated with discontinuation during the first 3 months on HAART. Nausea/vomiting and not having AIDS at the time of HAART initiation were associated with discontinuation due to an adverse event at any time, while a high viral load, and dizziness or anorexia/weight loss at the previous visit were associated with discontinuation due to an adverse event in the first 3 months on HAART.

Conclusions: Gastrointestinal adverse events of HAART are the most frequently cited reason for discontinuation of HAART. An effort should be made to educate patients about these events and to encourage continued adherence. Additionally, appropriate prophylaxes for these events are warranted.

Key Words: HIV/AIDS, antiretroviral therapy, adverse events, toxicity, tolerability, treatment

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The introduction of highly active antiretroviral therapy (HAART) in the United States in 1996 led to significant reductions in AIDS-related morbidity and mortality.[1–6] Consequently, HAART is now the standard of care for persons with HIV in the United States. Data from observational cohorts have served to document the favorable impact of HAART but have shown that the rates of HAART discontinuation are significantly higher in observational settings than in clinical trial settings.[7–9]

Since several observational studies have found that adverse events are the most commonly reported reason for discontinuation[7,10–14] a more detailed understanding of which specific adverse events lead to discontinuation and the temporality of the association could allow providers to target those events for intervention to reduce HAART discontinuation. The purpose of this study was to examine the patterns and correlates of discontinuation of the initial HAART regimen in an urban, outpatient cohort of antiretroviral-naive patients in the United States.

METHODS

The HIV Outpatient Clinic (HOP) is a public HIV clinic that is affiliated with the Medical Center of Louisiana, in New Orleans, and serves a large, urban, predominantly indigent population of about 2600 patients. Copies of the medical charts are abstracted every 6 months as part of the Adolescent and Adult Spectrum of Disease (ASD) Natural History of HIV Multicenter Study (funded by the Centers for Disease Control and Prevention).[15]

A total of 345 antiretroviral-naive patients who initiated HAART at the HOP clinic with any of 6 selected regimens between January 1997 and May 2001 were randomly selected. The regimens included in this study were chosen because they were the 6 regimens most frequently prescribed at the HOP clinic for antiretroviral-naive patients starting HAART during this period. One investigator reviewed records from each patient visit prior to and during the initial HAART regimen to collect information on the occurrence of signs or symptoms and data on sociodemographic characteristics, prior and concomitant conditions, indicators of disease staging, and concomitant medications. Data from the ASD database were in-

cluded to supplement sociodemographic data. The median time from initiation of HAART to record review was 2.8 years and the interquartile range (IQR) was 2.1–3.8 years.

Patient records were reviewed until the patient discontinued their initial HAART regimen, was lost to follow-up, or died. Discontinuation of the initial HAART regimen was defined as changing or stopping any drug in the regimen for at least 30 days. Reasons for discontinuation were recorded and classified into the following categories: treatment failure, adverse event, other reason, and no reason noted. For some analyses, similar adverse events were grouped together as follows.

- *Gastrointestinal abnormalities*: diarrhea, nausea, vomiting, ulcer, heartburn, gastrointestinal complaint, dyspepsia, or gastritis
- *Metabolic abnormalities*: diabetes or hypercholesterolemia
- *Central nervous system abnormalities*: dizziness, abnormal dreams, insomnia, confusion, or impaired thinking
- *Bone marrow suppression abnormalities*: anemia, leukopenia, granulocytopenia, or thrombocytopenia

Time to HAART discontinuation was calculated as the time from initiation of HAART until the date that the initial HAART regimen was discontinued. Patients who remained on their initial HAART regimen at the time of record review were censored at the date of review and classified as still on their initial regimen. Patients who did not discontinue HAART but were absent from the clinic for at least 1 year were classified as lost to follow-up and censored. Patients who died while on HAART were censored at their date of death. Discontinuations were noted as the decision of the patient without consultation with an HOP provider, the decision of an HOP provider, or the decision of an outside provider not affiliated with the HOP clinic, such as an emergency department or nursing home provider.

The Louisiana State University Health Sciences Center Institutional Review Board, the Tulane University Institutional Review Board, and the HIV Outpatient Clinic Research Committee approved the study.

