*Original Article*

DOI: 10.5582/ddt.2025.01011

# Clinical benefits of rapid initiation of antiretroviral therapy within 14 days for newly diagnosed late-presentation people living with human immunodeficiency virus (PLWH)

**Xiang Zhang[1,§], Hongjing Guan[2,§], Xiaoyun Di[1], Mengqing Li[2], Jingli Peng[1], Rentian Cai[3,*], Hongxia Wei[2,3,*]**

[1] Department of Infectious Disease, The Second Hospital of Nanjing, Affiliated to Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China;
[2] Department of Infectious Disease, The School of Public Health of Nanjing Medical University, The Second Hospital of Nanjing, Nanjing, Jiangsu, China;
[3] Department of Infectious Disease, The Second Hospital of Nanjing, Nanjing, Jiangsu, China.

**SUMMARY**: This study evaluated the impact of initiating antiretroviral therapy (ART) within 14 days compared to starting after 14 days in newly diagnosed, late-presenting people living with human immunodeficiency virus (PLWH). A total of 1,538 PLWH with a baseline $CD4^+$ T-cell count < 350 cells/μL who attended our outpatient clinic from January 2017 to June 2022 were included. Participants were divided into two groups based on ART initiation timing: rapid initiation (ART within 14 days) and delayed initiation (ART after 14 days). Rapid initiation led to significantly higher virologic suppression rates at 6 months (62.5% *vs.* 52.7%, $P < 0.05$) and 1 year (81.6% *vs.* 72.1%, $P < 0.01$) compared to delayed initiation. While overall treatment retention rates were comparable, rapid initiation improved retention at 6 months for those with baseline $CD4^+$ < 200 cells/μL and at 1 year for those with baseline $CD4^+$ between 200 and 350 cells/μL. No significant differences in $CD4^+$ T-cell counts or CD4/CD8 ratio were observed. A positive correlation was found between baseline viral load and time to virologic suppression, with rapid initiation of ART leading to faster suppression, especially in those with higher baseline viral loads. Multivariate analysis confirmed that ART initiation timing and baseline viral load were key determinants of virologic suppression. In conclusion, rapid ART initiation within 14 days was associated with higher virologic suppression at 6 months and 1 year. Rapid initiation of ART and lower baseline viral load were critical for virologic suppression, with improved retention for specific subgroups.

***Keywords***: Rapid ART initiation, virologic suppression rate, treatment retention rate, immune recovery

## 1. Introduction

Acquired immunodeficiency syndrome (AIDS), caused by the human immunodeficiency virus (HIV), has been a major global health concern since 1981. As of July 2022, approximately 84.2 million people worldwide have been infected, with 40.1 million deaths due to HIV-related illnesses (*1*). In China, 1.223 million people were reported to be living with HIV/AIDS by the end of 2022 (*2*). The introduction of combination antiretroviral therapy (cART) in 1996 significantly improved outcomes for people living with HIV (PLWH) (*3*). Since 2015, the WHO has recommended initiating ART for all HIV-positive individuals regardless of $CD4^+$ T-cell count (*4,5*), and China adopted this guideline in 2016 (*6*), resulting in nearly 600,000 PLWH starting ART the following year (*7*).

Recent evidence suggests that rapid ART initiation, defined variably as starting treatment within 5 to 14 days after diagnosis(*8,9*), can further improve clinical outcomes. Studies across multiple countries have demonstrated that immediate or same-day ART initiation leads to higher rates of virologic suppression, reduced treatment dropout, and significantly lower mortality (*8-19*). For example, rapid ART initiation has been associated with a 63% reduction in mortality (*10*) and faster virologic suppression in settings such as Haiti, Atlanta (USA), San Francisco (USA), and Guangxi (China) (*13,17-20*). These benefits are particularly pronounced in patients with advanced disease or low $CD4^+$ counts (*10,19*). Despite variations in implementation across regions, the trend toward rapid initiation is supported by strong clinical evidence.

