

## RESEARCH ARTICLE

# Effect of early highly active antiretroviral therapy on viral suppression among newly diagnosed men who have sex with men living with human immunodeficiency virus in Xi'an, China

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**Abstract**

**Background:** The number of men who have sex with men (MSM) living with human immunodeficiency virus (HIV) in China has increased rapidly and thus immediate highly active antiretroviral therapy (HAART) after diagnosis was implemented as a strategy to reduce the HIV transmission.

**Methods:** MSM who were diagnosed with HIV and received HAART between 2013 to 2015 in Xi'an were divided into three groups (>350, 200-350, and <200 cell/ $\mu$ L) according to their baseline CD4+ T cell count. The time of follow-up was calculated from the first date of receiving HAART to December 31, 2016. The CD4+ T cell count was detected with 1 week before or after HAART. The plasma viral loads were tested after 1, 2, and 3 years of treatment.

**Results:** Of 1442 subjects who received HAART, 690 (47.9%) cases were in >350 cell/ $\mu$ L group, whereas 400 (27.7%) cases and 352 (24.4%) cases were in the 200-350 cell/ $\mu$ L group and <200 cell/ $\mu$ L group, respectively. After 1 year of treatment, the viral suppression rate in the <200 cell/ $\mu$ L group was 91.1%, which was significantly lower than the other two groups. The logistic regression results show that the >350 cell/ $\mu$ L group and 200-350 cell/ $\mu$ L group predicted higher viral suppression rates.

**Conclusions:** Baseline CD4+ T cell count more than 350 cell/ $\mu$ L can improve viral suppression among MSM living with HIV. Furthermore, to reduce the transmission risk, the treatment compliance of people living with HIV with high CD4+ T cell levels should be improved, and their diagnosis to the treatment time should be decreased.

**KEYWORDS**

highly active antiretroviral therapy (HAART), human immunodeficiency virus (HIV), men who have sex with men (MSM), viral suppression

## 1 | INTRODUCTION

Highly active antiretroviral therapy (HAART) is the most effective treatment approach to suppress the human immunodeficiency virus (HIV). HAART not only prevents damage to organs and reduces HIV-related morbidity and mortality, but also reduces viral infectiousness and transmissibility.<sup>1,2</sup> The HIV Prevention

Trials Network clinical trial reported that early HIV treatment, defined as initiation of HAART for those with a CD4+ count between 350 and 550 cells per cubic millimeter, reduce up to 93%-96% viral transmission by sexual intercourse.<sup>3,4</sup> An analysis of two cases with transmission from partners who had received early treatment revealed that the transmission occurred before the treatment or at the beginning of the treatment when the virus

was not sufficiently suppressed.<sup>5</sup> This indicated that effective viral suppression is an important factor in preventing heterosexual transmission.<sup>5</sup> Furthermore, two prospective cohort studies have shown that in sero-discordant couples, high viral load (VL) is a significant risk factor for transmission, and that viral suppression treatment can significantly decrease HIV transmission probability.<sup>6,7</sup> Apart from reducing the sexual transmission of the virus between heterosexual persons, these studies have shown that viral suppression treatment can also reduce the sexual transmission risk among homosexual persons. Rodger et al<sup>8</sup> conducted a 1.3 years follow-up study in 1166 sero-discordant men who have sex with men (MSM) couples from 14 European countries, and found that in 11 cases of seroconversion among sexual partners of HAART treated patients with VL <200, viral transmission did not occur from their sexual partners, according to virus genotyping. Because the sexual transmission risk after the treatment is mainly dependent on the VL, American and Australian scientists have proposed a prevention strategy to reduce the sexual transmission through HAART, and further suggested that full viral suppression should aim to zero transmission ("undetectable equals untransmittable", "U = U").<sup>9,10</sup>

Research has shown that the earlier the treatments were applied, the faster the CD4+ T cell levels increased, and thus better viral suppression was achieved, but this difference did not seem to persist at 24 months.<sup>11</sup> Other studies have demonstrated that long-term (5 years after HAART initiation) CD4+ T cell recovery occurred after the treatment, regardless of the viral suppression status, and for approximately 30% of infected patients CD4+ T cell counts did not significantly increase even when the virus was fully suppressed (HIV-1 RNA load less than 50–200 copies/mL).<sup>12,13</sup> Even so, studies support that early treatment decreases the viral rebound by reducing the viral reservoirs, which means that early treatment should be advocated as a preventive measure.<sup>14</sup>