Statistical Methods

A person-years analysis was used to determine the incidence of discontinuation overall and by reason for discontinuation. Confidence intervals were calculated from the exact Poisson distribution.[16] Kaplan-Meier estimates were used to describe the cumulative probability of discontinuation of the initial HAART regimen.[17]

Proportional hazards and extended Cox regressions[18–20] with time-varying covariates were used to identify factors that were associated with the time from HAART initiation to discontinuation for any reason, due to an adverse event, and due to treatment failure. All tests of significance were 2 sided. Analyses were performed with SAS version 8.0 (SAS Institute, Cary, NC).

The following factors were identified at the time of HAART initiation and were included in models as time-fixed covariates: ethnicity (African American or non–African American), sex, age (≤35 years), year of HAART initiation (1997, 1998, 1999, or 2000–2001), time since HIV diagnosis (≤6 months), time in care at HOP clinic (≤1 month), prior diagnosis of any AIDS-defining illness, *Pneumocystis carinii pneumonia*, and hepatitis C, mode of HIV acquisition (male-to-male sexual contact, intravenous drug use, heterosexual contact, or other), self-reported history of illicit substance use, crack cocaine use, and alcohol abuse, history of depression and weight loss of ≥10 pounds, antiretrovirals prescribed in addition to lamivudine (zidovudine or stavudine, and efavirenz, nelfinavir, or indinavir), initiation of HAART as part of a clinical study, CD4 cell count (<100 cells/mL, 100–399 cells/mL, or ≥400 cells/mL), and viral load (<4.7 $\log_{10}$ copies/mL, 4.7–5.6 $\log_{10}$ copies/mL, or >5.6 $\log_{10}$ copies/mL).

The following factors were assessed at each clinic visit after HAART initiation and included in the models as time-varying covariates: CD4 cell count (<200 cells/mL, 200–499 cells/mL, or >499 cells/mL), viral load (≤2.6 $\log_{10}$ copies/mL, 2.6–4.0 $\log_{10}$ copies/mL, or >4.0 $\log_{10}$ copies/mL), body mass index (<18.5 kg/m^2, 18.5–24.9 kg/m^2, or >24.9 kg/m^2), and elevated blood pressure. Concomitant medications that were prescribed to at least 20 patients during follow-up were included with an indicator for prescription of each of the following: azithromycin, dapsone, fluconazole, clarithromycin, and trimethoprim sulfamethoxazole. Concomitant conditions or complaints that were reported for at least 30 patients during follow-up were included with an indicator for each of the following: diagnosed depression or suicide attempt, substance use, crack cocaine use, alcohol abuse, anemia, hepatitis, hypercholesterolemia, hypertension, fatigue, diarrhea, nausea or vomiting, headache, rash, abnormal dreams or insomnia, fever, ulcer/gastritis/dyspepsia, dizziness, and weight loss/anorexia. Grouped adverse events were also included with an indicator for each of the following: gastrointestinal abnormality, metabolic abnormality, central nervous system abnormality, and bone marrow suppression.

RESULTS

A total of 2337 visits were reviewed for the 345 sampled patients who initiated HAART on the selected initial regimens, resulting in 4128 person-months of follow-up. The study population was 68% male and 70% African American, with a median age of 34 years (IQR: 29–42) at the time of HAART initiation (Table 1). The selected initial HAART regimens were lamivudine (3TC)/zidovudine (AZT)/nelfinavir (39%), 3TC/stavudine (d4T)/nelfinavir (22%), 3TC/AZT/efavirenz (18%), 3TC/d4T/efavirenz (12%), 3TC/AZT/indinavir (5%), and 3TC/d4T/indinavir (4%).

TABLE 1. Study Population at the Time of HAART Initiation

	All Patients (n = 345) n (%)
Sex	
Male	233 (68)
Female	112 (33)
Race	
White	93 (27)
African-American	243 (70)
Other	9 (3)
Age at HAART initiation (y)	
Median	34
25th percentile	29
75th percentile	42
Mode of HIV acquisition	
Male-to-male sexual contact	103 (30)
Intravenous drug use	71 (20)
Heterosexual contact	50 (15)
Transfusion or transplant	7 (2)
Risk not specified	114 (33)
CD4 category (cell/mL)	
Median	182
25th percentile	33
75th percentile	379
Viral load category (copies/mL)	
Median	104,513
25th percentile	26,399
75th percentile	356,840
Time in care at HOP clinic	
<1 month	173 (50)
1–6 months	102 (30)
>6 months	70 (20)
Time since HIV diagnosis	
<1 month	41 (12)
1–6 months	167 (48)
>6 months–3 years	75 (22)
>3 years	62 (18)
AIDS diagnosis	210 (61)
History (self-report) of:	
Substance use (including crack cocaine)	168 (48)
Crack cocaine use	67 (19)
Alcohol abuse	80 (23)
Initial HAART regimen	
3TC/AZT/nelfinavir	135 (39)
3TC/d4T/nelfinavir	77 (22)
3TC/AZT/efavirenz	62 (18)
3TC/d4T/efavirenz	41 (12)
3TC/AZT/indinavir	16 (5)
3TC/d4T/indinavir	14 (4)

