Incidence and Predictors of Death, Retention, and Switch to Second-Line Regimens in Antiretroviral-Treated Patients in Sub-Saharan African Sites with Comprehensive Monitoring Availability

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Background. Antiretroviral treatment programs in sub-Saharan Africa have high rates of early mortality and loss to follow-up. Switching to second-line regimens is often delayed because of limited access to laboratory monitoring.

Methods. Retrospective analysis was performed of a cohort of adults who initiated a standard first-line antiretroviral treatment at 5 public sector sites in 3 African countries. Monitoring included routine CD4 cell counts, human immunodeficiency virus RNA measures, and records of whether appointments were kept. Incidence and predictors of death, loss to follow-up, and switch to second-line regimens were analyzed by time-to-event approaches.

Results. A total of 3749 patients were analyzed; at baseline, 37.1% were classified as having World Health Organization disease stage 3 or 4, and the median CD4 cell count was 192 cells/μL. First-line regimens were nevirapine based in 96.5% of patients; 17.7% of patients attended >95% of their drug pickup appointments. During 4545 person-years of follow-up, mortality was 8.6 deaths per 100 person-years and was predicted by lower baseline CD4 cell count, lower hemoglobin level, and lower body mass index (calculated as weight in kilograms divided by the square of height in meters); more-advanced clinical stage of infection; male sex; and more missed drug pickup appointments. Dropouts (which accrued at a rate of 2.1 dropouts per 100 person-years) were predicted by a lower body mass index, more missed visits and missed drug pickup appointments, and later calendar year. Incidence of switches to second-line regimens was 4.9 per 100 person-years; increased hazards were observed with lower CD4 cell count and earlier calendar year at baseline. In patients who switched, virological failure was predicted by combined clinical and CD4 criteria with 74% sensitivity and 30% specificity.

Conclusions. In an antiretroviral treatment program employing comprehensive monitoring, the probability of switching to second-line therapy was limited. Regular pickup of medication was a predictor of survival and was also strongly predictive of patient retention.

The majority of HIV-1–infected individuals live in sub-Saharan Africa [1]. In these countries, AIDS-related morbidity and mortality remain the highest in the world because of limited access to HIV diagnosis and treatment. In recent years, efforts have been made to expand access to antiretroviral treatment (ART) in several low-income countries. Short-term observations on the efficacy of ART in resource-limited settings show encouraging results [2–5]. Nevertheless, major concerns and unanswered questions remain regarding the durability of treatment response, the long-term effect
on mortality, the risk of patient loss to follow-up, and the emergence of drug resistance, with consequent treatment failure and the necessity for much more expensive and difficult-to-implement second-line regimens [6, 7].

We report the analysis of the rates and predictors of mortality, loss to follow-up, and switch to second-line ART in a cohort of adult nonpregnant patients who started a standard first-line ART regimen at 5 public sites with comprehensive monitoring availability, located in Mozambique, Malawi, and Guinea-Conakry.

PATIENTS AND METHODS

The DREAM Program. The DREAM Program, developed by the Community of Sant’Egidio (Rome, Italy), an international faith-based organization, is based on a comprehensive approach to the patient, whose treatment is entirely free of charge [8]. For patients who begin ART, clinical monitoring takes place after 2 and 4 weeks, at 3 months, and every 3 months thereafter. Laboratory monitoring of patients takes place through use of HIV-1 RNA measurements every 6 months, CD4 cell counts every 3 months, and complete blood cell counts and biochemistry assays to monitor laboratory toxicity every 3 months. Pharmacy appointments for medication pickup take place at day 1, every 2 weeks during the first month, and on a monthly basis thereafter. Peer community health care workers assist and monitor patients through home-care visits, counseling, and monitoring of patient adherence to medication and care. In addition, computer-based verification of patient appointment keeping (clinical visits and drug pickups) was established at each major site.

