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## Short-Term Clinical Disease Progression in HIV-Infected Patients Receiving Combination Antiretroviral Therapy: Results from the TREAT Asia HIV Observational Database

Preeyaporn Srasuebkul, Poh Lian Lim, Man Po Lee, Nagalingeswaran Kumarasamy, Jialun Zhou, Thira Sirisanthana, Patrick C. K. Li, Adeeba Kamarulzaman, Shinichi Oka, Praphan Phanuphak, Saphonn Vonthanak, Tuti P. Merati, Yi-Ming A. Chen, Somnuek Sungkanuparph, Goa Tau, Fujie Zhang, Christopher K. C. Lee, Rossana Ditangco, Sanjay Pujari, Jun Y. Choi, Jeffery Smith, and Matthew G. Law

National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Sydney, Australia (P.S., J.Z., M.J.L.); Tan Tock Seng Hospital, Singapore (P.L.L.); Queen Elizabeth Hospital, Hong Kong (M.P.L., P.C.K.L.), and Beijing Ditan Hospital, Beijing (F.Z.), China; Y. R. Gaitonde Centre for AIDS Research and Education, Chennai (N.K.), and Institute of Infectious Diseases, Pune (S.P), India; Research Institute for Health Sciences, Chiang Mai (T.S.), and HIV–Netherlands Australia Thailand/Thai Red Cross AIDS Research Centre (P.P.) and Ramathibodi Hospital, Mahidol University (S.S.), Bangkok, Thailand; University of Malaya (A.K.) and Hospital Sungai Buloh (C.K.C.L.), Kuala Lumpur, Malaysia; International Medical Centre of Japan, Tokyo, Japan (S.O.); National Center for HIV/AIDS, Dermatology and Sexually Transmitted Diseases, Phnom Penh, Cambodia (V.S.); Faculty of Medicine Udayana University and Sanglah Hospital, Bali, Indonesia (T.P.M.); Taipei Veterans General Hospital and AIDS Prevention and Research Centre, National Yang-Ming University, Taipei, Taiwan (Y.M.A.C.); Port Moresby General Hospital, Port Moresby, Papua New Guinea (G.T.); Research Institute for Tropical Medicine, Manila, Philippines (R.D.); Department of Internal Medicine, Division of Infectious Diseases, Yonsei University College of Medicine, Seoul, South Korea (J.Y.C.); and The Foundation for AIDS Research, New York, New York (J.S.).

### Abstract

**Objective**—The aim of our study was to develop, on the basis of simple clinical data, predictive short-term risk equations for AIDS or death in Asian patients infected with human immunodeficiency virus (HIV) who were included in the TREAT Asia HIV Observational Database.

**Methods**—Inclusion criteria were highly active antiretroviral therapy initiation and completion of required laboratory tests. Predictors of short-term AIDS or death were assessed using Poisson regression. Three different models were developed: a clinical model, a CD4 cell count model, and a CD4 cell count and HIV RNA level model. We separated patients into low-risk, high-risk, and very high-risk groups according to the key risk factors identified.

**Results**—In the clinical model, patients with severe anemia or a body mass index (BMI; calculated as the weight in kilograms divided by the square of the height in meters)  $\leq 18$  were at very high risk, and patients who were aged  $< 40$  years or were male and had mild anemia were at high risk. In the CD4 cell count model, patients with a CD4 cell count  $< 50$  cells/ $\mu$ L, severe anemia, or a BMI  $\leq 18$  were at very high risk, and patients who had a CD4 cell count of 51–200 cells/ $\mu$ L, were aged  $< 40$

years, or were male and had mild anemia were at high risk. In the CD4 cell count and HIV RNA level model, patients with a CD4 cell count  $<50$  cells/ $\mu\text{L}$ , a detectable viral load, severe anemia, or a BMI  $\leq 18$  were at very high risk, and patients with a CD4 cell count of 51–200 cells/ $\mu\text{L}$  and mild anemia were at high risk. The incidence of new AIDS or death in the clinical model was 1.3, 4.9, and 15.6 events per 100 person-years in the low-risk, high-risk, and very high-risk groups, respectively. In the CD4 cell count model the respective incidences were 0.9, 2.7, and 16.02 events per 100 person-years; in the CD4 cell count and HIV RNA level model, the respective incidences were 0.8, 1.8, and 6.2 events per 100 person-years.

**Conclusions**—These models are simple enough for widespread use in busy clinics and should allow clinicians to identify patients who are at high risk of AIDS or death in Asia and the Pacific region and in resource-poor settings.

Risk equations to identify HIV-infected patients at high risk of AIDS or death have been established on the basis of populations in developed country [1,2]. Use of these risk equations to identify HIV-infected patients at high short-term risk of AIDS or death would allow clinicians to attempt to intervene. The risk equations can also be used to stratify patient risk in randomized clinical trials, thus ensuring unbiased treatment comparisons [2].

Factors found to be related to disease progression or death are current hemoglobin level, CD4 cell count, body mass index (BMI; calculated as the weight in kilograms divided by the square of the height in meters), previous AIDS-defining illness, and injection drug use as the mode of HIV acquisition [2–8]. Risk equations have been developed predominantly for white populations in developed countries; their validity when extrapolated to other populations in developing countries is uncertain. Furthermore, the equations rely on diagnostic tests that are routinely used in developed countries but that are not widely available in resource-limited settings; thus, the application of these equations in developing countries may be problematic. For example, the recent model developed by Mocroft et al. [2] requires multiple CD4 cell count measurements for a CD4 cell count slope to be calculated; however, measurement of CD4 cell count may not be feasible in resource-limited settings.

There have been some efforts to develop simple predictive risk equations for use in resource-limited settings. The Anti-retroviral Treatment (ART) in Lower Income Countries (ART-LINC) Collaboration developed a risk equation for AIDS or death for patients who initiated HAART [9–11]. A short-term risk equation for patients receiving or not receiving ART was developed on the basis of limited follow-up data on Asian populations from the Therapeutics Research, Education, and AIDS Training in Asia HIV Observational Database (TAHOD) [7]. The purpose of this analysis was to develop short-term predictive risk equations for AIDS or death in Asian populations receiving ART with use of simple clinical data that would routinely be available in resource-limited settings.

## PATIENTS AND METHODS

Analyses were based on data from patients enrolled in TAHOD. TAHOD is a collaborative observational cohort study involving 17 sites in the Asia-Pacific region. Detailed methods are published elsewhere [12]. In brief, each site recruited 200 patients, including both patients initiating HAART and patients not initiating HAART. Recruitment was based on a consecutive series of patients who regularly attended a given site beginning at a particular time. Ethical approval for the study was obtained from the University of New South Wales Ethics Committee and other local ethics committees.