After a median follow-up of 8.1 months (IQR: 2.1–18.6 months), 211 patients (61%) discontinued their initial HAART regimen (Table 2). Twenty-one percent of patients who discontinued did so with an undetectable viral load at their last measurement. Just over half (52%) of discontinuations were initiated by the patient, 42% were in consultation with their HOP provider, and 6% were initiated by an outside provider. The incidence of discontinuation of the initial HAART regimen was 5.1 discontinuations per 100 person-months of follow-up (95% CI: 4.5–5.9). The cumulative probability of discontinuing the initial HAART regimen at 1 year after start of therapy was 51% (95% CI: 45–56%) (Fig. 1).

The reasons cited for discontinuation were adverse event (24%), treatment failure (12%), another reason (17%), and no reason noted (8%). Fifteen percent of patients were lost to follow-up (defined as no visit for ≥1 year), 11 patients (3%) died, and 21% of the patients were still on their initial HAART regimen at the time of record abstraction. The causes of death from the medical record or ASD were as follows: wasting/AIDS (1 patient), non-Hodgkin lymphoma (1 patient), wasting/AIDS/renal failure (1 patient), cocaine poisoning (1 patient), pulmonary Kaposi sarcoma/wasting/AIDS (2 patients), gunshot wound (1 patient), intracerebral hemorrhage/renal failure (1 patient), and unknown (3 patients).

Table 3 is a detailed presentation of reasons that were noted in the medical record to be the prompt for discontinuation for at least 4 patients. More than one reason may have been noted for each individual. Among those who discontinued due to an adverse event, nausea was the most frequently cited prompt for discontinuation (27%), followed by diarrhea (18%) and vomiting (16%). For 12%, the provider simply noted "gastrointestinal disturbance." When adverse events were grouped into categories, the most frequently cited cause for discontinuation due to an adverse event was a gastrointestinal abnormality, cited by 37 (44%) of those who discontinued because of an adverse event.

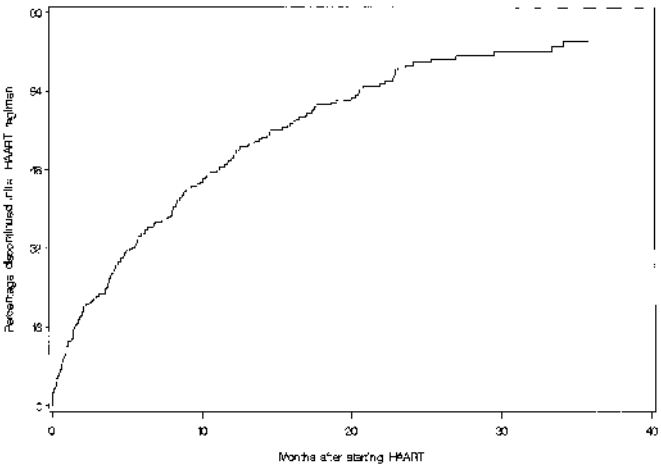

FIGURE 1. Kaplan-Meier estimate of the cumulative probability of discontinuation of the initial HAART regimen.