Late presentation remains a key barrier to effective HIV treatment, especially in low- and middle-income countries. In China, the proportion of late presenters

has decreased over the years, from 80% in 2008 to 29% in 2016 (*21,22*). However, many newly diagnosed individuals still present with $CD4^+$ counts below 350 or 200 cells/μL or with AIDS-defining conditions (*23*), placing them at higher risk for poor outcomes, including a tenfold increase in morbidity and mortality during the first year after diagnosis (*24,25*). Delayed diagnosis also contributes to ongoing transmission and incomplete immune recovery (*26-29*). Despite the urgency, there is a lack of focused research on late-presenting PLWH in China. This retrospective study analyzes such patients treated at Nanjing Second Hospital from 2017 to 2022, aiming to evaluate the impact of rapid versus delayed ART initiation on virologic suppression, treatment retention, and immune recovery over 1 year and 5 years.

## 2. Materials and Methods

### 2.1. Study subjects

This study is a single-center, retrospective, controlled study. The subjects were patients who visited the Infectious Diseases Department at Nanjing Second Hospital between January 1, 2017, and June 30, 2022. The study focused on treatment-naive individuals with a baseline $CD4^+$ T cell count below 350 cells/μL. Eligible patients were categorized into two groups based on the time to initiate ART after diagnosis: the rapid initiation group (ART started within 14 days of diagnosis) and the delayed initiation group (ART started more than 14 days after diagnosis).

#### 2.1.1. Inclusion criteria

Aged 18 years or older; Diagnosed with HIV/AIDS according to the People's Republic of China health industry standard (WS293-2019) - "Diagnosis of AIDS and HIV Infection"; Received initial antiviral treatment at Nanjing Second Hospital with complete follow-up data; Baseline $CD4^+$ T cell count below 350 cells/μL.

#### 2.1.2. Exclusion criteria

Prior receipt of any form of antiretroviral therapy; Absence of baseline viral load (VL) data; Coexisting conditions such as tuberculous meningitis, cryptococcal meningitis, or Kaposi's sarcoma that would preclude rapid initiation of ART; Patients transferred out during the follow-up period.

### 2.2. Study methods and data collection

#### 2.2.1. Study design

This study employs a single-center, retrospective design. This study was approved by the Ethics Committee of The Second Hospital of Nanjing, Affiliated to Nanjing University of Chinese Medicine (Approval No: 2024-LS-ky043). All procedures were conducted in accordance with the Declaration of Helsinki (2013 revision).

#### 2.2.2. Baseline assessment

Baseline data were collected before the initiation of ART, including general information (age, sex, marital status), immunological status ($CD4^+$ T cell count, CD4/CD8 ratio), HIV infection status (HIV-1 RNA viral load, time of HIV diagnosis, and time from diagnosis to treatment).

#### 2.2.3. Follow-up data collection

Participants were followed at regular intervals, with data collected at 3 months, 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years after initiating ART. Collected data included: HIV-1 RNA viral load; $CD4^+$ T cell count, $CD8^+$ T cell count; adherence to and interruption of treatment. Data from HIV-1 RNA and immune status tests conducted within 3 months before or after each follow-up visit were included in the analysis for that time point.

#### 2.2.4. Data sources

Data were sourced from the following: National AIDS Basic Prevention and Treatment Information System database; Electronic Medical Record System of Nanjing Second Hospital; Laboratory Information System (LIS); Patient paper records.

#### 2.2.5. Stratified analysis

Since the majority of late-presenting patients had $CD4^+$ T cell counts below 200 cells/μL, stratification by $CD4^+$ T cell count < 200 cells/μL was performed to account for variations in baseline $CD4^+$ T cell levels and their impact on achieving viral suppression.