Data collected in TAHOD included (1) demographic characteristics, (2) stage of disease (CD4 and CD8 cell counts, HIV RNA test date and result, AIDS-defining illness [defined according to the 1993 Center for Disease Control and Prevention revision of the AIDS case definition]

[13], and date and cause of death), and (3) treatment. All data were entirely observational; tests or interventions were performed according to clinical guidelines at each clinical site. Data were combined through standardized formats in Microsoft Excel and were transferred electronically (compressed with password protection) to the National Centre in HIV Epidemiology and Clinical Research (Sydney, Australia) for central aggregation and analysis. [12,14–17].

Analyses were based on data collected in the March 2007 data transfer. In Asia, particularly in low-income countries, standard monitoring tests, such as those used for measurement of CD4 cell count and HIV load, are not always routinely available. Therefore, in this study, we aimed to build 3 models to predict short-term disease progression, defined as a new AIDS-defining illness or death. The 3 models were (1) a clinical model (in which only clinical data were used), (2) a CD4 cell count model (in which clinical data and CD4 cell counts were used), and (3) a CD4 cell count and HIV RNA level model (in which clinical data, CD4 cell counts, and viral loads were used).

There were 3 inclusion criteria for TAHOD patients in these analyses. First, patients were included after they initiated HAART (treatment with  $\geq 3$  antiretroviral agents) and were only included if they had demographic data, BMI, hemoglobin levels, and alanine aminotransferase (ALT) levels available in TAHOD for the clinical model. Second, patients were included in the CD4 cell count model if they had all variables from the clinical model plus CD4 cell count measurements. Finally, patients included in the CD4 cell count and HIV RNA level model had all variables from the CD4 cell count model available in addition to viral load measurements. For example, if a patient initiated HAART on 15 June 2006 but had complete laboratory results for the clinical model on 15 December 2006, the first day of follow-up for this patient in the analysis would be 15 December 2006, and the characteristics at that time would be included in the analyses.

Poisson regression was used to determine factors associated with the short-term risk of clinical progression. The follow-up period began on the date of initiation of HAART (baseline) and ended at the time of first diagnosis of new AIDS, at the time of death from any cause, or at the last follow-up visit for patients who did not experience clinical progression. Patient follow-up was left-censored until the patient had all prognostic variables available. Explanatory variables were first included in univariate analyses. Baseline variables included sex, HIV exposure group, details of prior ART, date of HAART initiation, and AIDS diagnosis before HAART. Age, CD4 cell count, viral load, hemoglobin level, BMI, and whether or not patients were currently receiving any ART were all modeled as time-updated values, which meant that they were used to describe the risk of new AIDS or death over the short term. Continuous variables, such as CD4 cell count or age, were categorized a priori with use of commonly used cutoff values to ensure roughly equal numbers of events within each category and to allow calculation of event rates. Mild anemia was defined as a hemoglobin level of 80–120 g/L for male individuals and 80–140 g/L for female individuals. Severe anemia was defined as a hemoglobin level  $< 80$  g/L for both sexes. The ALT level was considered to be normal when it was  $< 5$  times the upper limit of normal and abnormal when it was  $\geq 5$  times the upper limit of normal. Variables with a  $P$  value  $< .1$  in univariate analyses were considered in multivariate models; categories were combined when appropriate, and a backwards stepwise procedure was used to remove variables that were not statistically significant—defined as  $P > .05$ —in this model.

We calculated risk scores for each patient with use of coefficients from Poisson regression results. Risk scores were then categorized into 3 groups (low, medium, and high) with use of cutoffs that gave roughly equal numbers of events in each class. The ability of the model to discriminate patient risk was assessed by calculating the observed incidence rate of AIDS or death within each risk score class. Statistical analyses were performed using Stata software, version 10 (StataCorp).

## RESULTS

### Patient characteristics

Of 3516 patients in TAHOD, 1679, 1663, and 1231 were eligible for inclusion in the clinical, CD4 cell count, and CD4 cell count and HIV RNA level models, respectively. Characteristics of the patients included in these 3 models are described in table 1. More than 80% of patients were aged  $\geq 30$  years in all 3 models. The majority of patients were men, and most patients had acquired HIV infection through heterosexual contact. Some degree of anemia had been experienced by ~50% of the patients at baseline (table 1).

In the clinical model, the median time at risk of disease progression or death was 1.7 years (range, <1 year to 4.20 years). There were 122 events, 87 (71.3%) of which were cases of new AIDS-defining illness and 35 (28.7%) of which were deaths. The incidence rate was 3.8 events per 100 person-years of follow-up (95% CI, 3.2–4.5 events per 100 person-years). In the CD4 cell count model, the median time at risk was 1.7 years (range, 0.003–4.20 years). There were 118 events, 84 (71.2%) of which were cases of new AIDS-defining illness and 34 (28.8%) of which were deaths. The incidence rate was 3.7 events per 100 person-years (95% CI, 3.1–4.4 events per 100 person-years). In the CD4 cell count and HIV RNA level model, the median time at risk was 2.0 years (range, 0.003–4.10 years). There were 57 events, 38 (66.7%) of which were cases of new AIDS-defining illness and 19 (33.3%) of which were deaths. The incidence rate was 2.2 events per 100 person-years (95% CI, 1.7–2.9 events per 100 person-years). Furthermore, patients received treatment for ~97% of the follow-up period, and 93% of the events in all 3 models occurred while patients were receiving ART.

### Predictive factors

Table 2–Table 4 show the significant univariate and multivariate incidence rate ratios (IRRs) of new AIDS and death, stratified by the 3 models. The TAHOD risk score was derived using the logarithm of the IRRs shown in table 2–table 4. The predictive factors for each model are detailed in the following paragraphs.

### Clinical model

Table 2 shows factors related to new AIDS or death in the clinical model. In the univariate analyses, factors related to AIDS and death were younger age ( $P < .001$ ), injection drug use as the mode of HIV transmission ( $P = .010$ ), reported previous AIDS-defining illness ( $P = .031$ ), low BMI ( $P < .001$ ), and any anemia ( $P < .001$ ).

In the multivariate model, older patients and female patients had significantly lower event rates. The rate of events was higher among patients who had a BMI  $\leq 18$  than it was among patients with a BMI of  $>18$  to 25 (IRR, 4.03; 95% CI, 2.63–6.16;  $P < .001$ ). Moreover, patients with anemia had higher rates of events than did patients with no anemia (mild anemia: IRR, 3.21 [95% CI, 2.13–4.83];  $P < .001$ ; severe anemia: IRR, 12.32 [95% CI, 5.76–26.37];  $P < .001$ ).

### CD4 cell count model

Table 3 shows factors related to new AIDS-defining illness or death in the CD4 cell count model. In univariate analyses, low CD4 cell count, in addition to the factors identified in the clinical model, was associated with AIDS or death.

Older age, higher BMI, and no anemia were all found to be associated with lower event rates in the model. Low CD4 cell count also predicted AIDS or death. The IRR among patients with a CD4 cell count of 201–350 cells/ $\mu\text{L}$  was 1.56 (95% CI, 0.84–2.86;  $P = .163$ ), the IRR among those with a CD4 cell count of 51–200 cells/ $\mu\text{L}$  was 3.79 (95% CI, 2.24–6.44;  $P < .001$ ), and

the IRR among those with a CD4 cell count  $\leq 50$  cells/ $\mu\text{L}$  was 13.38 (95% CI, 7.66–23.39;  $P < .001$ ).