In the past 5 years, the number of HIV reported cases in China has increased rapidly. Although there is a decline in risk behavior by people who inject drugs, there is an increase in viral transmission through sexual intercourse, especially among MSM.<sup>15,16</sup> In 2011, investigation in 15 large cities in China, including Xi'an, revealed that the prevalence of HIV in the MSM population was as high as 6.27%.<sup>17</sup> The increase in HIV transmission in this population has raised concern among Chinese government officials, causing them to implement new protocols, including increased HIV research funding,<sup>18</sup> expanding HIV testing, and expanding treatment coverage.<sup>19,20</sup> Beginning in 2013, immediate treatment after diagnosis was implemented as a prevention and control strategy to reduce HIV transmission among MSM. However, there are limited reports on the effectiveness of viral suppression and its contributing factors on HAART immediately after HIV diagnosis of MSM in China. Therefore, we performed a retrospective cohort study of MSM who were diagnosed with HIV between 2013 to 2015 in Xi'an, the most populous city in northwest China, to investigate the viral suppression effects of early HARRT.

## 2 | SUBJECT AND METHODS

### 2.1 | Participants

MSM who received HAART between January 1, 2013 and December 31, 2015 were recruited. To be eligible for HAART, MSM met the following criteria: (1) diagnosed with HIV infection or acquired immune deficiency syndrome (HIV/AIDS); (2) over 16 years of age; (3) resident of Xi'an city; and (4) demonstrate civil capacity. Participants with severe liver and kidney dysfunction who cannot receive in HARRT were excluded from the study.

### 2.2 | Study design

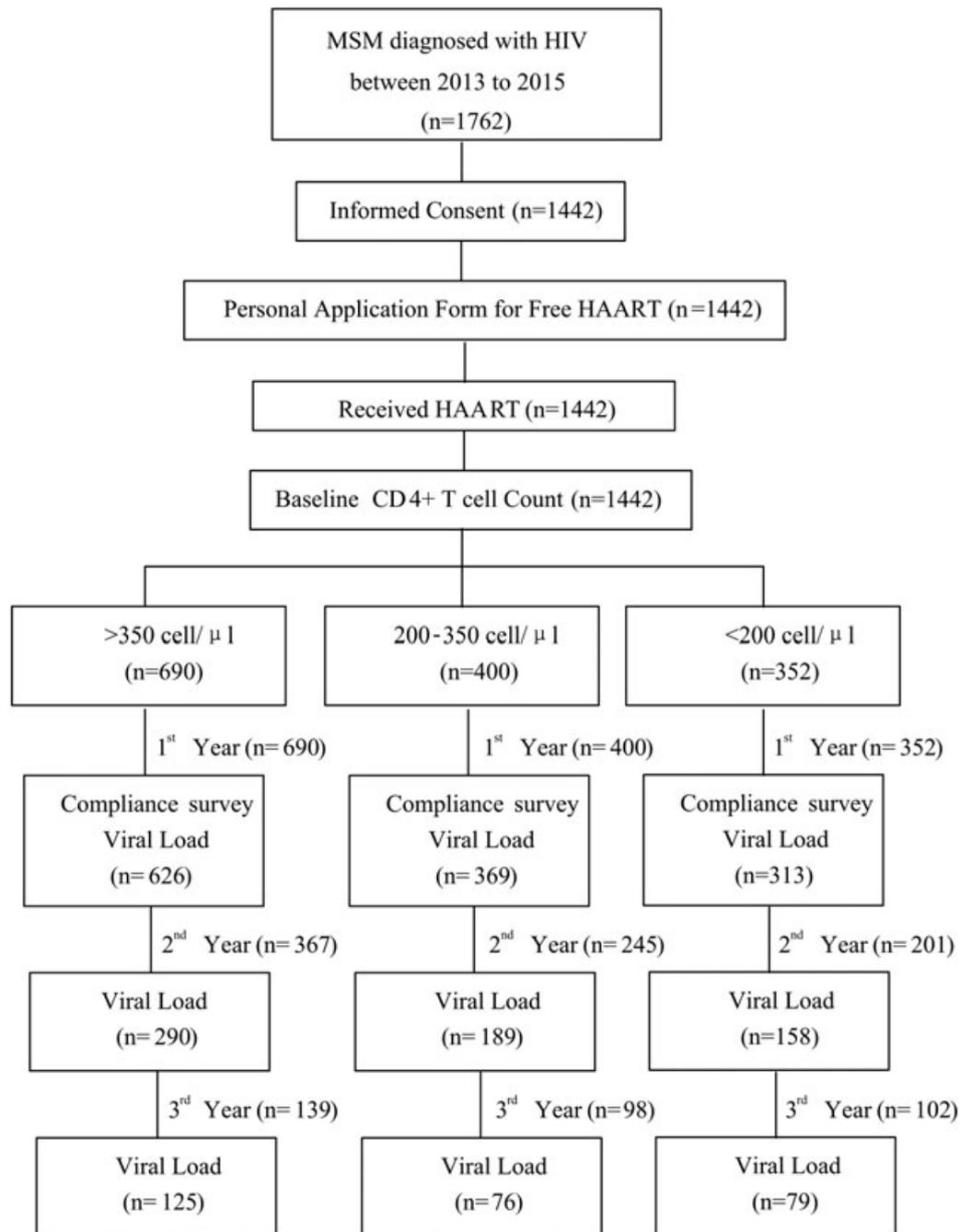
This study was performed retrospectively. The time of follow-up for each subject was calculated from the first date of HAART to December 31, 2016 (or the date of death, HAART withdrawal or loss to follow-up).