### 2.3. Study endpoints and definitions

#### 2.3.1. Primary endpoints

Viral suppression rate: The proportion of patients with plasma HIV-1 RNA < 50 copies/mL at 12 months post-treatment. Treatment retention rate: The ratio of actual treated patients to the number of patients eligible for treatment each year. $CD4^+$ T cell count and change from baseline: Measurement of $CD4^+$ T cell count and the difference from baseline at 12 months. CD4/CD8 ratio: The ratio of $CD4^+$ to $CD8^+$ T cells.

#### 2.3.2. Secondary endpoints

Viral suppression rate: Proportions of patients with plasma HIV-1 RNA < 50 copies/mL at 1 year, 2 years,

3 years, 4 years, and 5 years. Treatment retention rate: Treatment adherence rates at 1 year, 2 years, 3 years, 4 years, and 5 years. $CD4^+$ T cell count and change from baseline: Changes in $CD4^+$ T cell count from baseline at the specified time points. CD4/CD8 ratio: The CD4/CD8 ratio at each follow-up interval. Mortality rate and related factors: The mortality rate during the 5-year follow-up period and factors associated with mortality.

### 2.4. Statistical methods

Data were collected and initially processed using Excel, and statistical analyses were conducted with R Studio 4.3.0. All graphical representations were generated using Origin. Baseline characteristics of the population were described using appropriate methods based on data types. For continuous variables, median values and interquartile ranges (IQR) were reported. Comparisons between two groups for normally distributed data were performed using the Student's *t*-test, while non-normally distributed data were analyzed using the Wilcoxon rank-sum test. Categorical data were expressed as percentages, and comparisons between two groups were made using the chi-square test or Fisher's exact test.

Correlation curves were employed to describe the relationship between baseline viral load, time to ART initiation, and the duration required to achieve viral suppression. Cox proportional hazards regression analysis was used to identify factors associated with achieving viral suppression in late-presenting HIV patients post-treatment. Kaplan-Meier (K-M) curves illustrated the time to viral suppression for the rapid initiation group compared to the delayed initiation group, under various influencing factors.

Stratified analyses were performed based on baseline $CD4^+$ T cell counts, distinguishing between those with $CD4^+$ T cell counts < 200 cells/μL and those with counts between 200 and 350 cells/μL. These analyses evaluated changes in viral suppression rates, treatment retention rates, and immune recovery. Statistical significance was set at $P < 0.05$.

## 3. Results

### 3.1. Patient enrollment and study flow

Between January 1, 2017, and June 30, 2022, a total of 1,717 individuals with a baseline $CD4^+$ T cell count below 350 cells/μL were initially enrolled at the Infectious Diseases Department of Nanjing Second Hospital. Following exclusion of 58 cases with missing baseline viral load data, 16 cases with cryptococcal meningitis, tuberculous meningitis, or Kaposi's sarcoma, and 105 cases transferred from other institutions, 1,538 patients were included in the subsequent analysis (Figure 1).

Of these, 456 patients were in the rapid initiation group, and 1,082 patients were in the delayed initiation