Table 4 presents the factors that were associated, in the final adjusted Cox models, with time to the initial HAART regimen discontinuation for any reason, due to an adverse event, and due to treatment failure. Individuals with a $\log_{10}$ viral load from >2.6 to 4.0 at their last measurement had a hazard of discontinuation for any reason that was 2.56 (95% CI: 1.71–3.86) times higher than that of an individual with a

TABLE 2. Outcome of Initial HAART Regimen

		Discontinued Initial HAART n = 211 (61%)						
	Overall n = 211	Adverse Event n = 84 (24%)	Treatment Failure n = 40 (12%)	Other Reason n = 60 (17%)	No Reason Noted n = 28 (8%)	Lost to Follow-up n = 50 (15)	Died n = 11 (3%)	Still on Initial Regimen n = 73 (21%)
Time on HAART in months								
Median (IQR)	5.6 (1.5–12.2)	2.2 (0.7–6.3)	11.6 (7.4–20.5)	4.7 (1.2–12.4)	8.5 (4.5–12.5)	4.7 (1.0–15.9)	5.8 (2.2–10.2)	23.5 (16.1–34.2)
Last viral load <400 c/mL, n (%)	45 (21)	26 (31)	3 (8)	9 (15)	7 (25)	20 (40)	4 (36)	55 (75)
Decision to discontinue, n (%)								
Patient	109 (52)	34 (41)	0	51 (85)	—			
HOP clinic provider	89 (42)	44 (52)	37 (93)	6 (10)	—			
Outside provider	13 (6)	6 (7)	3 (8)	3 (5)	—			
Incidence of discontinuation (events/100 person-months)								
ID (95% CI)	5.1 (4.5–5.9)	2.0 (1.6–2.5)	1.0 (0.7–1.3)	1.5 (1.1–1.9)	0.7 (0.5–1.0)			
Cumulative probability of discontination at 1 year								
Probability (95% CI)	51 (45–56)	25 (20–31)	11 (7–16)	17 (13–22)	10 (6–15)			

TABLE 3. Reasons for Discontinuation of HAART

Adverse event (n = 84)	
Nausea	23 (27%)
Diarrhea	15 (18%)
Vomiting	13 (16%)
Gastrointestinal disturbance	10 (12%)
Dysphagia	9 (11%)
Headache	6 (7%)
Insomnia	6 (7%)
Hypersensitivity reaction/rash	5 (6%)
Tiredness/fatigue	5 (6%)
Dizziness	4 (5%)
Neuropathy	4 (5%)
Anemia	4 (5%)
Abnormal absolute neutrophil count	4 (5%)
Adverse event classes	
Gastrointestinal abnormalities	37 (44%)
Central nervous system abnormalities	8 (10%)
Bone marrow suppression	5 (6%)
Liver abnormalities	4 (5%)
Other reason (n = 60)	
Patient decision	16 (27%)
Incarceration	9 (15%)
Hospitalization	4 (7%)
Substance abuse	4 (7%)
Lost to follow-up (n = 50)	
Did not return	32 (64%)
Moved	14 (28%)

$\log_{10}$ viral load that was ≤2.6, while an individual with a $\log_{10}$ viral load >4.0 had a hazard of discontinuation that was 5.82 (95% CI: 4.06–8.34) times higher. During the first 3 months on HAART, individuals who reported experiencing nausea or vomiting at their previous visit had a hazard of discontinuation for any reason that was 2.60 (95% CI: 1.53–4.39) times higher than that of an individual who did not, and those who reported dizziness at their previous visit had a hazard of discontinuation that was 4.86 (95% CI: 1.94–12.16) times higher than that of an individual who did not.

During the first 3 months on HAART, patients who reported dizziness (HR, 5.97; 95% CI: 2.08–17.18) or anorexia/weight loss (HR, 3.95; 95% CI: 1.78–8.76), or who had a $\log_{10}$ viral load >4.0 (HR, 4.73; 95% CI: 2.36–9.47) were more likely to discontinue HAART due to an adverse event. Throughout follow-up, patients who reported nausea or vomiting at their previous visit (HR, 2.39; 95% CI: 1.42–4.00) were more likely to discontinue HAART due to an adverse event than those who did not, while patients in whom AIDS had been diagnosed before starting HAART were approximately 50% less likely to discontinue due to an adverse event (HR, 0.51; 95% CI: 0.33–0.80) compared with those in whom AIDS had not been diagnosed before starting HAART.

Predictors of discontinuation of the initial HAART regimen because of treatment failure were a history of anemia at the time of HAART initiation (HR, 4.03; 95% CI: 1.93–8.42), a CD4 cell count <200 cells/mL (HR, 3.42; 95% CI: 1.40–8.40) compared with at least 500 cells/mL, and having acquired HIV through male-to-male sexual contact compared with acquisition via heterosexual contact (HR, 4.79, 95% CI: 1.40–16.41). Patients taking a regimen that contained efavirenz had a significantly lower hazard of discontinuation due to treatment failure compared with those taking a regimen that contained either indinavir or nelfinavir (HR, 0.04; 95% CI: 0.01–0.33).