### CD4 cell count and HIV RNA level model

Factors related to new AIDS and death in the CD4 cell count and HIV RNA level model are shown in table 4. In univariate analyses, factors related to AIDS and death were low BMI ( $P < .001$ ), any anemia ( $P < .001$ ), low CD4 cell count ( $P < .001$ ), and detectable viral load ( $P < .001$ ).

In the multivariate analyses, factors associated with high event rates were found to be similar to those in the clinical and CD4 cell count models. CD4 cell count also predicted AIDS or death; the IRR among patients with a CD4 cell count of 201–350 cells/ $\mu\text{L}$  was 1.34 (95% CI, 0.63–2.85;  $P = .446$ ), the IRR among those with a CD4 cell count of 51–200 cells/ $\mu\text{L}$  was 2.44 (95% CI, 1.16–5.15;  $P = .019$ ), and the IRR among those with a CD4 cell count  $\leq 50$  cells/ $\mu\text{L}$  was 6.98 (95% CI, 2.99–16.29;  $P < .001$ ). Patients with a detectable viral load had an increased event rate (IRR, 3.22; 95% CI, 1.76–5.89;  $P = .005$ ), compared with patients with an undetectable viral load.

### Risk score and risk group

On the basis of the multivariate results from each model, we then classified the patients into 3 risk score classes: low, medium, and high. All 3 classes were defined using cutoff values that gave an equal number of events in each class. The observed incidence rates of AIDS and death in each risk score class for all 3 models are summarized in figure 1. For all 3 models, although the high-risk score class had higher observed rates of AIDS and death, the low-risk and medium-risk score classes did not discriminate patient risk well. This relative poor discrimination, combined with the complexity in calculating the risk score for a given patient, prompted the development of a much simpler risk classification based solely on patients having key risk factors. For example, in the clinical model, consideration of table 2 indicates that the highest incidence rates and rate ratios for AIDS and death were among patients with a BMI  $\leq 18$  and severe anemia. Moderately increased rate ratios were observed among patients aged  $< 40$  years, male patients, and those with mild anemia.

On the basis of these observations, we developed low-risk, high-risk, and very high-risk groups for each model. These groups were based on patients simply having certain prognostic factors. These predictive factor risk groups are summarized in table 5.

We then calculated incidence rates of AIDS or death in each patient factor risk group in each model (figure 2). The incidences in the clinical model were 1.3%, 4.9%, and 15.6% in the low-risk, high-risk, and very high-risk groups, respectively. The respective incidence rates of AIDS or death in the CD4 cell count model were 0.9%, 2.7%, and 16.02%, and such incidence rates in the CD4 cell count and HIV RNA level model were 0.8%, 1.8%, and 6.2% (figure 2). In all 3 models, these patient factor risk groups appeared to discriminate well, particularly for a small group of patients with very high short-term risk of AIDS or death.

Figure 3 shows the incidence rates of AIDS or death in each risk group in each model up to 12 months. Across all 3 models, event rates were very high during the first 3 months.

## DISCUSSION

In our study, we developed predictive risk equations for application to Asian populations. We developed equations for 3 models on the basis of increasingly expensive routine monitoring, so that a predictive risk equation would be available for clinical use in all settings. Although the full risk scores did, to some extent, discriminate patients at high risk, they did not

discriminate patients at low and moderate risk very well. In addition, the scores would be difficult to calculate in busy clinical settings. Therefore, we developed simple patient risk factor groups that were easy to calculate and that appeared to identify patients at very high short-term risk of AIDS or death.

Severe anemia and very low BMI were common predictive factors of high risk in all 3 models, even those that included CD4 cell count and HIV load testing. These factors have previously been found to be predictive in both developed [3,18–22] and developing [16,23,24] countries. Younger age and male sex were found to be associated with high short-term risk of AIDS or death in our analyses. Other studies have found that older age is associated with increased risk of AIDS, particularly in untreated HIV-infected populations [25,26]. Our finding would likely reflect increased adherence to HAART in older patients and in female patients [27,28]. There is some evidence to support this in our data; 46 (62%) of 74 injection drug users were male patients aged <40 years [29]. We also found in all 3 models that patients were at highest risk during the 3 months immediately after assessment; this was particularly true for patients identified to be at very high risk. This may reflect cohort effects: patients at high risk experience clinical failure early, and patients at lower risk remain in follow-up [30]. However, it does emphasize that our patient risk factor groups identify patients at very high short-term risk of AIDS or death and the need for clinicians to intervene quickly if feasible.

Our analyses have a number of limitations. First, they are based on data that are entirely observational, and the study did not have a fixed visit structure or mandated clinical or laboratory assessments. Thus, analyses had to be based on those patients who had assessments made according to local site criteria, and this may have introduced some biases in our analyses. Our data might be under-representative of patients at high short-term risk of developing AIDS or death. However, the prognostic factors should still be the same across the groups, because our results show prognostic factors similar to those in other studies [3,18–22]. Second, the relatively limited number of available clinical events prevented models from being developed on a training dataset and then validated on a separate independent dataset. It is well known that fitting and validating models on a single dataset can lead to over-optimistic estimates of predictive value [31,32]. Furthermore, the heuristic way in which our patient risk factor groups were developed prevented validation using formal bootstrap approaches. The regression results naturally divided the patients into the 3 groups [33]. The regression coefficients divided in those that had an extremely high risk, leading to the very high risk group, and then those with a statistically significantly elevated risk (but to a lesser degree), leading to the high risk group. The low risk group comprised patients with none of the risk factors. Our patient risk factor group models do have some face validity, in that the factors identified, particularly in patients at very high short-term risk, are those that have been seen in other studies. However, our models need testing and validating in independent datasets. Third, our analyses of more-complex models, particularly those that include HIV load, are more limited with regard to patients that could be included. It is notable that the patient risk factor groups in the CD4 cell count and HIV RNA level model had lower absolute risks than did the groups in the other models. We believe that this reflects the slightly different patient subgroups that were included in this analysis. These patients could possibly live in Asian countries with more-developed economies that presumably have more ART options (and other clinical treatments) available, leading to overall lower absolute risk of AIDS and death. In addition, these patients may have a higher rate of undetectable viral load than do untreated patients, and a significant proportion of patients who had detectable viral loads might have partial viral suppression, with a reduced rate of disease progression.

There is some strength to our analyses. First, we used the only risk equations developed in and for application to Asian populations in developing countries. Second, our patient risk factor group models are very simple to apply. Patients at very high short-term risk of AIDS

progression or death were simply identified using a limited number of laboratory tests and patient demographic factors; thus, these methods are feasible for use in even the busiest clinics. This contrasts with other risk equations, which often require complex calculations and more-expensive laboratory markers.