A baseline survey was conducted by physicians using the Personal Application Form according to the guidelines of the National Free HAART Program Handbook of the People's Republic of China (Third Edition, 2012). The Personal Application Form contains questions pertaining to demographic characteristics, such as age, education, marital status, employment status, and physical health status, such as body mass index (BMI), initial treatment scheme, diagnosed with tuberculosis or not, took sulfamethoxazole or not to treat opportunistic infections.

CD4+ T cell count was detected within 1 week before or after the initiation of HAART. In the AIDS diagnostic criteria of the People's Republic of China (WS 293-2008), a person living with HIV receives an AIDS diagnosis when the CD4+ T cell count is less than 200 cell/ $\mu$ L. In the guidelines of the National Free HAART Program Handbook of the People's Republic of China (Third Edition, 2012), it is recommended to start antiviral therapy when the CD4+ T cell count is no more than 350 cell/ $\mu$ L. In Xi'an and other seven cities in China where the immediate treatment after diagnosis was implemented, it is recommended to start antiviral therapy even when CD4+ T cell count is more than 350 cell/ $\mu$ L. All subjects were divided into three groups according to their baseline CD4+ T cell counts (>350, 200-350, and <200 cell/ $\mu$ L).

All patients received HAART in the Xi'an Infectious Disease Hospital which is the infectious disease treatment center of Shaanxi Province. The physicians who treat HIV/AIDS have vast experience in HIV care and treatment. Moreover, there is an AIDS Antivirus Treatment Center in Xi'an Infectious Disease Hospital which also trains physicians in Shaanxi Province in HIV management.

Follow-up surveys were performed 1 year after HAART initiation to document treatment compliance. In addition, plasma VLs of all three treatment groups after 1, 2, and 3 years of treatment were tested. Participants were followed-up until December 31, 2016. The study design is shown in Figure 1.



**FIGURE 1** Flow chart of study design and data collection. HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; MSM, men who have sex with men

### 2.3 | Laboratory tests

CD4+ T cell counts: BD FACSCalibur was used to detect the absolute number of CD4+ T cell in venous blood.

VL: Nuclisens Easy Q HIV-1 v2.0 Kit (easy MAG nucleic acid extraction system and Easy Q amplification detection system) was used to quantify the HIV RNA copies to estimate the VL.

### 2.4 | Related definition

#### 2.4.1 | Treatment compliance

Treatment compliance was determined by compliance with medication over the past 7 days, if the participant did not miss medication in the past 7 days, the compliance was good, otherwise, the compliance was poor.

## 2.4.2 | Viral suppression

Viral suppression was determined as HIV RNA copies were less than 400 copies/mL.

## 2.5 | Statistical analysis

The data were inputted into a Microsoft Excel database, which was subsequently converted to a Microsoft Access database. The data were analyzed using SPSS 13.0 software. The difference among groups was compared by one-way analysis of variance or *t* test for continuous variables and chi-squared statistic for categorical variables. Unconditional logistic regression models were used to analyze factors influencing viral suppression. Statistical significance was assessed using two-sided tests with  $\alpha = 0.05$  for all analyses.

## 2.6 | Ethics statement

The study was reviewed and approved by the Ethics Committee of Xi'an Jiaotong University. The written informed consent was obtained from each participant before receiving HAART as per guidance from the National Free HAART Program Handbook.