DISCUSSION

The initial HAART regimen is widely considered to be the most important regimen in HIV treatment because it is associated with the greatest probability of achieving sustained virologic response.[21,22] Switching from the initial HAART regimen results in a lower probability of virological suppression and frequent switching may exhaust future options for effective treatment.

Data from observational cohorts suggest that, among the reasons for discontinuation, the incidence is highest for discontinuation due to adverse events[7,10–14] and that discontinuation due to an adverse event occurs earlier in follow-up than discontinuation due to other reasons.[7,8,10,23] Gastrointestinal abnormalities have been cited as the most common reason for HAART discontinuation in cohort studies[7,10,12] as well as clinical trials.[24]

This retrospective cohort study used review of medical records to describe HAART discontinuation in an unselected cohort of patients. To date, few studies of this type have been published that consider individual HAART regimens instead of "any HAART," focus on specific adverse events instead of looking only at the occurrence of any adverse event, include concomitant medications and conditions as potential covariates in the models, and use time-dependent co-variates during follow-up instead of baseline correlates only. However, the design of this study also had several limitations. A retrospective review of medical records may potentially miss information that was not recorded correctly by the provider and data may be misclassified because of a lack of standardized assessments of endpoints at the time data were recorded. We were unable to collect information that was not part of the medical record, such as information on adherence to prescribed regimens.

The results of this study shed light on HAART regimen discontinuation in an "everyday" outpatient clinical setting. The cohort included patients who might not have met eligibility criteria for a clinical trial due to concomitant conditions, concomitant medications, or nonadherence to follow-up visits

TABLE 4. Adjusted Predictors of Time to Initial HAART Regimen Discontinuation

	Hazard Ratio	95% CI
Discontinuation of initial HAART regimen		
Log_{10} of viral load (copies/mL) at last measurement		
≤2.6	1.00	
>2.6–4.0	2.56	(1.71–3.86)*
>4.0	5.82	(4.06–8.34)*
Time on HAART		
<3 mo		
Nausea or vomiting at previous visit	2.60	(1.53–4.39)*
Dizziness at previous visit	4.86	(1.94–12.16)*
≥3 mo		
Nausea or vomiting at previous visit	1.56	(0.93–2.63)
Dizziness at previous visit	1.48	(0.60–3.65)
Discontinuation due to adverse event		
Time on HAART		
<3 mo		
Log_{10} of viral load at last measurement:		
≤12.6	1.00	
>2.6–4.0	1.17	(0.44–3.11)
>4.0	4.73	(2.36–9.47)*
Dizziness at previous visit	5.97	(2.08–17.18)*
Anorexia/weight loss at previous visit	3.95	(1.78–8.76)*
≥3 mo		
Log_{10} of viral load at last measurement:		
≤2.6	1.00	
>2.6–4.0	1.70	(0.84–3.46)
>4.0	1.83	(0.87–3.82)
Dizziness at previous visit	2.21	(0.51–9.54)
Anorexia/weight loss at previous visit	1.44	(0.51–4.10)
Nausea or vomiting at previous visit	2.39	(1.42–4.00)*
AIDS-defining diagnosis at HAART initiation	0.51	(0.33–0.80)†
Discontinuation due to treatment failure		
History of anemia at HAART initiation	4.03	(1.93–8.42)*
Efavirenz in the HAART regimen (vs. a protease inhibitor)	0.04	(0.01–0.33)†
CD4 (cells/mL) at last measurement		
<200	3.42	(1.40–8.40)†
200–499	2.24	(0.98–5.11)
≥500	1.00	
Mode of HIV acquisition		
Male-to-male sexual contact	4.79	(1.40–16.41)‡
Intravenous drug use	2.37	(0.52–10.86)
Heterosexual contact	1.00	
Other/unknown	3.05	(0.87–10.72)

*$P < 0.001$.
†$P < 0.01$.
‡$P < 0.05$.

as well as patients who were unwilling to participate in a clinical trial (only 7% of patients in this cohort initiated HAART as part of a clinical study). The data from this study describe adverse event experiences among patients treated in the usual manner by experienced clinicians who were free to choose what they believed to be the optimal regimen for the patient and to change the regimen and, thus, provided a realistic description of patients' experiences on their initial HAART regimen.