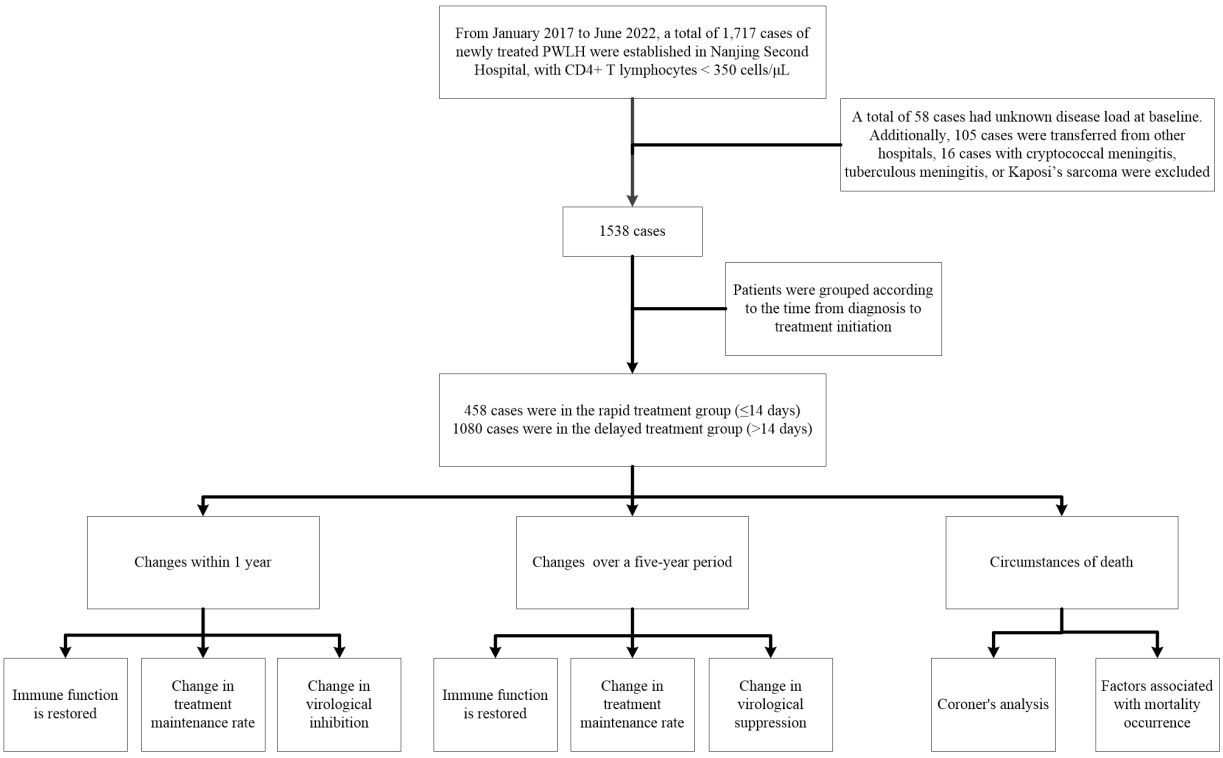


**Figure 1. Baseline enrollment status.**

group (Table 1). Overall, the cohort comprised 1,419 males (92.3%) and 119 females (7.7%). The median age of the patients was 38 years (IQR: 30-54 years). Education levels showed that 959 patients (62.4%) had attained a high school diploma or higher.

The median time from diagnosis to treatment initiation showed a decreasing trend over the years: 26 days (IQR: 14-69.5) in 2018; 26 days (IQR: 13-68.5) in 2019; 20 days (IQR: 13-48) in 2020; 20 days (IQR: 13-42) in 2021; and 18 days (IQR: 11-39.75) in 2022.

The median baseline $CD4^+$ T cell count for the overall cohort was 181 cells/μL (IQR: 66-266 cells/μL). The largest proportion of patients had $CD4^+$ T cell counts between 200 and 350 cells/μL (712 patients, 46.3%), followed by those with counts between 100 and 199 cells/μL (331 patients, 21.5%), counts below 50 cells/μL (309 patients, 20.1%), and counts between 50 and 99 cells/μL (186 patients, 12.1%).

The median log10 value of baseline VL was 4.8 log10 copies/mL (IQR: 4.3-5.2 log10 copies/mL). The baseline VL was significantly higher in the rapid initiation group compared to the delayed initiation group (4.8 log10 copies/mL *vs.* 4.7 log10 copies/mL, $P = 0.048$).

### 3.2. Viral suppression rates, treatment retention rates, and immune recovery within 1 year of ART

#### 3.2.1. Viral suppression rates

We found that rapid ART initiation resulted in significantly higher one-year viral suppression rates than delayed initiation in patients with advanced HIV. As shown in Table 2, the overall viral suppression rate within one year for late-stage people living with HIV exhibited an increasing trend over time. The rapid initiation group demonstrated significantly higher viral suppression rates compared to the delayed initiation group at 6 months (62.5% *vs.* 52.7%, $P = 0.022$) and at 1 year (81.6% *vs.* 72.1%, $P = 0.001$).