Study sites and patients. Patients were selected from 5 public sector sites, all of which are in partnership with the DREAM Program. Two sites are located in Mozambique (the Machava Center in the city of Matola, Maputo Province, and the Manga Chingoussura Center, Sofala Province), 2 sites are located in Malawi (in the cities of Blantyre and Lilongwe), and 1 site is located in Guinea-Conakry (the city of Conakry). These sites initiated the ART program between February 2002 (Machava) and January 2006 (Conakry).

Included in the analysis were nonpregnant adults (age, ≥15 years) who were observed at 1 of the aforementioned sites and who initiated a standard first-line ART regimen with available pretherapy visit, laboratory examinations, and at least 1 clinical follow-up. Clinicians could decide to switch ART to a second-line regimen on the basis of clinical, CD4 cell count, and HIV-1 RNA criteria, as per the recommendations of country-specific or World Health Organization (WHO) guidelines [9]. This study was approved by the Ministries of Health of Mozambique and Guinea-Conakry and by the National Health Sciences Research Committee of the Ministry of Health of Malawi.

Treatment regimens and outcome definitions. Standard first-line regimen was defined as any 3-drug group that was based on 2 nucleoside reverse-transcriptase inhibitors plus a nonnucleoside reverse-transcriptase inhibitor or on 3 allowed nucleoside reverse-transcriptase inhibitors. Standard second-line regimen was defined as any combination of ≥3 drugs, given at therapeutic doses, that included a protease inhibitor. Substitutions within the first-line regimen for toxicity reasons were ignored. Generic drugs were employed throughout the program, in fixed-dose combinations, when available. The date of loss to follow-up was defined as the date on which the patient was last seen before being lost for >3 months, unless they returned later. Patient adherence was estimated by missed scheduled clinical visits and missed scheduled drug pickup appointments, allowing for 7 days of delay. The proportion of missed appointments was calculated and dichotomized using 95% thresholds. Deaths were ascertained using information from hospitals and families and by actively searching, using telephone calls and home visits, for patients who did not show up.

Variables collected. All data were extracted from the DREAM Program database, which centrally collects the computer records from the different program sites. With allowance for a maximum of 180 days before ART initiation, at the last pretreatment examination, available hemoglobin, body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters), CD4 cell count, viral load (bDNA assay, version 3.0; Siemens Diagnostics), and type of first-line regimen were retrieved for analysis. Clinical stage [10] was electronically recorded by staff at the examination sites beginning December 2005; therefore, that information was available for 61% of the patient sample. In addition, the percentage of missed clinical visits and drug pickup appointments, the date of last follow-up, the reasons for follow-up interruption (i.e., death, loss to follow-up, transfer out, or other reasons), and complete treatment history were also retrieved. To establish which WHO guideline–defined treatment-failure criteria were present before switching to second-line therapy [9], we considered all new or recurrent WHO stage 4 clinical episodes, as well as all follow-up CD4 cell counts and last CD4 and HIV RNA available information in the range of −180 to +15 days from the date of switching. Virological failure was defined as an HIV RNA level >10,000 copies/mL at >6 months after treatment initiation; immunological failure was defined as CD4 cell counts <100 cells/μL at all measures available in the specified time range or decreasing to below pretreatment values, or decreasing >50% below the peak value reached during treatment. Clinical failure was defined as the presence of any new or recurrent WHO stage 4 event >6 months after treatment initiation. To detect the presence of significant viremia in patients with immunological failure, we also explored which percentage of patients had a viral load >1000 copies/mL.
Statistical analysis. Patient follow-up began on the date of ART initiation. Time-to-event analysis was performed using the following outcomes: death due to any cause, loss to follow-up, or switch to second-line ART. For patients who did not reach a specific outcome, follow-up was right-truncated at the first of the following dates: last observation, transfer out, death, or 30 June 2007. The incidence of the outcomes was determined. Kaplan-Meier estimates and Cox proportional hazards regression models were employed to analyze estimated probabilities and predictors of the outcome events. In the multivariate Cox models, covariates were analyzed using the forward conditional method. This allows a stepwise entry in the model only for covariates with significant adjusted correlation with the outcome. Because pre-ART WHO stage was available for a subset of the sample, the multivariate analysis for predictors of death was performed using separate models with or without the WHO stage covariate. All analyses were performed using SPSS software, version 14 (SPSS).

