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Nationwide Cohort Study of Antiretroviral Therapy Timing: Treatment Dropout and Virological Failure in China, 2011–2015

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Background. People living with human immunodeficiency virus (PLWH) are still being diagnosed late, rendering the benefits of “early” antiretroviral therapy (ART) unattainable. Therefore, we aimed to evaluate the benefits of “immediate” ART.

Methods. A nationwide cohort of PLWH in China who initiated ART January 1, 2011, to December 31, 2014 and had baseline CD4 results ≥200 cells/μL were censored at 12 months, dropout, or death, whichever came first. Treatment dropout and virological failure (viral load ≥400 copies/mL) were measured. Determinants were assessed by Cox and log-binomial regression.

Results. The cohort included 123,605 PLWH. The ≤30 days group had a significantly lower treatment dropout rate of 6.72%, compared to 8.91% for the 91–365 days group and to 12.64% for the >365 days group. The ≤30 days group also had a significantly lower virological failure rate of 5.45% (31–90 days: 7.39%; 91–365 days: 9.64%; >365 days: 12.67%). Greater risk of dropout (91–365 days: adjusted hazard ratio [aHR] = 1.33, 95% confidence interval [CI] = 1.25–1.42; >365 days: aHR = 1.55, CI = 1.47–1.54), and virological failure (31–90 days: adjusted risk ratio [aRR] = 1.35, CI = 1.26–1.45; 91–365 days: aRR = 1.66, CI = 1.55–1.78; >365 days: aRR = 1.85, CI = 1.74–1.97) were observed for those who delayed treatment.

Conclusions. ART within 30 days of HIV diagnosis was associated with significantly reduced risk of treatment failure, highlighting the need to implement test-and-immediately-treat policies.

Keywords. HIV/AIDS; antiretroviral therapy; treatment dropout; virological failure; China.

The benefits of “early” antiretroviral therapy (ART) initiation when CD4 counts are still high are well accepted. Studies have shown reduced risk of clinical events, increased odds of virological suppression, and prolonged survival [1, 2], as well as reduced risk of tuberculosis and some cancers [3, 4], and decreased sexual and mother-to-child transmission [5–7]. Thus, early ART is now recommended for all people living with human immunodeficiency virus (PLWH) [8, 9]. However, in real-world settings, many PLWH continue to be diagnosed late. These “late presenters” already have low CD4 counts and thereby have missed the opportunity to receive “early” ART.

Therefore, in many settings, the focus has turned from “early” to “immediate” ART [2, 10–12], or ART initiation quickly after diagnosis, regardless of CD4 count.

Several projects in China have strived for earlier human immunodeficiency virus (HIV) diagnosis, faster ART initiation, and better retention in care, by expanding testing and treatment and streamlining the care cascade. Newly diagnosed PLWH were encouraged to promptly initiate ART regardless of CD4 count despite national guidelines restricting ART eligibility by CD4 level until early 2016. One study since found that time from diagnosis to ART initiation was reduced to a median of 5 days, ART initiation rose to 91% within 1 year, and mortality fell by 62% [13]. In another study, odds of achieving testing completeness (HIV, CD4, and viral load [VL] testing) within 30 days increased 20-fold, odds of initiating ART within 90 days increased 3.5-fold, and mortality declined by nearly 60% [14].

We hypothesized that immediate ART would reduce treatment dropout and virological failure, and we conducted a nationwide cohort study of patients in China’s National Free ART Program (NFATP) to evaluate these outcomes and their determinants.
**METHODS**

**Design**
A nationwide observational cohort study was conducted among NFATP patients who initiated ART between January 1, 2011, and December 31, 2014. Figure 1 describes the study design. For each participant, the beginning of follow-up was the date of first ART initiation. All were followed until the date of dropout, death, or 12-month follow-up, whichever came first. The study ended December 31, 2015.

**Enrolment**
All individuals who had records of first ART initiation between January 1, 2011, and December 31, 2014 were screened for eligibility.Criteria were (a) age ≥18 years on date of first ART initiation, (b) HIV infection route self-reported as sexual contact or injecting drug use, and (c) baseline CD4 count ≥200 cells/μL. PLWH with CD4 <200 cells/μL were not eligible because of their increased odds of rapid ART uptake due to severe symptoms. Participants were excluded for inability to link their records between the 2 databases or for having no follow-up records.