Furthermore, the data demonstrated superior viral suppression with rapid ART in both low (< 200 cells/μL) and moderate (200-350 cells/μL) $CD4^+$ T cell count groups. When stratified by baseline $CD4^+$ T cell levels, the viral suppression rate within one year showed an increasing trend regardless of the baseline $CD4^+$ T cell count. For individuals with baseline $CD4^+$ T cell counts < 200 cells/μL, the viral suppression rate at 1 year was significantly higher in the rapid initiation group compared to the delayed initiation group (77.3% *vs.* 66.6%, $P < 0.05$). In the cohort with baseline $CD4^+$ T cell counts between 200 and 350 cells/μL, the rapid initiation group exhibited significantly higher viral suppression rates at 6 months (76.7% *vs.* 62.9%, $P < 0.05$) and at 1 year (86.0% *vs.* 77.6%, $P < 0.05$) compared to the delayed initiation group.

To identify key predictors of viral suppression, we conducted comprehensive univariate and multivariate Cox regression analyses. Univariate and multivariate Cox regression models were employed to analyze the factors influencing viral suppression, with factors

**Table 1. General characteristics between the two groups**

| Feature | Total (n = 1538) | Rapid ART (n = 456) | Delayed ART (n = 1082) | *P* |
|---|---|---|---|---|
| Age, years | | | | 0.932 |
| Median (IQR) | 38 (30-54) | 38 (30-55) | 38 (30-54) | |
| Gender | | | | 0.57 |
| Male, n (%) | 1419 (92.3) | 418 (91.7) | 1001 (92.5) | |
| Female, n (%) | 119 (7.7) | 38 (8.3) | 81 (7.5) | |
| Education Level | | | | 0.377 |
| Primary and Below, n (%) | 88 (5.7) | 30 (6.6) | 58 (5.4) | |
| Junior High, n (%) | 189 (12.3) | 50 (11.0) | 139 (12.8) | |
| High School and Above, n (%) | 959 (62.4) | 278 (61.0) | 681 (62.9) | |
| Unknown, n (%) | 302 (19.6) | 98 (21.5) | 204 (18.9) | |
| Marital Status | | | | 0.191 |
| Single, Divorced, Widowed, n (%) | 989 (64.3) | 282 (61.8) | 707 (65.3) | |
| Married or Cohabiting, n (%) | 549 (35.7) | 174 (38.2) | 375 (34.7) | |
| Baseline CD4+ T Cells, cells/μL | | | | 0.268 |
| <50, n (%) | 309 (20.1) | 105 (23.0) | 204 (18.9) | |
| 50-99, n (%) | 186 (12.1) | 57 (12.5) | 129 (11.9) | |
| 100-199, n (%) | 331 (21.5) | 93 (20.4) | 238 (22.0) | |
| 200-349, n (%) | 712 (46.3) | 201 (44.1) | 511 (47.2) | |
| Baseline VL, log10copies/ml | | | | 0.048* |
| Median (IQR) | 4.8 (4.3-5.2) | 4.8 (4.4-5.2) | 4.7 (4.3-5.2) | |
| Time from Diagnosis to Treatment (day) | | | | |
| 2018, Median (IQR) | 26 (14-69.5) | 12 (7-12) | 40 (26-230) | < 0.001*** |
| 2019, Median (IQR) | 26 (13-68.5) | 10 (5-12) | 35 (21-154) | < 0.001*** |
| 2020, Median (IQR) | 20 (13-48) | 12 (7-13) | 33 (21-89) | < 0.001*** |
| 2021, Median (IQR) | 20 (13-42) | 12 (8-13) | 31 (20-114.5) | < 0.001*** |
| 2022, Median (IQR) | 18 (11-39.75) | 8.5 (5-12) | 33 (19.25-81.5) | < 0.001*** |

IQR: interquartile ranges ; *: $P < 0.05$; ***: $P < 0.001$.