## 3 | RESULTS

### 3.1 | General information

From 2013 to 2015, a total of 1762 MSM were newly diagnosed with HIV/AIDS. Of these, 222 cases did not receive HAART because they had not lived in Xi'an more than 2 years, and 98 cases did not receive HAART until 2016. Finally, 1442 cases were eligible for the study. Six hundred and ninety (47.9%) cases were in the >350 cell/ $\mu$ L group, whereas 400 (27.7%) cases and 352 (24.4%) cases were in the 200-350 cell/ $\mu$ L group and <200 cell/ $\mu$ L group, respectively. The mean age of the subjects was 34.3 years  $\pm$  11.2 years, with the highest mean age in the <200 cell/ $\mu$ L group (38.0  $\pm$  11.4 years) and the lowest in the >350 cell/ $\mu$ L group (31.6  $\pm$  10.0 years). The >350 cell/ $\mu$ L group included the highest percentage of patients with high school or higher education (81.3%), the lowest percentage of (heterosexual) married cases (23.2%). Meanwhile, the <200 cell/ $\mu$ L group contained the highest ratio of patients diagnosed with tuberculosis in the recent 12 months (8.5%), highest proportion of patients that received treatment within 1 month after diagnosis (64.2%), and the highest percentage of cases treated with sulfamethoxazole (50.6%; Table 1).

**TABLE 1** Participant characteristics in three baseline CD4+ T cell count groups

| Characteristics                                    | >350 cell/ $\mu$ L<br>( $n_1 = 690$ ) | 200-350 cell/ $\mu$ L<br>( $n_2 = 400$ ) | <200 cell/ $\mu$ L t<br>( $n_3 = 352$ ) | Total (N = 1442) |
|--|---------------------------------------|--|---|------------------|
| Age in years, mean (SD)                            | 31.6 (10.0) <sup>a</sup>              | 35.6 (11.8) <sup>b</sup>                 | 38.0 (11.4) <sup>c</sup>                | 34.3 (11.2)      |
| Education, n (%)                                   |                                       |  |   |                  |
| Secondary school or lower                          | 129 (18.7)                            | 84 (21.0) <sup>b</sup>                   | 107 (30.4) <sup>c</sup>                 | 320 (22.2)       |
| High school or higher                              | 561 (81.3)                            | 316 (79.0)                               | 245 (69.6)                              | 1122 (77.8)      |
| Marital status, n (%)                              |                                       |  |   |                  |
| Single   | 455 (65.9) <sup>a</sup>               | 217 (54.3) <sup>b</sup>                  | 151 (42.9) <sup>c</sup>                 | 823 (57.1)       |
| Married or have a regular partner                  | 160 (23.2)                            | 127 (31.8)                               | 142 (40.3)                              | 429 (29.8)       |
| Divorced, separated, or widowed                    | 75 (10.9)                             | 56 (14.0)                                | 59 (16.8)                               | 190 (13.2)       |
| Employment, n (%)                                  |                                       |  |   |                  |
| Yes  | 266 (38.6) <sup>a</sup>               | 127 (31.8)                               | 118 (33.5)                              | 511 (35.4)       |
| No   | 424 (61.4)                            | 273 (68.3)                               | 234 (66.5)                              | 931 (64.6)       |
| BMI, n (%)   |                                       |  |   |                  |
| <18.5  | 73 (10.7)                             | 32 (8.2) <sup>b</sup>                    | 65 (18.8) <sup>c</sup>                  | 170 (12.0)       |
| 18.5-24.0  | 452 (66.3)                            | 267 (68.8)                               | 215 (62.3)                              | 934 (66.0)       |
| >24.0  | 157 (23.0)                            | 89 (22.9)                                | 65 (18.8)                               | 311 (22.0)       |
| Initial treatment scheme                           |                                       |  |   |                  |
| 3TC + EFV/NVP + TDF/D4T/AZT                        | 689 (99.9)                            | 399 (99.8)                               | 350 (99.4)                              | 1438 (99.7)      |
| 3TC + TDF + LPV/r                                  | 1 (0.1)                               | 1 (0.3)                                  | 2 (0.6)                                 | 4 (0.3)          |
| Tuberculosis, n (%)                                |                                       |  |   |                  |
| Yes  | 3 (0.4) <sup>a</sup>                  | 7 (1.8) <sup>b</sup>                     | 30 (8.5) <sup>c</sup>                   | 40 (2.8)         |
| No   | 687 (99.6)                            | 393 (98.3)                               | 322 (91.5)                              | 1402 (97.2)      |
| Time period between diagnosis and treatment, n (%) |                                       |  |   |                  |
| <1 mo  | 288 (41.7) <sup>a</sup>               | 229 (57.3) <sup>b</sup>                  | 226 (64.2) <sup>c</sup>                 | 743 (51.5)       |
| 1-6 mo   | 293 (42.5)                            | 132 (33.0)                               | 111 (31.5)                              | 536 (37.2)       |
| >6 mo  | 109 (15.8)                            | 39 (9.8)                                 | 15 (4.3)                                | 163 (11.3)       |
| Sulfamethoxazole, n (%)                            |                                       |  |   |                  |
| Yes  | 0 (0.0) <sup>a</sup>                  | 5 (1.3) <sup>b</sup>                     | 178 (50.6) <sup>c</sup>                 | 183 (12.7)       |
| No   | 690 (100.0)                           | 395 (98.8)                               | 174 (49.4)                              | 1259 (87.3)      |