**Data**
Data were extracted from China’s HIV/AIDS Comprehensive Response Information Management System (CRIMS) [15], a nationwide, real-time, reporting system that is controlled and maintained by the National Center for AIDS/STD Control and Prevention (NCAIDS) of the Chinese Center for Disease Control and Prevention (China CDC). In China, all new cases of confirmed HIV infection require CRIMS reporting. CRIMS has been described elsewhere [15], but in brief, records include demographics, HIV test dates, transmission routes, and CD4 test dates and results.

Upon initiation of ART, information must be reported into the NFATP Data System, a subsystem of CRIMS also controlled and maintained by NCAIDS, China CDC. Although the NFATP and its data system have been described previously [16–18], 2 important programmatic changes occurred during the study period in 2012. First, tenofovir disoproxil fumarate (TDF) was recommended for first-line ART regimens. Second, although the CD4 count-based ART eligibility criterion was ≤350 cells/μL over the entire study period, an exception for pregnant women, serodiscordant couples, and individuals with tuberculosis or hepatitis B coinfection was made, and these individuals were encouraged to begin ART regardless of CD4 level. NFATP Data System records include ART initiation dates, details of ART regimens, CD4 test dates and results, and VL test dates and results.

According to standard practice in China during our study, free CD4 testing was performed at treatment baseline and then repeated every 6–12 months after ART initiation. After
ART initiation, clinical follow-ups were performed at 2 weeks, 1 month, 2 months, 3 months, and every 3 months thereafter. Free VL testing was performed once every 12 months after ART initiation. Study data were extracted on June 30, 2016.

**Subgroups**

All participants were categorized into 4 groups based on their time interval from the date of HIV diagnosis and the date of first ART initiation. Patients who initiated ART within 30 days of HIV diagnosis were categorized as the “≤30 days group.” Patients who initiated ART after 30 days but within 90 days were categorized as the “31–90 days group.” Patients who initiated ART after 90 days but within 1 year were categorized as the “91–365 days group.” Finally, patients who initiated ART after 1 year were categorized as the “>365 days group.” The first outcome, treatment dropout, was assessed after this initial categorization. Subsequently, only those remaining in the cohort at the end of the 12-month follow-up period (i.e., those who did not dropout or die), and had VL test results, were again categorized into the “≤30 days group,” the “31–90 days group,” the “91–365 days group,” and the “>365 days group” for assessment of the second outcome, virological failure (Figure 1).

**Outcomes**

Treatment dropout events were defined as loss to follow-up or discontinuation of ART within 12 months after first ART initiation. Patients were censored at death or at last follow-up or at the end of the 12-month follow-up period. Virological failure was defined as VL >400 copies/mL at between 6 and 18 months after ART initiation. Because ART patients in China were provided free VL testing only once each year after ART initiation, we expanded the observational window for the virological failure outcome to ensure that we captured at least one VL test result for each participant. For those who had more than one VL test result during this window, the result nearest the 12-month follow-up date was selected. Determinants of treatment dropout and virological failure were also assessed.

**Analysis**

**Main Analyses**

Continuous variables were summarized using median and interquartile range (IQR) and categorical variables using number and percent. Characteristics of participants were compared using rank-sum test for continuous variables and χ² test for categorical variables. First ART initiation date was subtracted from latest censored date to calculate observed time, which was expressed in person-years (PY). Cox proportional hazards regression was used to assess determinants of treatment dropout, generating hazard ratios (HRs) and 95% confidence intervals (CIs). Univariate and multivariate log-bi-nomial regression models were used to assess determinants of virological failure, producing risk ratios (RRs) and CIs. All P-values were 2-sided, and P < .05 was considered statistically significant.

**Post hoc Analyses**

We performed 3 additional analyses. First, to evaluate whether there was any additional benefit to ART initiation in intervals less than 30 days, we divided the ≤30 days group into 3 smaller groups: ≤1 day, 2–7 days, and 8–30 days, and present treatment dropout and virological failure rates. Second, to evaluate whether outcomes were different for those who initiated ART at higher CD4 counts, we created a subgroup with baseline CD4 count results >350 cells/μL and present treatment dropout and virological failure rates stratified by time interval from diagnosis to treatment. Finally, to evaluate virological failure using an “intent-to-treat” (ITT) approach, all individuals who either died or dropped out of treatment were included as failures, and ITT virological failure rates are presented stratified by baseline CD4 count and time interval from diagnosis to treatment.