In this study, the 1-year probability of discontinuing the initial HAART regimen was approximately 50%. After a median follow-up of 8.1 months, we found that 24% of patients discontinued HAART due to an adverse event, a finding that was similar to the discontinuation proportions reported from the Antiprotéases Cohorte Study (APROCO) (24%),[7] the Italian Cohort of Antiretroviral-Naive Patients (ICONA) (21%),[10] and the Swiss HIV Cohort Study (20%).[12] Approximately one-third of those who discontinued HAART because of an adverse event in this cohort did so with an undetectable viral load, suggesting that these individuals "gave up" a regimen that was still potent. Although in most cases, the HOP provider made the decision to discontinue the regimen, it is important to note that for 41% of those who discontinued because of an adverse event, the decision was made by the patient without consultation with the provider. For these patients, treatment was frequently interrupted, not immediately changed, and it is possible that discontinuation could have been avoided for a number of them with appropriate management of the adverse event.

Experiencing nausea or vomiting was associated with overall discontinuation and discontinuation due to an adverse event. Nausea and vomiting were among the most frequent incident events during follow-up (data not shown) and were among the most commonly reported adverse events specifically cited as the reason for discontinuation. Although no studies to our knowledge have examined individual adverse events as predictors of HAART discontinuation, nausea has been implicated as a cause of nonadherence to HAART in the ICONA cohort.[25] In our study, experiencing dizziness was associated with overall discontinuation and with discontinuation due to an adverse event during the first 3 months of HAART. That dizziness was a significant predictor of discontinuation early in follow-up may reflect that patients either find dizziness to be immediately intolerable, or that dizziness resolves after a few weeks on HAART, such as has been reported for patients taking efavirenz.[26] Experiencing anorexia/weight loss was also predictive of discontinuing the initial HAART regimen because of an adverse event during the first 3 months of HAART.

Higher viral loads were associated with discontinuation for any reason throughout follow-up and because of an adverse event during the first 3 months of HAART. A similar association between higher viral loads during follow-up and regimen discontinuation was reported in a cohort of patients from the Royal Free Hospital in the United Kingdom[8] and in the Women's Interagency HIV Study cohort.[27]

Individuals in whom AIDS had been diagnosed at the time of HAART initiation had a lower risk of discontinuation because of an adverse event. This is not surprising, because patients who started HAART after AIDS was diagnosed were more likely to be experiencing symptoms of the disease, with significant interruption of daily activity. They may have been less bothered by the nuisance adverse events if therapy improved disease symptoms, or perhaps the gravity of the AIDS diagnosis made them more committed to therapy.

Although this study was not designed to assess the association between a particular antiretroviral agent and discontinuation, we considered each drug as a potential predictor in the models. The final adjusted models were re-run with the indicators for each drug in the regimen, but where inclusion of these variables did not change the effect estimates, they were removed from the final model. In the subset of patients taking nelfinavir, we compared discontinuation rates between those taking nelfinavir 2 or 3 times a day and found no significant differences attributable to differences in dosing schedules.

Although we could not assess the persistence of adverse events, the prescribing information for many antiretrovirals suggests that prevalence of nuisance adverse events declines during follow-up[28,29]; patients should be counseled about the tendency of some adverse events to decline over time. For events that do not decline, particularly those associated with discontinuation or loss to follow-up, patients should be queried about the severity of events. To prevent the development of drug resistance secondary to suboptimal adherence, providers may consider a change of regimen if the patient feels that the event is excessively bothersome. There is some evidence that although switching the initial HAART regimen due to intolerance does limit further treatment options, it is not associated with an unfavorable virologic outcome later.[7,21]

The most commonly reported reason for discontinuation of the initial HAART regimen was an adverse event. Given the high rates of HAART discontinuation in this cohort, and prior findings that perceived side effect severity is associated with poor adherence to HAART,[30,31] the prevention and treatment of adverse events would be a key intervention to keep patients on their initial HAART regimen for a longer period, increasing their likelihood of a sustained virologic response to HAART.

Although adverse events are often considered to be an unavoidable consequence of effective treatment, this study suggests that adverse events may in fact hinder effective treatment of HIV disease and should be the targets of further research to maximize available treatments. Patients on HAART would benefit greatly from more effective management of adverse events, in particular gastrointestinal events such as nausea, vomiting, and diarrhea.

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