RESULTS

Baseline patient characteristics. There were 4125 patients who were prescribed ART and who had at least 1 documented pre-ART visit and laboratory examination; 4070 patients picked up medications at least once, and 3749 patients had at least 1 follow-up visit and were included in the analysis. There were 2325 female patients (62.0%). At ART initiation, median patient age was 34 years (interquartile range [IQR], 28–41 years), median CD4 cell count (available for 3320 patients) was 192 cells/μL (IQR, 90–293 cells/μL), median HIV-1 RNA level (3105 patients) was $4.6 \log_{10}$ copies/mL (IQR, 3.9–5.1 log$_{10}$ copies/mL), median hemoglobin concentration was 10.7 g/dL (IQR, 9.1–12.2 g/dL), median BMI was 20 (IQR, 18–23), and median calendar year was 2006 (IQR, 2004–2006); 37.1% of patients had disease assessed as WHO clinical stage 3 or stage 4.

Treatments and patient appointment keeping. The most frequently used initial first-line ART regimens were stavudine plus lamivudine plus nevirapine (65.1% of patients) and zidovudine plus lamivudine plus nevirapine (31.4%). Systematic records of which clinical appointments and drug pickup appointments were kept were available for 3740 (99.8%) of 3749 patients; 888 (23.7%) and 664 (17.7%) of patients missed $\geqslant$5% of clinical visits or drug pickup appointments, respectively.

Mortality and its predictors. During a cumulative follow-up of 4545 person-years, 393 patients died (8.6 per 100 person-years). The Kaplan-Meier survival curve showed a steeper decrease during the initial 6 months, with a 0.94 cumulative estimated survival probability at this time point (figure 1A). Thereafter, the percentage of patients who survived showed a slower decrease over time, with an estimated 3-year survival probability of 0.88.

For univariate analysis, variables associated with a longer time to death were as follows: female sex, higher baseline hemoglobin level, higher BMI, higher baseline CD4 cell count, and attendance at $\geqslant$95% of the drug pickup appointments, whereas a higher viral load and baseline status of WHO stage 3 or 4 were associated with a higher mortality risk (table 1). In the multivariate model, higher baseline CD4 cell counts,
hemoglobin levels, and BMI; female sex; and missing <5% of scheduled drug pickup appointments were all independently associated with a reduced hazard of death. In a second model that included the WHO stage, the more advanced clinical stage was also independently predictive of time to death, without significantly affecting the association of the other predictors, except that the proportion of missed drug pickup appointments showed only a correlation trend (P = .06), whereas later calendar year of program entry was an independent predictor of lower hazard of death.

**Patient loss to follow-up and its predictors.** One hundred six patients were classified as dropouts (2.1 patients per 100 person-years). The estimated percentage of patients who were still receiving care showed a slow linear decrease, to 92% after 3 years (figure 1B). Independent predictors of patient retention were higher baseline BMI, missing <5% of scheduled clinical visits and <5% of scheduled drug pickup appointments, and earlier calendar year at ART initiation (table 2).

**Switches to second-line therapy: incidence, criteria, and predictors.** Two hundred twenty-two patients switched to a second-line regimen (4.9 patients per 100 person-years). The 1-year and 3-year estimated probabilities of continuing to receive on a first-line regimen were 0.98 and 0.80, respectively (figure 1C). The Kaplan-Meier curve showed a biphasic decrease, with an increased percentage of patients starting to switch during the second or third year of treatment.