All statistical analyses were performed using SAS software (version 9.1.3, SAS Institute Inc., USA).

**Ethics**

This study was approved by the Institutional Review Board of NCAIDS, China CDC. All NFATP patients signed an informed consent upon entry. No additional informed consent was sought. All records were de-identified prior to analysis.

**RESULTS**

A total of 256,486 individuals were screened for study eligibility, and a total of 123,605 (48.2%) were included in the study cohort (Figure 1). Characteristics of participants are shown in Table 1. Median age was 36 years (IQR: 28–46). A majority was male (70.5%) and reported that their HIV infection route was heterosexual contact (63.5%). Median baseline CD4 count was 308 cells/μL (IQR: 257–379).

Among the 123,605 participants in our cohort, 28,883 (23.4%) initiated ART within 30 days of HIV diagnosis (≤30 days group), whereas 21,918 (17.7%) initiated ART between 31 and 90 days after HIV diagnosis (31–90 days group), 25,635 (20.7%) initiated ART between 91 and 365 days after HIV diagnosis (91–365 days group), and 47,169 (38.2%) initiated ART more than 365 days after HIV diagnosis (>365 days group; Figure 1, Table 1). Median time between HIV diagnosis and ART initiation for the ≤30 days group was 14 days (IQR: 7–21), for the 31–90 days group was 51 days (IQR: 40–67), for the 91–365 days group was 190 days (IQR: 132–264), and for the >365 days group was 998 days (IQR: 622–1649; data not shown).

Those in the ≤30 days group tended to be older (age >50: 26.4% vs 21.8% in the 31–90 days group, 19.0% in the 91–365 days group, and 10.6% in the >365 days group). A greater proportion of those in the ≤30 days group reported their HIV infection route as heterosexual contact (73.0% vs 64.5%, 64.5%, and
56.6%), whereas a larger proportion of those in the >365 days group reported injecting drug use as their route of HIV infection (25.8% vs 7.0% in the 91–365 days group, 3.4% in the 31–90 days group, and 2.4% in the ≤30 days group). A greater proportion of those in the >365 days group had higher baseline CD4 counts (>350 cells/μL: 35.9% vs 30.4%, 25.8%, and 28.0%).

### Treatment Dropout and Determinants

A total of 11,663 participants dropped out of treatment within the 12-month follow-up period (Figure 1). As shown in Table 2, the overall dropout rate for the entire study cohort was 9.44% (CI = 9.27–9.60). Treatment dropout rate was lowest for the ≤30 days group at 6.72% (CI = 6.43–7.01) and the 31–90 days group at 6.73% (CI = 6.39–7.06), followed by the 91–365 days group at 8.91% (CI = 8.56–9.26) and the >365 days group at 12.64% (CI = 12.34–12.94). Details of treatment dropout rate overall and by time from diagnosis to treatment group stratified by participant characteristics can be found in Supplementary Table S1.

As shown in Table 3, 123,605 participants contributed 114,475 PY of observed time, during which a total of 11,663 participants dropped out of treatment, for an overall dropout rate of 10.19 per 100 PY. Significantly greater risk of dropout was found among those who were aged >50 years (adjusted HR [aHR] = 1.30, CI = 1.23–1.38), reported their route of HIV infection as heterosexual contact (aHR = 2.44, CI = 2.28–2.62) or injecting drug use (aHR = 5.31, CI = 4.94–5.71), had a baseline CD4 count >350 cells/μL (aHR = 1.19, CI = 1.14–1.24), and were in the 91–365 days group (aHR = 1.33, CI = 1.25–1.42) or the >365 days group (aHR = 1.55, CI = 1.47–1.54).
Our study revealed that those who initiated ART within 30 days after diagnosis had significantly reduced rates of treatment dropout and virological failure. Furthermore, those who initiated ART in 31–90 days had a 35% greater risk of virological failure, those who initiated in 91–365 days had a 33% greater risk of treatment dropout and 66% greater risk of virological failure, and finally, those who initiated ART in >365 days had a 55% greater risk of dropout and an 85% greater risk of virological failure. Notably, individuals in our delayed ART groups tended to be middle-aged, injecting drug users, and/or have higher CD4 counts, factors that may have influenced their ability to access care. Nevertheless, this reflects real-world conditions in China. We also noticed that individuals infected via heterosexual contact had 2.44 times greater risk of dropout and 1.78 times greater risk of virological failure, compared to those infected via homosexual contact. It is possible that homosexuals in urban areas, have better access to care, and have a better compliance.