<sup>a</sup>>350 cell/ $\mu$ L vs 200-350 cell/ $\mu$ L,  $P < .017$ .

<sup>b</sup>200-350 cell/ $\mu$ L vs <200 cell/ $\mu$ L,  $P < .017$ .

<sup>c</sup>>350 cell/ $\mu$ L vs <200 cell/ $\mu$ L,  $P < .017$ .

**TABLE 2** Viral load detection rates in three baseline CD4+ T cell count groups, % (n/N)

|     | Total            | >350 cell/ $\mu$ L | 200-350 cell/ $\mu$ L | <200 cell/ $\mu$ L | $\chi^2$ | P    |
|-----|------------------|--------------------|-----------------------|--------------------|----------|------|
| 1 y | 90.7 (1308/1442) | 90.7 (626/690)     | 92.3 (369/400)        | 88.9 (313/352)     | 2.463    | .292 |
| 2 y | 78.4 (637/813)   | 79.0 (290/367)     | 77.1 (189/245)        | 78.6 (158/201)     | .315     | .854 |
| 3 y | 82.6 (280/339)   | 89.9 (125/139)     | 77.6 (76/98)          | 77.5 (79/102)      | 8.812    | .012 |

### 3.2 | Cohort maintenance and virus load detection

Because this study was a dynamic cohort study, 339, 474, and 629 cases were recruited in 2013, 2014, and 2015, respectively. Thus, 339, 813, and 1442 cases could be followed-up for 3, 2, and 1 year of treatment, respectively.

VL was detected in 280, 637, and 1308 cases with corresponding detection rates of 82.6%, 78.4%, and 90.7% in 3-year, 2-year, and 1-year follow-up, respectively. During follow-up, 15 cases died, 61 cases were transferred to another city to receive treatment, and some patients were unable to complete a blood draw for VL detection. The VL detection rates showed no significant differences among different baseline CD4+ T cell count groups in 1-year and 2-year follow-up, but in the 3rd year the detection rate in the >350 cell/ $\mu$ L group was significantly higher than in the other two groups ( $P < .05$ ; Table 2).

### 3.3 | Compliance

Of the 1308 participants who tested VL after 1 year treatment, only five (0.4%) had missed their medication in the previous 7 days. The number of participants who missed their medication in the past 7 days in the three groups was one (0.2%), three (0.8%), and one (0.3%), respectively, and no statistical difference was found ( $\chi^2 = 2.644$ ,  $P = .267$ ).

### 3.4 | Viral suppression

The viral suppression rates after one, two, and three years of treatment increased gradually, which were 95.7%, 95.9%, and 97.1%, respectively. After 1 year of treatment, the viral suppression rate in the <200 cell/ $\mu$ L group was significantly lower than in the other two groups ( $P < .05$ ), whereas no significant differences were found after 2 and 3 years of treatment (Table 3).

### 3.5 | Contributing factors to viral suppression after HAART for 1 year

Among the 1442 cases, VLs were detected in 1308 cases after HAART for 1 year, and VLs less than 400 copies/mL were found in

1252 cases (viral suppression rate was 95.7%). After 1 year, the viral suppression rates in the >350 cell/ $\mu$ L group and 200-350 cell/ $\mu$ L group, were higher than 97.1%, whereas in the <200 cell/ $\mu$ L group were the lowest (91.1%). Moreover, patients with high school or higher education and with good compliance, (ie, being adherent to medications over past 7 days), showed high viral suppression rates, whereas patients that suffered from tuberculosis in the recent 1 year and took sulfamethoxazole for treatment displayed low viral suppression rates (Table 4).