At the date of switch, treatment failure criteria were as follows: WHO-defined clinical criteria for 12 (6.3%) of 192 patients with available information, CD4 criteria for 136 (67.0%) of 203 patients, and virological criteria for 90 (48.9%) of 184 patients. Among patients who met clinical treatment failure, 5 (50%) of 10 also met virological criteria, and 8 (80%) of 10 met immunological criteria. Among patients who met immunological failure criteria, 61 (49.2%) of 124 with available information about viral load also experienced virological failure, and an additional 39 (31.5%) had a viral load of 1000–10,000 copies/mL. Among the 90 patients who met virological failure criteria, 60 (68.2%) of 88 evaluable patients also experienced immunological failure, and 1 additional patient experienced clinical failure; therefore, 27 (30.7%) of 88 patients switched because they met virological failure criteria only. Overall, 27 (14.7%) of 184 patients who switched regimens and who had virological follow-up data available met virological failure criteria only. In 158 patients who switched and who had complete clinical, CD4 cell count, and viral load information available, the combined clinical and CD4 cell count criteria showed a 73.6% sensitivity to detect virological failure (53 of 72 patients who experienced virological failure had true-positive results) and a 30.2% specificity (26 of 86 patients who did not experience virological failure had true-negative results). Results of both univariate and multivariate analyses indicated that starting first-line ART during a more recent calendar year and with higher CD4 cell counts was significantly associated with a lower risk of switching to second-line ART (table 3).

To estimate the number of switches to second-line regimens because of immunological failure that were theoretically prevented by virological monitoring, we selected patients who experienced immunological failure 6–36 months after ART initiation who did not switch to a second-line ART and for whom at least 1 viral load measurement during follow-up was available. In 354 (89.8%) of 394 cases of immunological failure

### Table 1. Predictors of the time to death.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis$^a$</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>HR for death (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td>Female vs. male sex</td>
<td>0.58 (0.48–0.71)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age, &gt;26 years vs. &lt;26 years</td>
<td>0.89 (0.67–1.12)</td>
<td>.46</td>
</tr>
<tr>
<td>Baseline Hb level, per 1 g/dL increase</td>
<td>0.75 (0.71–0.78)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline BMI, per 1-increment increase</td>
<td>0.81 (0.78–0.84)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline CD4 cell count, per 100 cells/μL increase</td>
<td>0.67 (0.61–0.73)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline HIV RNA level, per log$_{10}$ copies/mL increase</td>
<td>1.27 (1.12–1.45)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>WHO stage, 3 or 4 vs. 1 or 2 (n = 2271)</td>
<td>3.03 (2.33–3.85)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Attended &gt;95% of drug pickup appointments</td>
<td>0.73 (0.58–0.91)</td>
<td>.006</td>
</tr>
<tr>
<td>Attended &gt;95% visits</td>
<td>1.10 (0.88–1.38)</td>
<td>.40</td>
</tr>
<tr>
<td>Calendar year, per 1-year increase</td>
<td>0.98 (0.91–1.05)</td>
<td>.53</td>
</tr>
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</table>

NOTE. There were 393 deaths. BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); Hb, hemoglobin; HR, hazard ratio; NC, not computed; NE, not entered; WHO, World Health Organization.

$^a$ Two separate models were fitted, as follows: model 1 excluded WHO stage, because 39% of patients had missing values, and model 2 included it (see Patients and Methods).
(CD4 cell count below that of baseline or <100 cells/µL), all available viral loads were <10,000 copies/mL.

### DISCUSSION

The success of ART programs in low-income countries is usually associated with cost-free treatment and access to programs [11–16], provision of cotrimoxazole prophylaxis [11, 17], and active adherence and implementation [18–20]. The use of CD4 cell counts to monitor ART efficacy reduces morbidity and mortality in a resource-limited setting [21].