Our findings add important additional dimensions to two recent studies of interventions meant to accelerate time from testing to treatment in China. The results of those studies were dramatically increased rates of timely diagnosis and thorough clinical assessment, substantially reduced time from diagnosis to ART initiation, significantly greater rates of ART initiation, and meaningfully improved survival [13, 14]. Furthermore, an even more recent nationwide cohort study of PLWH who had baseline CD4 counts >500 cells/μL found that those who entered China’s NEATP and immediately initiated ART (<30 days after diagnosis, compared to >30 days) experienced 63% lower mortality [19]. Thus, the benefit of immediate ART is meaningful, even for those who are not diagnosed late. Of note, another recent study in China found that those with CD4 counts >500 cells/μL at baseline had greater probability of attrition (i.e., loss to follow-up or ART cessation), suggesting that these patients may require additional support to promote retention in care over time [20].

Consistent with our study, a clinical trial of a new rapid ART initiation algorithm (ART in a single clinic visit) in South Africa

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**Table 2. Main Outcome Measures and Results of Post hoc Analyses**

| Time From Diagnosis to Treatment | Entire Cohort (Baseline CD4 >200 Cells/μL) | Subgroup Including Only Those With Baseline CD4 >350 Cells/μL |
|---------------------------------|------------------------------------------|-------------------------------------------------------------|
|                                 | Treatment Dropout Rate, % (CI)            | Treatment Dropout Rate, % (CI)                              |
|                                 | Virological Failure Rate, % (CI)          | Virological Failure Rate, % (CI)                            |
|                                 | Intent-to-Treat Virological Failure Rate, % (CI) | Intent-to-Treat Virological Failure Rate, % (CI) |
| 1 day group                     | 7.86 (6.50–9.22)                          | 8.56 (6.14–10.98)                                          |
| 2–7 days group                  | 7.45 (6.79–8.11)                          | 8.72 (7.47–9.96)                                           |
| 8–30 days group                 | 6.43 (6.10–6.76)                          | 6.18 (5.55–6.81)                                           |
| ≤30 days group                  | 6.72 (6.43–7.01)                          | 7.00 (6.52–7.48)                                           |
| 31–90 days group                | 6.73 (6.39–7.06)                          | 8.12 (6.85–9.42)                                           |
| 91–365 days group               | 6.91 (6.56–7.26)                          | 9.94 (8.53–11.34)                                          |
| >365 days group                 | 12.64 (12.34–12.94)                       | 14.04 (13.51–14.56)                                        |
| Overall                         | 9.44 (9.27–9.60)                          | 10.91 (10.60–11.22)                                        |

Main outcome measures of treatment dropout and virological failure overall and for the ≤30 days group, the 31–90 days group, the 91–365 days group, and the >365 days group is presented inside the red box. Post hoc analyses for the entire cohort as well as only those participants with baseline CD4 count results >350 cells/mm², and assessed at a range of earlier time points are also presented.

Abbreviation: CI, confidence interval.
observed both an increase in retention and in viral suppression at 10 months follow-up [21]. A study in rural Uganda and Kenya found that delay in ART initiation of more than 30 days after HIV diagnosis was associated with elevated rates of treatment dropout at 12 months [22]. In Myanmar, 94% of ART-eligible study participants were on ART by 90 days, and only 3% had dropped out of treatment in a median of 13 months of follow-up [23]. A very large, retrospective analysis of newly diagnosed PLWH in high-income countries has found that immediate initiation of ART increases viral suppression earlier in follow-up [24]. Finally, a smaller study of a same-day ART intervention in the United States found reduced time to virological suppression [25]. We believe that in the China context, immediate ART eliminates the chance that newly diagnosed PLWH receive confusing or incorrect messages about HIV/AIDS treatment and care, a problem known to contribute to losses to follow-up in the pre-ART period.