Because of the non-randomized group allocation at the time of treatment entry and the incomplete equilibrium between the three groups, variables such as age, marital status, occupation, education, time period between diagnosis and treatment, CD4+ T cell levels at the beginning of the treatment, the initial treatment scheme, BMI, tuberculosis in recent year, sulfamethoxazole treatment, and compliance, were analyzed by logistic regression. The logistic regression results show that the baseline CD4+ T cell count group and compliance were the contributing factors for viral suppression after 1 year of treatment. Compared with the <200 cell/ $\mu$ L group, >350 cell/ $\mu$ L group, and 200-350 cell/ $\mu$ L group predicted higher viral suppression rates after treatment for 1 year; the OR was 3.240 (95% CI: 1.744-6.019) and 4.380 (95% CI: 1.936-9.909), respectively. Poor compliance predicted lower viral suppression rates with OR value of 0.019 (95% CI: 0.003-0.131; Table 5).

## 4 | DISCUSSION

To improve the quality of life and decrease mortality of MSM living with HIV, the threshold to recommend free HAART in China decreased in recent years; from CD4+ T cell counts <200 cell/ $\mu$ L in 2004, to <350 cell/ $\mu$ L in 2008, and then to <500 cell/ $\mu$ L from 2014 to date.<sup>21</sup> Therefore, we assessed the effectiveness of the immediate treatment after diagnosis, since the free treatment of MSM living with HIV in Xi'an was no longer limited by the baseline CD4+ T cell levels from 2013. Previous results from the Henan Province, located in central China, have shown a significant increase in early treatment

**TABLE 3** Viral suppression rates in three baseline CD4+ T cell count groups, % (n/N)

|     | Total            | >350 cell/ $\mu$ L | 200-350 cell/ $\mu$ L | <200 cell/ $\mu$ L | $\chi^2$ | P     |
|-----|------------------|--------------------|-----------------------|--------------------|----------|-------|
| 1 y | 95.7 (1252/1308) | 97.1 (608/626)     | 97.3 (359/369)        | 91.1 (285/313)     | 21.860   | <.001 |
| 2 y | 95.9 (611/637)   | 95.5 (277/290)     | 96.8 (183/189)        | 95.6 (151/158)     | .565     | .754  |
| 3 y | 97.1 (272/280)   | 98.4 (123/125)     | 97.4 (74/76)          | 94.9 (75/79)       | 2.111    | .348  |

**TABLE 4** Viral suppression rates in participants with different characteristics

| Characteristics                                    | viral suppression           |                          | t/ $\chi^2$ | P    |
|--|-----------------------------|--------------------------|-------------|------|
|  | Yes (n <sub>1</sub> = 1252) | No (n <sub>2</sub> = 56) |             |      |
| Age in years, mean (SD)                            | 34.2 (11.0)                 | 37.4 (12.4)              | 2.128       | .033 |
| Education, n (%)                                   |                             |                          |             |      |
| Secondary school or lower                          | 264 (93.3)                  | 19 (6.7)                 | 5.214       | .022 |
| High school or higher                              | 988 (96.4)                  | 37 (3.6)                 |             |      |
| Marital status, n (%)                              |                             |                          |             |      |
| Single   | 712 (96.3)                  | 27 (3.7)                 | 2.451       | .294 |
| Married or have a regular partner                  | 370 (94.4)                  | 22 (5.6)                 |             |      |
| Divorced, separated, or widowed                    | 170 (96.0)                  | 7 (4.0)                  |             |      |
| Employment, n (%)                                  |                             |                          |             |      |
| Yes  | 442 (95.7)                  | 20 (4.3)                 | 0.004       | .950 |
| No   | 810 (95.7)                  | 36 (4.3)                 |             |      |
| Baseline CD4+ T cell count (cell/ $\mu$ L)         |                             |                          |             |      |
| <200   | 285 (91.1)                  | 28 (8.9)                 | 21.860      | <.01 |
| 200-350  | 359 (97.3)                  | 10 (2.7)                 |             |      |
| >350   | 608 (97.1)                  | 18 (2.9)                 |             |      |
| Time period between diagnosis and treatment, n (%) |                             |                          |             |      |
| <1 mo  | 652 (94.9)                  | 35 (5.1)                 | 4.221       | .121 |
| 1-6 mo   | 456 (96.0)                  | 19 (4.0)                 |             |      |
| >6 mo  | 144 (98.6)                  | 2 (1.4)                  |             |      |
| Initial treatment scheme                           |                             |                          |             |      |
| 3TC + EFV/   | 1249 (95.7)                 | 56 (4.3)                 | 0.134       | .714 |
| NVP + TDF/D4T/AZT                                  |                             |                          |             |      |
| 3TC + TDF + LPV/r                                  | 3 (100.0)                   | 0 (0.0)                  |             |      |
| BMI, n (%)   |                             |                          |             |      |
| <18.5  | 139 (94.6)                  | 8 (5.4)                  | 0.627       | .731 |
| 18.5-24.0  | 810 (96.0)                  | 34 (4.0)                 |             |      |
| >24.0  | 279 (95.9)                  | 12 (4.1)                 |             |      |
| Tuberculosis, n (%)                                |                             |                          |             |      |
| Yes  | 30 (88.2)                   | 4 (11.8)                 | 4.770       | .029 |
| No   | 1222 (95.9)                 | 52 (4.1)                 |             |      |
| Sulfamethoxazole, n (%)                            |                             |                          |             |      |
| Yes  | 147 (91.9)                  | 13 (8.1)                 | 6.572       | .010 |
| No   | 1105 (96.3)                 | 43 (3.7)                 |             |      |
| Compliance, n (%)                                  |                             |                          |             |      |
| Poor   | 2 (40.0)                    | 3 (60.0)                 | 38.024      | <.01 |
| Good   | 1250 (95.9)                 | 53 (4.1)                 |             |      |