In this analysis, we developed simple patient risk factor groups that were developed in and for application to Asia populations that identify patients at high short-term risk of AIDS or death. The models are simple enough to allow widespread use in busy clinics, with different models developed for different resource settings. These models should allow clinicians to identify patients at highest short-term risk of AIDS or death and to possibly provide early intervention.

## THE TREAT ASIA HIV OBSERVATIONAL DATABASE

C. V. Mean,<sup>a</sup> V. Saphonn,<sup>a</sup> and K. Vohith (National Center for HIV/AIDS, Dermatology & STDs, Phnom Penh, Cambodia); F. J. Zhang<sup>a,b</sup>, H. X. Zhao, and N. Han (Beijing Ditan Hospital, Beijing, China); P. C. K. Li<sup>a,c</sup> and M. P. Lee (Queen Elizabeth Hospital, Hong Kong, China); N. Kumarasamy<sup>a</sup> and S. Saghayam (YRG Centre for AIDS Research and Education, Chennai, India); S. Pujari<sup>a</sup> and K. Joshi (Institute of Infectious Diseases, Pune, India); T. P. Merati<sup>a</sup> and F. Yuliana (Faculty of Medicine Udayana University & Sanglah Hospital, Bali, Indonesia); S. Oka<sup>a,c</sup> and M. Honda (International Medical Centre of Japan, Tokyo, Japan); J. Y. Choi<sup>a</sup> and S. H. Han (Division of Infectious Diseases, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea); C. K. C. Lee<sup>a</sup> and R. David (Hospital Sungai Buloh, Kuala Lumpur, Malaysia); A. Kamarulzaman<sup>a</sup> and A. Kajindran (University of Malaya, Kuala Lumpur, Malaysia); G. Tau<sup>a</sup> (Port Moresby General Hospital, Port Moresby, Papua New Guinea); R. Ditangco<sup>a</sup> and R. Capistrano (Research Institute for Tropical Medicine, Manila, Philippines); Y. M. A. Chen,<sup>a</sup> W. W. Wong, and Y. W. Yang (Taipei Veterans General Hospital and AIDS Prevention and Research Centre, National Yang-Ming University, Taipei, Taiwan); P. L. Lim,<sup>a</sup> C. C. Lee, and E. Foo (Tan Tock Seng Hospital, Singapore); P. Phanuphak<sup>a</sup> and M. Khongphattanyothing (HIV-NAT/Thai Red Cross AIDS Research Centre, Bangkok, Thailand); S. Sungkanuparph<sup>a</sup> and B. Piyavong (Ramathibodi Hospital, Mahidol University, Bangkok, Thailand); T. Sirisanthana<sup>a</sup> and W. Kotarat (Research Institute for Health Sciences, Chiang Mai, Thailand); J. Chuah<sup>a</sup> (Gold Coast Sexual Health Clinic, Miami, Queensland, Australia); K. Frost,<sup>a</sup> J. Smith,<sup>a</sup> and B. Nakornsri (The Foundation for AIDS Research, New York); and D. A. Cooper,<sup>a</sup> M. G. Law,<sup>a</sup> K. Petoumenos, R. Oyomopito, and J. Zhou<sup>a</sup> (National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Sydney, Australia).

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<sup>a</sup>Steering committee member

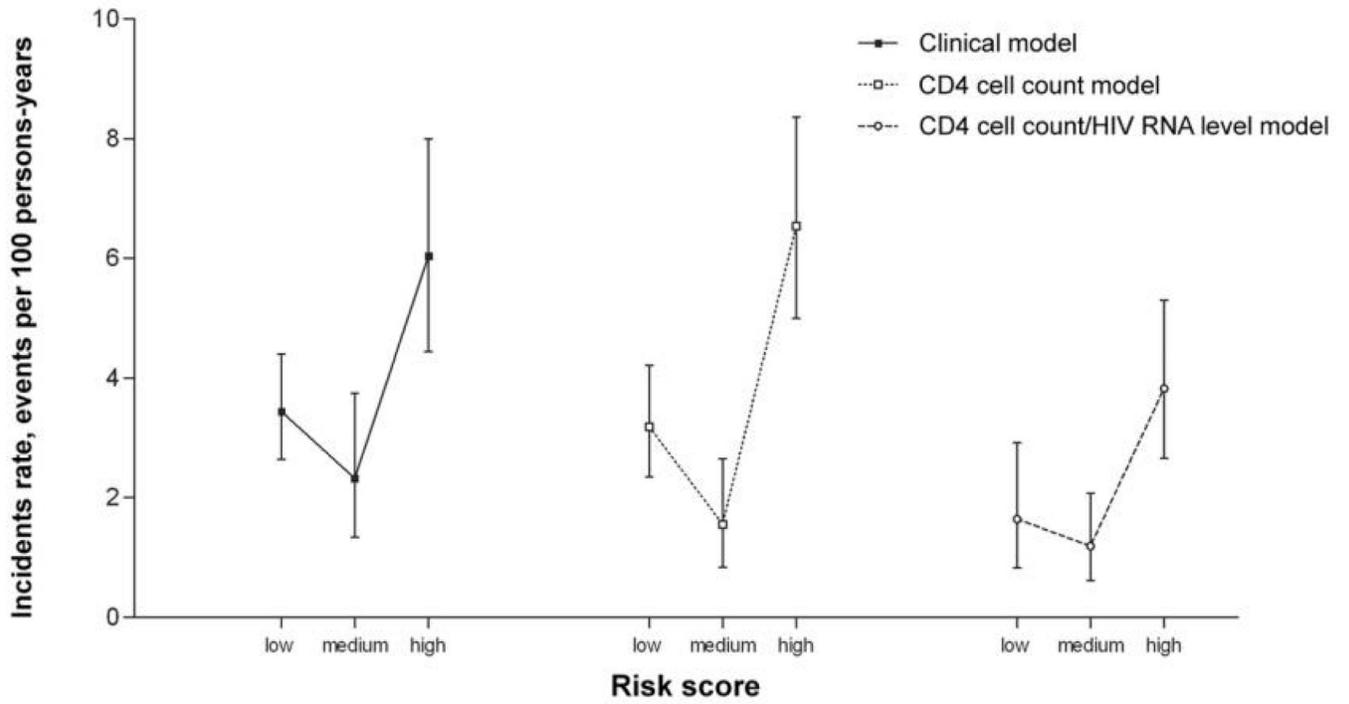
<sup>b</sup>Current steering committee chair

<sup>c</sup>Cochair.