These results from around the globe make a good case for movement to test-and-immediately-treat policies. However, implementation will be challenging. For China, this means that some 200,000 diagnosed but untreated PLWH should be started on ART as quickly as possible. Streamlining of the HIV care cascade will be required. To cope with increased demand for HIV services, China’s NFATP will again need to be rapidly scaled up. Moreover, close surveillance of HIV VL in ART patients via regular testing will be important for early detection of treatment failure.

Table 3. Determinants of Treatment Dropout

| Characteristics                      | Entire Cohort, N | Observed Time, PY | Dropped Out, N | Dropout Rate, per 100 PY | Unadjusted HR (CI) | P Value | Adjusted HR (CI) | P Value |
|--------------------------------------|------------------|-------------------|----------------|--------------------------|--------------------|---------|-----------------|---------|
| Overall                              | 123,605          | 114,475           | 11,663         | 10.19                    |                    |         |                 |         |
| Age, years                           |                  |                   |                |                          |                    |         |                 |         |
| 18–30                                | 39,887           | 37,545            | 3,386          | 9.02                     | 1.00               | .000    |                 |         |
| 31–50                                | 61,451           | 56,911            | 5,883          | 10.34                    | 1.14 (1.09–1.19)   | <.001   | 0.90 (0.86–0.94)| <.001   |
| >50                                  | 22,267           | 20,019            | 2,394          | 11.96                    | 1.31 (1.25–1.38)   | <.001   | 1.30 (1.23–1.38)| <.001   |
| Sex                                  |                  |                   |                |                          |                    |         |                 |         |
| Male                                 | 87,161           | 80,716            | 8,056          | 9.98                     | 0.93 (0.90–0.97)   | <.001   | 1.05 (1.01–1.10)| .061    |
| Female                               | 36,444           | 33,759            | 3,607          | 10.68                    | 1.00               |         |                 |         |
| HIV infection route                  |                  |                   |                |                          |                    |         |                 |         |
| Homosexual contact                   | 29,735           | 28,887            | 1,142          | 3.95                     | 1.00               | .000    |                 |         |
| Heterosexual contact                 | 78,465           | 72,460            | 7,402          | 10.22                    | 2.55 (2.40–2.72)   | <.001   | 2.44 (2.28–2.62)| <.001   |
| Injecting drug use                   | 15,405           | 13,128            | 3,119          | 23.76                    | 5.79 (5.41–6.19)   | <.001   | 5.31 (4.94–5.71)| <.001   |
| TB coinfection                       |                  |                   |                |                          |                    |         |                 |         |
| Yes                                  | 31,05            | 27,80             | 3,55           | 12.77                    | 1.25 (1.12–1.39)   | <.001   | 1.06 (0.95–1.17)| .32     |
| No                                   | 120,500          | 111,695           | 11,308         | 10.12                    | 1.00               |         |                 |         |
| Hepatitis B coinfection              |                  |                   |                |                          |                    |         |                 |         |
| Yes                                  | 41,216           | 38,158            | 3,683          | 9.65                     | 1.00               | .000    |                 |         |
| No                                   | 82,220           | 76,660            | 7,39           | 9.65                     | 1.09 (1.01–1.18)   | .022    | 1.15 (1.06–1.24)| .001    |
| Not tested                           | 74,169           | 68,656            | 7,241          | 10.55                    | 1.00 (0.92–1.08)   | .998    | 1.10 (1.01–1.19)| .022    |
| Serodiscordant couple                |                  |                   |                |                          |                    |         |                 |         |
| Yes                                  | 28,175           | 26,113            | 2,630          | 10.07                    | 1.00               | .000    |                 |         |
| No                                   | 95,430           | 88,362            | 9,033          | 10.22                    | 1.01 (0.97–1.06)   | .522    | 1.10 (1.06–1.15)| <.001   |
| Baseline CD4 count (cells/μL)        |                  |                   |                |                          |                    |         |                 |         |
| 200–350                              | 85,220           | 79,217            | 7,475          | 9.44                     | 1.00               | .000    |                 |         |
| >350                                 | 38,385           | 35,258            | 4,188          | 11.88                    | 1.26 (1.21–1.30)   | <.001   | 1.19 (1.14–1.24)| <.001   |
| Initial ART regimen                  |                  |                   |                |                          |                    |         |                 |         |
| TDF not included                     | 75,827           | 70,074            | 7,346          | 10.48                    | 1.08 (1.04–1.12)   | <.001   | 1.21 (1.16–1.26)| <.001   |
| TDF included                         | 47,778           | 44,401            | 4,317          | 9.72                     | 1.00               |         |                 |         |
| Year ART initiated                   |                  |                   |                |                          |                    |         |                 |         |
| 2011                                 | 18,772           | 17,466            | 1,764          | 10.10                    | 1.00               | .000    |                 |         |
| 2012                                 | 25,454           | 23,515            | 2,513          | 10.69                    | 1.06 (1.00–1.13)   | .082    | 1.18 (1.11–1.25)| <.001   |
| 2013                                 | 34,411           | 31,439            | 3,805          | 12.10                    | 1.20 (1.13–1.27)   | <.001   | 1.43 (1.35–1.52)| <.001   |
| 2014                                 | 44,968           | 42,055            | 3,581          | 8.52                     | 0.85 (0.80–0.90)   | <.001   | 1.13 (1.06–1.20)| <.001   |
| Time of ART initiation               |                  |                   |                |                          |                    |         |                 |         |
| <30 days group                       | 28,883           | 27,285            | 1,941          | 7.11                     | 1.00               | .000    |                 |         |
| 31–90 days group                     | 21,918           | 20,699            | 1,474          | 7.12                     | 1.00 (0.94–1.07)   | .983    | 1.05 (0.99–1.13)| .13     |
| 91–365 days group                    | 25,635           | 23,819            | 2,284          | 9.58                     | 1.34 (1.26–1.43)   | <.001   | 1.33 (1.25–1.42)| <.001   |
| >365 days group                      | 47,169           | 42,672            | 5,964          | 13.98                    | 1.94 (1.84–2.04)   | <.001   | 1.55 (1.47–1.54)| <.001   |