Abbreviation: BMI, body mass index.

administration for newly diagnosed MSM living with HIV (from 9.8% in 2008 to 48.4% in 2013).<sup>22</sup> This indicates that the immediate treatment after diagnosis strategy, which was applied to MSM living with HIV in Xi'an from 2013, promoted the administration of free HAART to patients with high CD4 +T cell levels.

The monitoring of viral suppression is not only an important part of HAART evaluation, but also provides important indexes to

calculate viral transmission probability.<sup>6-9</sup> In this study, VL <400 copies/mL was considered as complete suppression, and the viral suppression rates after 1, 2, and 3 years of treatment were as high as 95.7%, 95.9%, and 97.1%, respectively. The viral suppression rate was 91.1% even in the <200 cell/ $\mu$ L group after 1 year of treatment, which is much higher than the reported results in South Africa, Henan, and other eight provinces in China.<sup>23-26</sup> This difference may be because of better patients' assessment by more experienced physicians and achievement of better patients' compliance in specialized infectious disease hospitals which in Xi'an, than rural township hospitals in other provinces. In an annual VL detection report of 9594 patients that had received HAART in Zhejiang Province from 2009-2014, the viral suppression rate with less than 400 copies/mL was also as high as 93.2%,<sup>27</sup> however, these results were on the basis of the last VL detection rate during the treatment period.

Patient compliance with drug administration is an important factor to guarantee treatment efficiency. Several studies have shown that poor treatment compliance can lead to the failure of HAART and development of drug resistance.<sup>28-30</sup> One major concern of the early treatment was poor patient compliance,<sup>31</sup> but after 1-year treatment our findings showed there were no significant differences between the three groups, indicating that early treatment did not increase poor compliance risk. Both single- and multi-factor analyses suggest that good compliance was a beneficial factor for HAART effectiveness, demonstrating that improvement of compliance is important for enhancing the HAART effects in both >350 cell/ $\mu$ L group and <200 cell/ $\mu$ L group.

The baseline CD4+ T cell levels were closely related to the viral suppression after the treatment. Similar to the report by Voirin et. al,<sup>11,32,33</sup> our study also showed that the higher the baseline CD4+ T cell levels, the higher the viral suppression rates after 1-year of treatment, indicating that early treatment promoted viral suppression. However, a previous study that had been conducted in Henan Province showed that, except from the HAART for 4 years, the viral suppression rates of early treatment after treatment for 6 months, 1, 2, 3, and 5 years were lower than the normal treatment group.<sup>23</sup> However, this might have been caused by the selection bias of subjects in that study, and by the lower quality of primary care provided in health clinics in small towns. Apart from the beneficial effects of increasing the baseline CD4+ T cell levels for treatment, studies have shown that timely treatment also promotes the HAART effects,<sup>34</sup> although the timeline of treatment was also affected by several other factors. Tang et al<sup>35</sup> has shown that the promptness of patients infected through homosexual transmission was relatively low, and so did the patients with higher CD4+ T cell levels. In this study, we also demonstrated that patients with CD4+ T cell counts >350 cell/ $\mu$ L, which received early treatment, showed the lowest promptness (treatment received within 1 month after diagnosis), which was 40.2%. Furthermore, patients in the <200 cell/ $\mu$ L group, displayed the highest promptness (63.0%), as well as the highest percentages of tuberculosis and sulfamethoxazole administration, which were 8.8% and 52.2%, respectively. These results suggest that