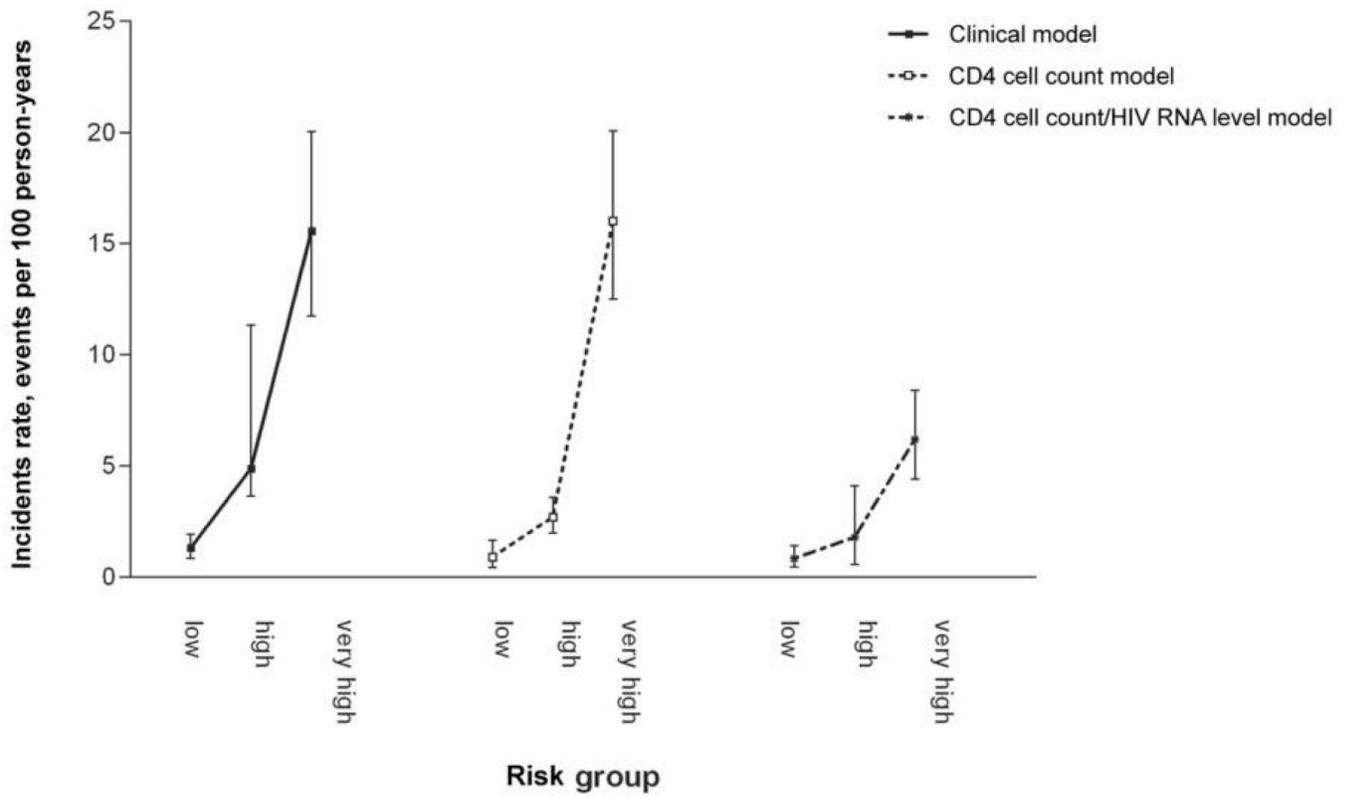
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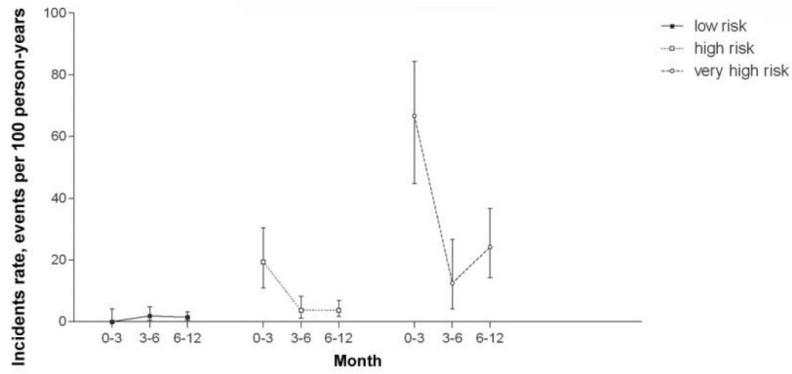
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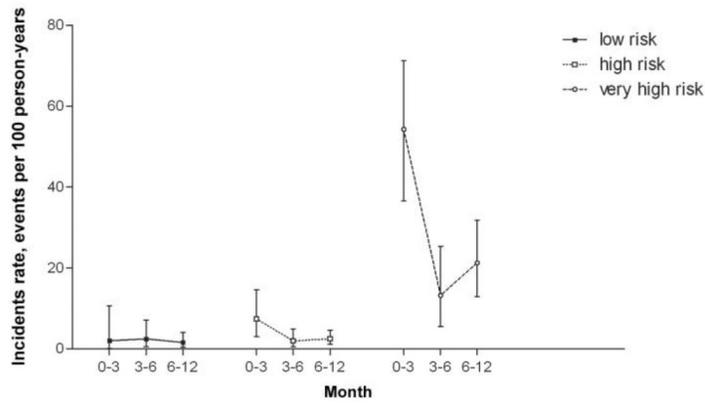
**Figure 1.**  
Incidence of new AIDS or death, by risk score class



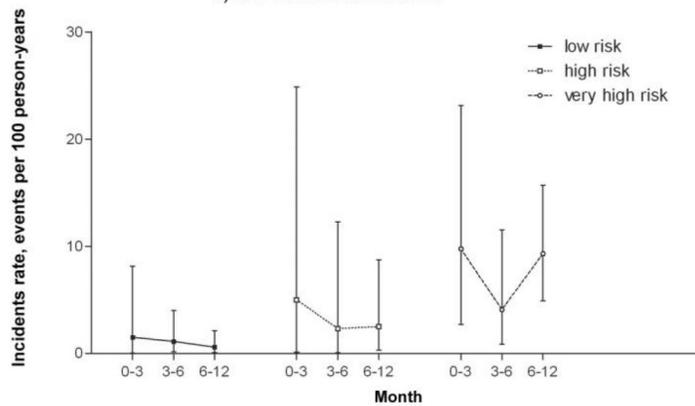
**Figure 2.**  
Incidence of new AIDS or death, by patient risk factor group



a) Clinical Model



b) CD4 cell count model



c) CD4 cell count/HIV RNA level model

**Figure 3.** Incidence of new AIDS or death in the clinical model (a), CD4 cell count model (b), and CD4 cell count and HIV RNA level model (c) during the 12-month follow-up period, by patient risk factor group.