Treatment dropout, observed time, dropout rate, and determinants of treatment dropout as assessed by Cox regression modeling in China, 2011–2015.

Abbreviations: ART, antiretroviral therapy; CI, 95% confidence interval; HIV, human immunodeficiency virus; HR, hazard ratio; PY, person-years; TB, tuberculosis; TDF, tenofovir disoproxil fumarate.
of virological failure and prompt switching to second-line therapy. Dramatic scale up of VL testing capacity and aggressive pursuit of new point-of-care technologies allowing decentralization and increased coverage will be needed. Finally, an estimated 300,000 PLWH in China still do not know their status [26]. China must redouble its case-finding efforts to help these people get the care they need.

Our study had some limitations. First, our study was conducted among subjects in routine HIV care. Thus, participants were not randomly assigned to groups, creating potential for bias. Second, missing values for some variables in our data set could have resulted in under- or overestimation of the outcomes of interest. Third, although unlikely, it is possible that some misclassification bias occurred, due to treatment interruptions or unascertained deaths being counted as dropouts. If an individual stopped and restarted ART during our 12-month follow-up period, they were still counted as on ART at 12 months. Moreover, all deaths among PLWH in China are recorded in CRIMS, causing them to be classified as died, not dropped out.

Our results demonstrate that immediate ART is associated with reduced treatment dropout and virological failure. Taken together with the results of other recent studies in China [13, 14, 19], and other settings [21–25, 27], it is clear that shortening the time from diagnosis to treatment maximizes health and survival and should be an urgent priority. Moreover, movement toward a test-and-immediately-treat policy could help China