In the present study, we report a mortality rate of 8 deaths per 100 person-years after ART initiation at sites in 3 sub-Saharan African countries. As shown by other studies, mortality was higher during the initial 6 months of treatment [22–25]. Higher baseline CD4 cell counts, BMI, and hemoglobin levels; female sex; less advanced clinical stage; and higher adherence to drug pickup appointments were all independently associated with a reduced hazard of death. BMI and hemoglobin level are indicators of patient nutritional status but may also be influenced by late-stage AIDS conditions, such as wasting syndrome and opportunistic infections, or by the HIV itself [26, 27]. Our results confirm and extend previous observations that have shown rates of 20 dropouts per 100 person-years [37] or the loss to follow-up of 7%–8% of patients at 6–8 months after ART initiation [3, 38]. This is probably the result of the active adherence implementation and of active patient follow-up in this program (see Patients and Methods) [37]. Most importantly, treatment, monitoring, and care were cost free in the entire program, an important element for maintaining long-term treatment adherence in sub-Saharan Africa [39, 40]. In this study, loss to follow-up was predicted by a lower BMI; because this was also a mortality predictor, it might indicate that some of the patients who were lost to follow-up are represented by untraceable deaths or individuals who were too sick to return for care [41, 42]. Irregular attendance at scheduled visits and/or at drug pickup appointments was strongly associated with a higher hazard of being lost to follow-up. This finding suggests that lack of adherence during the program was a relevant predictor of being lost to the ART program itself and underscores the importance of recording these parameters in low-income settings as a patient- and program-monitoring

**Table 2. Predictors of time to loss to follow-up.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td></td>
<td>HR for loss to</td>
<td>HR for loss to</td>
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<tr>
<td></td>
<td>follow-up (95% CI)</td>
<td>follow-up (95% CI)</td>
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<td></td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>Female vs. male sex</td>
<td>0.70 (0.48–1.03)</td>
<td>.07</td>
</tr>
<tr>
<td>Age, ≥26 years vs. &lt;26 years</td>
<td>0.45 (0.30–0.68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline Hb level, per 1 g/dL increase</td>
<td>1.00 (0.92–1.09)</td>
<td>.98</td>
</tr>
<tr>
<td>Baseline BMI, per 1-increment increase</td>
<td>0.96 (0.91–1.02)</td>
<td>.20</td>
</tr>
<tr>
<td>Baseline CD4 cell count, per 100 cells/µL increase</td>
<td>1.02 (0.93–1.12)</td>
<td>.64</td>
</tr>
<tr>
<td>Baseline HIV RNA level, per log_{10} copies/µL increase</td>
<td>0.96 (0.84–1.08)</td>
<td>.47</td>
</tr>
<tr>
<td>WHO stage, 3 or 4 vs. 1 or 2 (n = 2271)</td>
<td>1.06 (0.58–1.91)</td>
<td>.85</td>
</tr>
<tr>
<td>Attended ≥95% of drug pickup appointments</td>
<td>0.04 (0.02–0.07)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Attended ≥95% visits</td>
<td>0.05 (0.03–0.11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Calendar year, per 1-year increase</td>
<td>0.98 (0.84–1.14)</td>
<td>.77</td>
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</table>

**NOTE.** One hundred six patients were lost to follow-up. BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); Hb, hemoglobin; HR, hazard ratio; NC, not computed; NE, not entered.
Multivariate analysis
munological failure criteria in the present study can be ex-
a specificity of 32%. The higher sensitivity of clinical and im-
terapy, the combined clinical and CD4 cell count failure cri-
cringly, we found that, for patients who switched to second-line

criteria (defined as viral loads over, sensitivity of these criteria for detecting virological failure
substantial increase in treatment complexity and cost. More-
ment switch revealed that immunological failure was the most
quent cause, followed by virological failure. Clinical failures
were extremely rare, which indicates that laboratory monitoring
allowed a regimen switch, in most situations, before clinical
progression. The majority of ART programs in resource-limited
settings use clinical and sometimes CD4 cell count monitoring. Access to viral load monitoring is limited by cost
and by lack of adequate infrastructure. Studies have shown that the use of WHO-recommended clinical criteria alone or clinical
criteria combined with CD4 cell count failure criteria to de-
termined the need to switch to second-line therapy often trans-
lates to an unnecessary use of second-line regimens, with a
substantial increase in treatment complexity and cost. More-
over, sensitivity of these criteria for detecting virological failure
(defined as viral loads >50 or >400 copies/mL according to
distinct studies) had a range of 25%–30% [44–46]. Interest-
ingly, we found that, for patients who switched to second-line
therapy, the combined clinical and CD4 cell count failure cri-
teria detected virological failure with a sensitivity of 74% and
a specificity of 32%. The higher sensitivity of clinical and im-
nunological failure criteria in the present study can be ex-
plained by the required virological failure confirmation. Vi-
rological monitoring was useful for switching treatment for 27
individuals (15%) who experienced virological failure that
would have remained undetected with use of clinical and CD4
cell count monitoring alone and who would have unnecessarily
continued to further accumulate drug resistance [47]. Overall,
we estimated that the number of unnecessary switches for im-
munological failure without virological confirmation that were
theoretically prevented by the use of virological monitoring in
this cohort outweighed the observed number of switches to
second-line ART for treatment failure detected by virological
monitoring alone. This may explain the limited number of
switches observed in this study. Nevertheless, an understanding
of the most cost-effective criteria and timing for switching to
second-line ART in resource-limited settings requires more in-
vestigation [48].