**Table 2. Virological suppression rates at different $CD4^+$ T cell counts within one year**

| Population group / Time Point | Total Population | | | $CD4^+$ T Cells < 200 cells/μL | | | $CD4^+$ T Cells 200-350 cells/μL | | |
|---|---|---|---|---|---|---|---|---|---|
| | ≤ 14 Days | > 14 Days | *P* | ≤ 14 Days | > 14 Days | *P* | ≤ 14 Days | > 14 Days | *P* |
| 3 M Viral Suppression Rate | 0.327 | 0.31 | 0.759 | 0.276 | 0.24 | 0.366 | 0.402 | 0.393 | 0.875 |
| 6 M Viral Suppression Rate | 0.625 | 0.527 | 0.022* | 0.512 | 0.435 | 0.113 | 0.767 | 0.629 | 0.009** |
| 9 M Viral Suppression Rate | 0.816 | 0.721 | 0.001*** | 0.773 | 0.666 | 0.005** | 0.86 | 0.776 | 0.021* |

M: month; *: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$.

**Table 3. Factors associated with virological suppression in late-presenting PLWH: Cox regression analysis**

| Factors | Univariate HR (95% CI) | *P* | Multivariate HR (95% CI) | *P* |
|---|---|---|---|---|
| Age | 0.996 (0.990, 1.000) | 0.053 | 0.997 (0.993, 1.000) | 0.079 |
| Initial VL Measurement, copies/mL | | | | |
| $< 10^5$ | 1 | | | |
| $> 10^5$ | 0.623 (0.556, 0.698) | < 0.001*** | 0.631 (0.563, 0.708) | < 0.001*** |
| Initial CD4+ T Cells, cells/μL | | | | |
| < 50 | 1 | | | |
| 50-150 | 0.918 (0.889, 1.200) | 0.314 | | |
| > 150 | 1.322 (1.208, 1.474) | < 0.001*** | 1.180 (0.989, 1.408) | 0.066 |
| Time from Diagnosis to Treatment, days | | | | |
| Within 14 Days | 1 | | | |
| Greater than 14 Days | 0.721 (0.777, 0.936) | < 0.001*** | 0.711 (0.632, 0.800) | < 0.001*** |
| Use of Co-Trimoxazole | | | | |
| No | 1 | | | |
| Yes | 0.762 (0.724, 0.913) | < 0.001*** | 0.975 (0.838, 1.130) | 0.739 |

*: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$.

showing $P < 0.1$ in univariate analysis included in the multivariate model. The univariate analysis identified several significant factors: age ($P = 0.053$), baseline viral load ($P < 0.001$), baseline $CD4^+$ T cell count ($P < 0.001$), whether ART was initiated rapidly ($P < 0.001$), and the use of co-trimoxazole for prophylaxis ($P < 0.001$).

The multivariate Cox regression model, employing the forward likelihood ratio method, revealed that a baseline VL < $10^5$ copies/mL (HR: 0.623, 95% CI: 0.556–0.698, $P < 0.001$) and ART initiation within 14 days of diagnosis (HR: 0.71, 95% CI: 0.632–0.800, $P < 0.001$) were significantly associated with a higher likelihood of achieving viral suppression (Table 3).

The survival analysis revealed two critical determinants of viral suppression timing in late-stage PLWH: treatment initiation speed and baseline viral load. As illustrated in Figures 2A1 and A2, the time to achieve viral suppression in late-stage PLWH is influenced by the time from diagnosis to treatment initiation and baseline viral load levels. The Kaplan-Meier curves demonstrate that, within the rapid initiation group, the median time to achieve 50% viral suppression is significantly shorter, indicating that earlier initiation of ART leads to quicker attainment of viral suppression ($P < 0.001$). Additionally, for treatment-naive late-stage PLWH, those with a baseline VL below $10^5$ copies/mL achieve viral suppression more rapidly ($P < 0.001$).