| Characteristics                  | Virological Failure, N (%) | Unadjusted RR (CI) | P Value | Adjusted RR (CI) | P Value |
|----------------------------------|---------------------------|--------------------|---------|------------------|---------|
| Overall                          | 9235 (100)                |                    |         |                  |         |
| Age, years                       |                           |                    |         |                  |         |
| 18–30                            | 2764 (29.9)               | 1.0                | .002    | 0.91 (0.87–0.95) | <.001   |
| 31–50                            | 4767 (51.6)               | 1.15 (1.10–1.20)   | .002    | 1.17 (1.10–1.24) | <.001   |
| >50                              | 1704 (18.5)               | 1.18 (1.11–1.25)   | <.001   | 1.17 (1.10–1.24) | <.001   |
| Sex                              |                           |                    |         |                  |         |
| Male                             | 6574 (71.2)               | 1.05 (1.00–1.09)   | .030    | 1.14 (1.09–1.19) | <.001   |
| Female                           | 2661 (28.8)               | 1.0                | .002    |                  |         |
| HIV infection route              |                           |                    |         |                  |         |
| Homosexual contact               | 1344 (14.6)               | 1.0                | .002    |                  |         |
| Heterosexual contact             | 5713 (61.9)               | 1.78 (1.68–1.88)   | <.001   | 1.78 (1.67–1.90) | <.001   |
| Injecting drug use               | 2178 (23.6)               | 4.47 (4.19–4.76)   | <.001   | 4.08 (3.81–4.73) | <.001   |
| TB coinfection                   |                           |                    |         |                  |         |
| Yes                              | 268 (2.9)                 | 1.26 (1.12–1.41)   | <.001   | 1.05 (0.94–1.18) | .38     |
| No                               | 8967 (97.1)               | 1.0                | .002    |                  |         |
| Hepatitis B coinfection          |                           |                    |         |                  |         |
| Yes                              | 656 (7.1)                 | 1.0                | .002    |                  |         |
| No                               | 4873 (52.8)               | 0.81 (0.75–0.88)   | <.001   | 0.83 (0.77–0.89) | <.001   |
| Not tested                       | 3706 (40.1)               | 1.15 (1.06–1.24)   | <.001   | 1.18 (1.09–1.28) | <.001   |
| Serodiscordant couple            |                           |                    |         |                  |         |
| Yes                              | 2307 (25.0)               | 1.0                | .002    |                  |         |
| No                               | 6928 (75.0)               | 0.89 (0.85–0.93)   | <.001   | 0.95 (0.91–1.00) | .038    |
| Baseline CD4 count (cells/μL)    |                           |                    |         |                  |         |
| 200–350                          | 6204 (67.2)               | 1.0                | .002    |                  |         |
| >350                             | 3031 (32.8)               | 1.08 (1.03–1.12)   | <.001   | 1.07 (1.03–1.12) | .002    |
| Initial ART regimen              |                           |                    |         |                  |         |
| TDF not included                 | 6201 (67.1)               | 1.30 (1.25–1.36)   | <.001   | 1.34 (1.28–1.40) | <.001   |
| TDF included                     | 3034 (32.9)               | 1.0                | .002    |                  |         |
| Year ART initiated               |                           |                    |         |                  |         |
| 2011                             | 1771 (19.2)               | 1.0                | .002    |                  |         |
| 2012                             | 1964 (21.3)               | 0.81 (0.76–0.86)   | <.001   | 0.92 (0.87–0.98) | .009    |
| 2013                             | 2499 (27.1)               | 0.78 (0.74–0.83)   | <.001   | 1.00 (0.94–1.06) | .90     |
| 2014                             | 3001 (32.5)               | 0.69 (0.65–0.73)   | <.001   | 0.99 (0.93–1.05) | .74     |
| Time of ART initiation           |                           |                    |         |                  |         |
| ≤30 days                         | 1337 (14.5)               | 1.0                | .002    |                  |         |
| 31–90 days                       | 1353 (14.7)               | 1.36 (1.26–1.46)   | <.001   | 1.35 (1.26–1.45) | <.001   |
| 91–365 days                      | 1985 (21.5)               | 1.77 (1.65–1.89)   | <.001   | 1.66 (1.55–1.78) | <.001   |
| >365 days                        | 4560 (49.4)               | 2.33 (2.19–2.47)   | <.001   | 1.85 (1.74–1.97) | <.001   |

Virological failure and determinants of virological failure as assessed by univariate and multivariate log binomial regression modeling in China, 2011–2015.

Abbreviations: ART, antiretroviral therapy; CI, 95% confidence interval; HIV, human immunodeficiency virus; RR, risk ratio; TB, tuberculosis; TDF, tenofovir disoproxil fumarate.
meet the UNAIDS 90-90-90 targets, if it can overcome the many implementation challenges.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author Contributions. Y. Z. and Z. W. designed the study. Y. Z. and S. Y. performed the statistical analysis. Y. Z., Z. W., and J. M. M. interpreted the results and developed the initial manuscript draft. All authors contributed to manuscript revisions and approved the final version for publication. Z. W. had full access to all the data and had final responsibility for the decision to submit for publication.

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