Time to switch to second-line regimens was prolonged dur-
ing more-recent calendar years. This might reflect a better use
of first-line regimens, including improved expertise in man-
aging treatment-related complications, as well as a more pru-
dent attitude toward treatment failure, which required an ad-
ditional adherence check and intervention before switching to
second-line therapy or, consistent with the higher proportion
of patients lost to follow-up, a reduced capacity to monitor
and detect the failure of first-line ART caused by lack of capacity
at the treatment sites.

In conclusion, the longer follow-up of patients receiving ART
in sub-Saharan Africa, with comprehensive laboratory and ad-
herence monitoring and adherence implementation, was as-
associated with limited mortality after the initial 6 months, high
patient retention, and a limited number of switches to second-
line ART. The monitoring of drug pickup appointment keeping
could be used for planning interventions at individual, site, and
program levels.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
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<th>Multivariate analysis</th>
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<tr>
<td></td>
<td>HR for switch</td>
<td>P</td>
<td>HR for switch</td>
<td>P</td>
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<td></td>
<td>(95% CI)</td>
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<td>(95% CI)</td>
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<tr>
<td>Female vs. male sex</td>
<td>0.92 (0.70–1.20)</td>
<td>.54</td>
<td>NE</td>
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<td>Age, ≥26 years vs. &lt;26 years</td>
<td>0.72 (0.52–1.00)</td>
<td>.05</td>
<td>NE</td>
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<tr>
<td>Baseline Hb level, per 1 g/dL increase</td>
<td>1.03 (0.98–1.09)</td>
<td>.22</td>
<td>NE</td>
<td></td>
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<tr>
<td>Baseline BMI, per 1-increment increase</td>
<td>1.01 (0.97–1.04)</td>
<td>.70</td>
<td>NE</td>
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<tr>
<td>Baseline CD4 cell count, per 100 cells/μL increase</td>
<td>0.92 (0.84–0.99)</td>
<td>.041</td>
<td>0.89 (0.82–0.97)</td>
<td>.007</td>
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</tr>
<tr>
<td>Baseline HIV RNA level, per log10 copies/mL increase</td>
<td>0.96 (0.88–1.04)</td>
<td>.32</td>
<td>NE</td>
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<tr>
<td>WHO stage, 3 or 4 vs. 1 or 2 (n = 2271)</td>
<td>0.99 (0.59–1.64)</td>
<td>.96</td>
<td>NC</td>
<td></td>
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<tr>
<td>Attended ≥95% of drug pickup appointments</td>
<td>0.93 (0.69–1.27)</td>
<td>.66</td>
<td>NE</td>
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<tr>
<td>Attended ≥95% visits</td>
<td>0.94 (0.72–1.24)</td>
<td>.67</td>
<td>NE</td>
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<tr>
<td>Calendar year, per 1-year increase</td>
<td>0.81 (0.75–0.88)</td>
<td>&lt;.001</td>
<td>0.76 (0.70–0.83)</td>
<td>&lt;.001</td>
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**NOTE.** There were 222 switches to second-line antiretroviral treatment. BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); Hb, hemoglobin; HR, hazard ratio; NC, not computed; NE, not entered.

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Table 3. Predictors of time to switch to second-line antiretroviral treatment.
Acknowledgments

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References