Our correlation analysis demonstrates that baseline viral load significantly impacts the viral suppression timeline in late-stage PLWH, with differential effects across viral load strata. Overall, higher baseline viral load in late-stage PLWH is associated with a longer time to achieve viral suppression ($R = 0.24$, $P < 0.01$), as shown in Figure 2B1. Further stratification by baseline VL thresholds of $10^5$ copies/mL reveals that in the group with VL < $10^5$ copies/mL, there is a positive correlation between the time from diagnosis to treatment and the time to achieve viral suppression ($R = 0.099$, $P = 0.0027$). This correlation is more pronounced in the group with VL > $10^5$ copies/mL ($R = 0.17$, $P < 0.001$), indicating a stronger relationship (Figures 2B2 and 2B3).

Additionally, a positive correlation was observed between the time to initiate ART and the time to achieve viral suppression, meaning that earlier initiation of ART is associated with a shorter time to achieve viral suppression ($R = 0.16$, $P < 0.001$) (Figure 2B4).

3.2.2. Treatment retention rates

For late-stage PLWH undergoing ART, treatment retention rates were assessed at various time points. At 3 months, the retention rates were 98.7% in the rapid initiation group and 96.1% in the delayed initiation group ($P = 0.316$) (Table 4). At 6 months, retention rates were 98.1% in the rapid initiation group compared to 95.7% in the delayed initiation group ($P = 0.563$). At 1 year, the treatment retention rates were 96.8% for the rapid initiation group and 93.6% for the delayed initiation