**Table 1**

Baseline characteristics of the study patients.

| Characteristic                     | No. (%) of patients          |                                          |                                                               |
|------------------------------------|------------------------------|------------------------------------------|---------------------------------------------------------------|
|                                    | Clinical model<br>(n = 1679) | CD4<br>cell count<br>model<br>(n = 1663) | CD4<br>cell count and<br>HIV RNA level<br>model<br>(n = 1231) |
| Age, years                         |                              |                                          |                                                               |
| ≥40                                | 693 (41.27)                  | 688 (41.37)                              | 571 (46.39)                                                   |
| 30–39                              | 767 (45.68)                  | 760 (45.70)                              | 538 (43.70)                                                   |
| ≤29                                | 219 (13.04)                  | 215 (12.93)                              | 122 (9.91)                                                    |
| Sex                                |                              |                                          |                                                               |
| Male                               | 1207 (71.89)                 | 1199 (72.10)                             | 907 (73.68)                                                   |
| Female                             | 472 (28.11)                  | 464 (27.90)                              | 324 (26.32)                                                   |
| Mode of HIV transmission           |                              |                                          |                                                               |
| Heterosexual sex                   | 1217 (72.48)                 | 1203 (72.34)                             | 816 (66.29)                                                   |
| IDU                                | 74 (4.41)                    | 72 (4.33)                                | 44 (3.57)                                                     |
| MSM                                | 310 (18.46)                  | 310 (18.64)                              | 304 (24.70)                                                   |
| Other                              | 78 (4.65)                    | 78 (4.69)                                | 67 (5.44)                                                     |
| ART status before HAART initiation |                              |                                          |                                                               |
| Naive                              | 1351 (80.46)                 | 1336 (80.34)                             | 935 (75.95)                                                   |
| Experienced                        | 328 (19.54)                  | 327 (19.66)                              | 296 (24.05)                                                   |
| Previous AIDS-defining illness     |                              |                                          |                                                               |
| No                                 | 830 (49.43)                  | 821 (49.37)                              | 630 (51.18)                                                   |
| Yes                                | 849 (50.57)                  | 842 (50.63)                              | 601 (48.82)                                                   |
| BMI category                       |                              |                                          |                                                               |
| ≤18                                | 195 (16.74)                  | 192 (11.55)                              | 114 (9.26)                                                    |
| >18 to 25                          | 1203 (71.65)                 | 1191 (71.62)                             | 897 (72.87)                                                   |
| >25                                | 281 (16.74)                  | 280 (16.84)                              | 220 (17.87)                                                   |
| ART status                         |                              |                                          |                                                               |
| Not receiving ART                  | 51 (3.04)                    | 51 (3.07)                                | 39 (3.17)                                                     |
| Receiving ART                      | 1628 (96.96)                 | 1612 (96.93)                             | 1192 (96.83)                                                  |
| Anemia                             |                              |                                          |                                                               |
| None                               | 855 (50.92)                  | 854 (51.35)                              | 734 (59.63)                                                   |
| Mild                               | 797 (47.47)                  | 783 (47.08)                              | 490 (39.81)                                                   |
| Severe                             | 27 (1.61)                    | 26 (1.56)                                | 7 (0.57)                                                      |
| ALT level, IU/L                    |                              |                                          |                                                               |
| Normal                             | 1664 (99.11)                 | 1647 (99.04)                             | 1223 (99.35)                                                  |
| Abnormal                           | 15 (0.89)                    | 16 (0.96)                                | 8 (0.65)                                                      |
| CD4 cell count, cells/μL           |                              |                                          |                                                               |
| ≤50                                | ...                          | 135 (8.12)                               | 44 (3.57)                                                     |
| 51–200                             | ...                          | 431 (25.92)                              | 257 (20.88)                                                   |
| 201–350                            | ...                          | 499 (30.01)                              | 401 (32.58)                                                   |
| >350                               | ...                          | 598 (35.96)                              | 529 (42.97)                                                   |

| Characteristic      | No. (%) of patients          |                                          |                                                               |
|---------------------|------------------------------|------------------------------------------|---------------------------------------------------------------|
|                     | Clinical model<br>(n = 1679) | CD4<br>cell count<br>model<br>(n = 1663) | CD4<br>cell count and<br>HIV RNA level<br>model<br>(n = 1231) |
| HIV load, copies/mL |                              |                                          |                                                               |
| ≤500                | ...                          | ...                                      | 934 (75.87)                                                   |
| >500                | ...                          | ...                                      | 297 (24.13)                                                   |

**NOTE.** ALT, alanine aminotransferase; ART, antiretroviral treatment; BMI, body mass index (calculated as the weight in kilograms divided by the square of the height in meters); IDU, injection drug use; MSM, men who have sex with men.

**Table 2**  
 Predictive factors for AIDS or death outcome in 1679 patients in the clinical model.

| Factor                         | Person-years | No. of events | Incidence rate | Univariate analysis |       | Multivariate analysis |       |
|--------------------------------|--------------|---------------|----------------|---------------------|-------|-----------------------|-------|
|                                |              |               |                | IRR (95% CI)        | P     | IRR (95% CI)          | P     |
| Overall                        | 3205.72      | 122           | 3.80           | ...                 | <.001 | ...                   | <.001 |
| Age, years                     |              |               |                |                     |       |                       |       |
| ≥40                            | 1561.97      | 44            | 2.82           | 1.00                |       | 1.00                  |       |
| 30–39                          | 1381.73      | 55            | 3.98           | 1.41 (0.95–2.10)    | .089  | 1.55 (1.03–2.33)      | .034  |
| ≤29                            | 262.02       | 23            | 8.78           | 3.12 (1.86–5.21)    | <.001 | 3.17 (1.88–5.37)      | <.001 |
| Sex                            |              |               |                |                     |       |                       |       |
| Male                           | 2401.50      | 98            | 4.08           | 1.00                |       | 1.00                  |       |
| Female                         | 804.22       | 24            | 2.98           | 0.73 (0.46–1.15)    | .174  | 0.54 (0.33–0.87)      | .011  |
| Mode of HIV transmission       |              |               |                |                     |       |                       |       |
| Heterosexual sex               | 2282.40      | 91            | 3.99           | 1.00                |       | ...                   |       |
| IDU                            | 122.48       | 11            | 8.98           | 2.25 (1.19–4.28)    | .013  | ...                   |       |
| MSM                            | 632.92       | 15            | 2.37           | 0.59 (0.34–1.03)    | .063  | ...                   |       |
| Other                          | 167.91       | 5             | 2.98           | 0.75 (0.30–1.85)    | 0.528 | ...                   |       |
| ART status before HAART        |              |               |                |                     |       |                       |       |
| Naive                          | 2354.04      | 97            | 4.12           | 1.00                | ...   | ...                   |       |
| Experienced                    | 851.67       | 25            | 2.93           | 0.71 (0.46–1.11)    | 0.136 | ...                   |       |
| Previous AIDS-defining illness |              |               |                |                     |       |                       |       |
| No                             | 1553.39      | 47            | 3.02           | 1.00                |       | ...                   |       |
| Yes                            | 1652.33      | 75            | 4.54           | 1.50 (1.04–2.17)    | .031  | ...                   |       |
| BMI                            |              |               |                |                     |       |                       |       |
| ≤18                            | 285.88       | 41            | 14.34          | 5.05 (3.38–7.53)    | <.001 | 4.03 (2.63–6.16)      | <.001 |
| >18 to 25                      | 2357.44      | 67            | 2.84           | 1.00                |       | 1.00                  |       |
| >25                            | 562.39       | 14            | 2.49           | 0.88 (0.49–1.56)    | .652  | 1.02 (0.57–1.82)      | .942  |
| ART status                     |              |               |                |                     |       |                       |       |
| Not receiving ART              | 82.710       | 8             | 9.67           | 1.00                |       | ...                   |       |
| Receiving ART                  | 3123.01      | 114           | 3.65           | 0.38 (0.19–0.76)    | .006  | ...                   |       |
| Anemia                         |              |               |                |                     |       |                       |       |
| None                           | 1944.09      | 33            | 1.70           | 1.00                | <.001 | 1.00                  | <.001 |
| Mild                           | 1221.49      | 78            | 6.38           | 3.76 (2.51–5.65)    | <.001 | 3.21 (2.13–4.83)      | <.001 |