**TABLE 5** Predictors of viral suppression

|  | B      | S.E.  | Wald    | df | Sig.  | Exp(B) | 95% C.I. for EXP(B) |       |
|--|--------|-------|---------|----|-------|--------|---------------------|-------|
|  |        |       |         |    |       |        | Lower               | Upper |
| Baseline CD4+ T cell count (cell/ $\mu$ L) |        |       | 20.004  | 2  | 0.000 |        |                     |       |
| >350                                       | 1.175  | 0.316 | 13.829  | 1  | 0.000 | 3.240  | 1.744               | 6.019 |
| 200-350                                    | 1.477  | 0.417 | 12.576  | 1  | 0.000 | 4.380  | 1.936               | 9.909 |
| Poor compliance                            | -3.941 | 0.973 | 16.407  | 1  | 0.000 | 0.019  | 0.003               | 0.131 |
| Constant                                   | 2.366  | 0.204 | 134.616 | 1  | 0.000 | 10.654 |                     |       |

the treatment might be delayed because of the absence of any physical symptoms in patients in the >350 cell/ $\mu$ L group, which may consider good perceived health, and thus assume that they do not need immediate treatment. A study has shown that in people living with HIV with baseline CD4+ T cell levels >350 cell/ $\mu$ L, there was a longer treatment delay after diagnosis, and lower viral suppression rates,<sup>22</sup> but the effects of this delay on the viral suppression were not reported. Still, high transmission risk exists in newly diagnosed infected person because of the presence of high VLs and high-risk sexual behaviors.<sup>36,37</sup> Therefore, to reduce the transmission risk, the treatment compliance of people living with HIV with high CD4+ T cell levels could be improved, and their diagnosis to treatment time should be decreased.

The first line of HIV treatment scheme that was applied in the study in the Henan Province was the combined administration of D4T/AZT + didanosine (DDI) + NVP/EFV, which showed low viral suppression rates.<sup>23</sup> In our study, different treatment schemes were applied and showed no significant effects on viral suppression rates. This discrepancy might have been caused by the administration of 3TC in place of DDI and the use of TDF instead of and D4T in our study, but also because of the gradual optimization of the national first-line treatment scheme.<sup>21</sup> The current results also indicate that both first-line and second-line treatments have good therapeutic effects on patients infected through homosexual contact in Xi'an.

Expanding the treatment coverage has not only decreased the HIV mortality rates but has also decreased its incidence.<sup>38,39</sup> The 90-90-90 strategy (90% of HIV-infected individuals diagnosed, 90% will receive HAART, and 90% will achieve sustained virologic suppression) was proposed by the Joint United Nations Programme on HIV and AIDS in 2014 and is expected to make significant progress by 2020.<sup>40</sup> Our study has shown good HAART outcomes, and the viral suppression rate is in accord with the 2020 target set by the United Nations. However, the current study also revealed that among the newly diagnosed MSM living with HIV in Xi'an from 2013-2015, 24.2% were in the <200 cell/ $\mu$ L group, and that this was associated with the lowest viral suppression rates after 1-year of treatment. These results indicate that HIV testing should be expanded and further and treatment strategy could be implemented continuously to encourage more asymptomatic persons to undergo early diagnosis and treatment. With this approach, overall HAART effects can be

further improved, resulting in further prevention of HIV transmission and reduction of new infections.

#### 4.1 | Limitations of the study

This study was a dynamic cohort study, so cut-off cases may weaken or enhance the results of virus suppression. In addition, the VL detection rate failed to reach 100% because of death, interruption of treatment, and transfer. However, this study had a large sample size, and the complete viral suppression after 1-year treatment demonstrates that the treatment is successful.

In conclusion, this study found that the implementation of strategy as an immediate treatment after diagnosis among MSM living with HIV in Xi'an from 2013 to 2015 prompted more people with high CD4+ cell levels to receive HAART. The baseline CD4+ T cell count >350 cell/ $\mu$ L group had the highest viral suppression rate 1 year after treatment, and the risk of missing medication in the recent 7 days did not increase. Despite this, 24.2% of the patients are still in the <200 cell/ $\mu$ L group. We need to strengthen the strategy of "early diagnosis and early treatment" in this population, so as to reduce disease transmission.

#### AUTHOR CONTRIBUTIONS

XW and LW gave the concept. YZ and HZ curated the data. LW and YZ conducted the formal analysis. GZ and HL administrated the project. LW and AJS visualized the study. XW, LW, and AJS wrote the original draft. LW, AJS reviewed and edited the paper.

#### CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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