| Factor          | Person-years | No. of events | Incidence rate | Univariate analysis |       | Multivariate analysis |       |
|-----------------|--------------|---------------|----------------|---------------------|-------|-----------------------|-------|
|                 |              |               |                | IRR (95% CI)        | P     | IRR (95% CI)          | P     |
| Severe          | 39.13        | 11            | 28.1           | 16.56 (8.25–33.23)  | <.001 | 12.32 (5.76–26.36)    | <.001 |
| ALT level, IU/L |              |               |                |                     |       |                       |       |
| Normal          | 3185.22      | 121           | 3.80           | 1.00                | ...   | ...                   | ...   |
| Abnormal        | 20.491       | 1             | 4.88           | 1.28 (0.18–9.034)   | .801  | ...                   | ...   |

**NOTE.** ALT, alanine aminotransferase; ART, antiretroviral therapy; BMI, body mass index (calculated as the weight in kilograms divided by the square of the height in meters); IDU, injection drug use; IRR, incidence rate ratio; MSM, men who have sex with men.

**Table 3**  
 Predictive factors for AIDS or death outcome on 1663 patients in the CD4 cell count model.

| Factor                         | Person-years | No. of events | Incidence rate | Univariate analysis |       | Multivariate analysis |       |
|--------------------------------|--------------|---------------|----------------|---------------------|-------|-----------------------|-------|
|                                |              |               |                | IRR (95% CI)        | P     | IRR (95% CI)          | P     |
| Overall                        | 3198.18      | 118           | 3.69           | ...                 | ...   | ...                   | ...   |
| Age, years                     |              |               |                |                     |       |                       |       |
| ≥ 40                           | 1557.84      | 43            | 2.76           | 1.00                |       | 1.00                  | <.011 |
| 30–39                          | 1380.13      | 52            | 3.77           | 1.36 (0.91–2.05)    | .133  | 1.22 (0.81–1.84)      | .344  |
| ≤ 29                           | 260.21       | 23            | 8.84           | 3.20 (1.91–5.37)    | <.001 | 2.36 (1.41–3.96)      | .001  |
| Sex                            |              |               |                |                     |       |                       |       |
| Male                           | 2395.38      | 96            | 4.01           | 1.00                |       | ...                   | ...   |
| Female                         | 802.80       | 22            | 2.74           | 0.68 (0.43–1.09)    | .111  | ...                   | ...   |
| Mode of HIV transmission       |              |               |                |                     |       |                       |       |
| Heterosexual sex               | 2277.95      | 88            | 3.87           | 1.00                |       | ...                   | ...   |
| IDU                            | 119.72       | 10            | 8.35           | 2.16 (1.10–4.24)    | .025  | ...                   | ...   |
| MSM                            | 632.92       | 15            | 2.37           | 0.61 (0.35–1.06)    | .081  | ...                   | ...   |
| Other                          | 167.59       | 5             | 2.98           | 0.77 (0.31–1.91)    | .577  | ...                   | ...   |
| ART status before HAART        |              |               |                |                     |       |                       |       |
| Naive                          | 2348.44      | 94            | 4.00           | 1.00                |       | ...                   | ...   |
| Experienced                    | 849.74       | 24            | 2.82           | 0.71 (0.45–1.11)    | .133  | ...                   | ...   |
| Previous AIDS-defining illness |              |               |                |                     |       |                       |       |
| No                             | 1551.52      | 44            | 2.83           | 1.00                |       | ...                   | ...   |
| Yes                            | 1646.66      | 74            | 4.49           | 1.58 (1.09–2.31)    | .017  | ...                   | ...   |
| BMI                            |              |               |                |                     |       |                       |       |
| ≤ 18                           | 285.16       | 41            | 14.38          | 5.37 (3.58–8.05)    | <.001 | 2.61 (1.71–3.97)      | <.001 |
| >18 to 25                      | 2351.23      | 63            | 2.68           | 1.00                |       | 1.00                  |       |
| >25                            | 561.79       | 14            | 2.49           | 0.93 (0.52–1.66)    | .806  | 1.12 (0.64–1.98)      | .685  |
| ART status                     |              |               |                |                     |       |                       |       |
| Not receiving ART              | 82.71        | 8             | 9.67           | 1.00                |       | ...                   | ...   |
| Receiving ART                  | 3115.47      | 110           | 3.53           | 0.36 (0.18–0.73)    | .005  | ...                   | ...   |
| Anemia                         |              |               |                |                     |       |                       |       |
| None                           | 1942.84      | 32            | 1.65           | 1.00                |       | 1.00                  | <.001 |
| Mild                           | 1215.72      | 76            | 6.25           | 3.79 (2.51–5.73)    | <.001 | 2.02 (1.35–3.04)      | .001  |

| Factor                         | Person-years | No. of events | Incidence rate | Univariate analysis |       | Multivariate analysis |       |
|--------------------------------|--------------|---------------|----------------|---------------------|-------|-----------------------|-------|
|                                |              |               |                | IRR (95% CI)        | P     | IRR (95% CI)          | P     |
| Severe                         | 38.62        | 10            | 25.89          | 15.72 (7.64–32.33)  | <.001 | 7.73 (3.84–15.55)     | .001  |
| CD4 cell count, cells/ $\mu$ L |              |               |                |                     |       |                       |       |
| $\leq 50$                      | 108.53       | 37            | 34.09          | 26.94 (15.82–45.86) | .094  | 13.38 (7.66–23.39)    | <.001 |
| 51–200                         | 573.43       | 40            | 6.98           | 5.51 (3.23–9.41)    | <.001 | 3.79 (2.24–6.44)      | <.001 |
| 201–350                        | 935.98       | 21            | 2.24           | 1.77 (0.96–3.27)    | .066  | 1.55 (0.84–2.86)      | .163  |
| >350                           | 1580.25      | 20            | 1.27           | 1.00                |       | 1.00                  |       |
| ALT level, IU/L                |              |               |                |                     |       |                       |       |
| Normal                         | 3177.69      | 117           | 3.68           | 1.00                | ...   | ...                   |       |
| Abnormal                       | 20.49        | 1             | 4.88           | 1.32 (0.19–9.32)    | .777  | ...                   |       |

**NOTE.** ALT, alanine aminotransferase; ART, antiretroviral therapy; BMI, body mass index (calculated as the weight in kilograms divided by the square of the height in meters); IDU, injection drug use; IRR, incidence rate ratio; MSM, men who have sex with men.

**Table 4**  
 Predictive factors for AIDS or death in 1231 patients in the CD4 cell count and HIV RNA level model.

| Factor                         | Person-years | No of events | Incidence rate | Univariate analysis |       | Multivariate analysis |       |
|--------------------------------|--------------|--------------|----------------|---------------------|-------|-----------------------|-------|
|                                |              |              |                | IRR (95% CI)        | P     | IRR (95% CI)          | P     |
| Overall                        | 2568.02      | 57           | 2.2            | ...                 | ...   | ...                   | ...   |
| Age, years                     |              |              |                |                     |       |                       |       |
| ≥40                            | 1367.05      | 29           | 2.12           | 1.00                | .004  | ...                   | ...   |
| 30–39                          | 1043.23      | 21           | 2.01           | 0.95 (0.54–1.664)   | .855  | ...                   | ...   |
| ≤29                            | 157.77       | 7            | 4.43           | 2.09 (0.92–4.76)    | .079  | ...                   | ...   |
| Sex                            |              |              |                |                     |       |                       |       |
| Male                           | 1939.82      | 45           | 2.32           | 1.00                | ...   | ...                   | ...   |
| Female                         | 628.23       | 12           | 1.91           | 0.82 (0.43–1.56)    | .550  | ...                   | ...   |
| Mode of HIV transmission       |              |              |                |                     |       |                       |       |
| Heterosexual sex               | 1733.82      | 35           | 2.02           | 1.00                | .554  | ...                   | ...   |
| IDU                            | 66.12        | 3            | 4.54           | 2.25 (0.69–7.35)    | .180  | ...                   | ...   |
| MSM                            | 621.71       | 15           | 2.41           | 1.19 (0.65–2.19)    | .564  | ...                   | ...   |
| Other                          | 146.40       | 4            | 2.73           | 1.35 (0.47–3.86)    | .572  | ...                   | ...   |
| ART status before HAART        |              |              |                |                     |       |                       |       |
| Naive                          | 1784.76      | 44           | 2.47           | 1.00                | ...   | ...                   | ...   |
| Experienced                    | 783.29       | 13           | 1.66           | 0.67 (0.36–1.25)    | .212  | ...                   | ...   |
| Previous AIDS-defining illness |              |              |                |                     |       |                       |       |
| No                             | 1304.85      | 24           | 1.84           | 1.00                | ...   | ...                   | ...   |
| Yes                            | 1263.20      | 33           | 2.61           | 1.42 (0.84–2.41)    | .192  | ...                   | ...   |
| BMI                            |              |              |                |                     |       |                       |       |
| ≤18                            | 200.99       | 19           | 9.45           | 5.99 (3.33–10.76)   | <.001 | 2.98 (1.56–5.68)      | .004  |
| >18 to 25                      | 1901.22      | 30           | 1.58           | 1.00                | <.001 | 1.00                  | .001  |
| >25                            | 465.83       | 8            | 1.72           | 1.09 (0.50–2.38)    | .832  | 1.23 (0.56–2.70)      | .604  |
| ART status                     |              |              |                |                     |       |                       |       |
| Not receiving ART              | 59.17        | 4            | 6.76           | 1.00                | ...   | ...                   | ...   |
| Receiving ART                  | 2508.88      | 53           | 2.11           | 0.31 (0.12–0.84)    | .021  | ...                   | ...   |
| CD4 cell count, cells/μL       |              |              |                |                     |       |                       |       |
| ≤50                            | 50.32        | 15           | 29.81          | 29.87 (15.29–58.36) | <.001 | 6.98 (2.99–16.29)     | <.001 |
| 51–200                         | 346.80       | 15           | 4.32           | 4.33 (2.09–8.98)    | <.001 | 2.44 (1.16–5.15)      | .019  |

| Factor              | Person-years | No of events | Incidence rate | Univariate analysis |       | Multivariate analysis |       |
|---------------------|--------------|--------------|----------------|---------------------|-------|-----------------------|-------|
|                     |              |              |                | IRR (95% CI)        | P     | IRR (95% CI)          | P     |
| 201–350             | 767.83       | 13           | 1.69           | 1.70 (0.80–3.60)    | .169  | 1.34 (0.63–2.85)      | .446  |
| >350                | 1403.09      | 14           | 1.00           | 1.00                |       | 1.00                  |       |
| HIV load, copies/mL |              |              |                |                     |       |                       |       |
| ≤ 500               | 2129.95      | 24           | 1.13           | 1.00                |       | 1.00                  |       |
| >500                | 438.10       | 33           | 4.53           | 6.68 (3.96–11.27)   | <.001 | 3.22 (1.76–5.89)      | <.001 |
| Anemia              |              |              |                |                     |       |                       |       |
| None                | 1705.83      | 23           | 1.35           | 1.00                |       | 1.00                  |       |
| Mild                | 836.21       | 34           | 4.07           | 3.01 (1.78–5.11)    | <.001 | 1.77 (1.07–2.93)      | .028  |
| Severe              | 26.01        | 0            | 0.00           | 0                   | <.001 | 0                     | <.001 |
| ALT level, IU/L     |              |              |                |                     |       |                       |       |
| Normal              | 2553.11      | 56           | 2.19           | 1.00                |       | ...                   |       |
| Abnormal            | 14.93        | 1            | 6.70           | 3.05 (0.43–21.45)   | .262  | ...                   |       |

**NOTE.** ALT, alanine aminotransferase; ART, antiretroviral therapy; BMI, body mass index (calculated as the weight in kilograms divided by the square of the height in meters); IDU, injection drug use; IRR, incidence rate ratio; MSM, men who have sex with men.

**Table 5**

Characteristics of patients in each risk group, by type of model.

| Model                            | Risk group                                                                                         |                                                                          |                                                                                     |
|----------------------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
|                                  | Very high risk                                                                                     | High risk                                                                | Low risk                                                                            |
| Clinical                         | Severe anemia or BMI $\leq 18$                                                                     | Age <40 years or male sex and mild anemia                                | Age $\geq 40$ years, female sex, BMI >18, and no anemia                             |
| CD4 cell count                   | CD4 cell count $\leq 50$ cells/ $\mu$ L or severe anemia or BMI $\leq 18$                          | CD4 cell count of 51–200 cells/ $\mu$ L or age <40 years and mild anemia | No anemia and age $\geq 40$ years                                                   |
| CD4 cell count and HIV RNA level | CD4 cell count $\leq 50$ cells/ $\mu$ L or detectable viral load or severe anemia or BMI $\leq 18$ | CD4 cell count of 51–200 cells/ $\mu$ L and mild anemia                  | Undetectable viral load, BMI >18, CD4 cell count >200 cells/ $\mu$ L, and no anemia |

**NOTE.** BMI, body mass index (calculated as the weight in kilograms divided by the square of the height in meters).