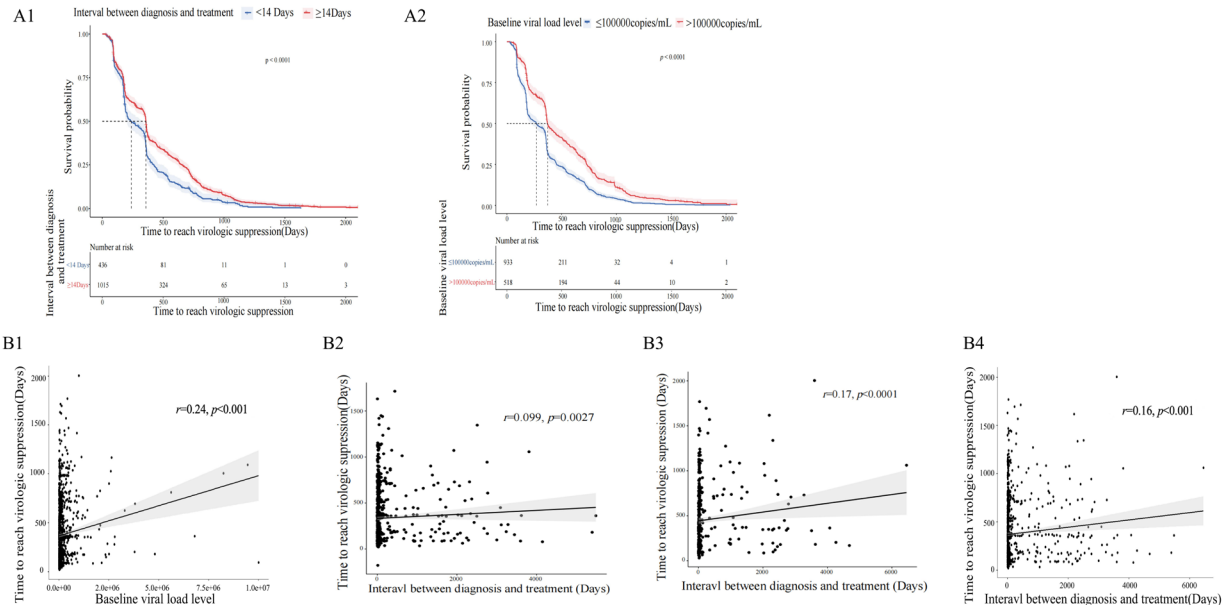


**Figure 2. Kaplan-Meier (K-M) curves for achieving virological suppression and correlations with achieving virological suppression after treatment.** (**A1**) K-M curves for the rapid start and delayed start treatment groups. (**A2**) K-M curves for different baseline viral loads. (**B1**) Correlation between baseline viral load and achieving virological suppression after treatment. (**B2**) Correlation between baseline viral load < $10^5$ copies/mL and achieving virological suppression after treatment. (**B3**) Correlation between baseline viral load > $10^5$ copies/mL and achieving virological suppression after treatment. (**B4**) Correlation between time from diagnosis to initiation of antiretroviral therapy and achieving virological suppression after treatment.

**Table 4. Treatment maintenance rates at different CD4$^+$ T cell counts within one year**

| Population group | Total Population | | | Baseline CD4$^+$ T Cell Count < 200 cells/μL | | | Baseline CD4$^+$ T Cell Count: 200-350 cells/μL | | |
|---|---|---|---|---|---|---|---|---|---|
| Time Point | ≤ 14 Days | > 14 Days | *P* | ≤ 14 Days | > 14 Days | *P* | ≤ 14 Days | > 14 Days | *P* |
| 3 M Treatment Retention Rate | 0.987 | 0.961 | 0.316 | 0.988 | 0.954 | 0.084 | 0.986 | 0.969 | 0.880 |
| 6 M Treatment Retention Rate | 0.981 | 0.951 | 0.563 | 0.983 | 0.937 | < 0.001*** | 0.979 | 0.966 | 0.218 |
| 12 M Treatment Retention Rate | 0.968 | 0.936 | 0.510 | 0.973 | 0.924 | 0.160 | 0.962 | 0.951 | 0.009** |

M: month; **: $P < 0.01$; ***: $P < 0.001$.

group ($P = 0.510$). Differences between the groups were not statistically significant.

Further stratification by baseline CD4$^+$ T cell count revealed differences in retention rates. For individuals with a baseline CD4$^+$ T cell count < 200 cells/μL, the treatment retention rate at 6 months was significantly higher in the rapid initiation group compared to the delayed initiation group (98.3% *vs.* 93.7%, $P < 0.001$). For those with baseline CD4$^+$ T cell counts between 200 and 350 cells/μL, the retention rate at 1 year was notably higher in the rapid initiation group compared to the delayed initiation group (96.2% *vs.* 95.1%, $P < 0.05$).

3.2.3. Immune recovery

Longitudinal immune reconstitution monitoring demonstrated substantial post-treatment improvements in both quantitative and functional immunological parameters for late-stage PLWH. As illustrated in Figure 3A, the recovery of CD4$^+$ T cell counts and related metrics in late-stage PLWH post-treatment shows a marked improvement. Overall, CD4$^+$ T cell counts increased from a baseline of 183 cells/μL to 342 cells/μL within one year, representing a rise of 159 cells/μL over this period. The most rapid increase in CD4$^+$ T cell counts was observed at 3 months post-treatment (Figure 3A1 and A2).

The CD4/CD8 ratio also exhibited an upward trend over the year, increasing from a baseline of 0.17 to 0.39 by the end of the year, reflecting an improvement of 0.22 (Figure 3A3).

The comparative analysis revealed comparable immune recovery including CD4$^+$ T cell counts and CD4/CD8 ratio between rapid and delayed ART initiation groups in late-stage PLWH at one-year follow-up. Immune recovery in late-stage PLWH improved following treatment. However, at one year, there were no significant statistical differences between the rapid initiation and delayed initiation groups in terms of CD4$^+$ T cell counts (336 cells/μL *vs.* 347 cells/μL; *P*

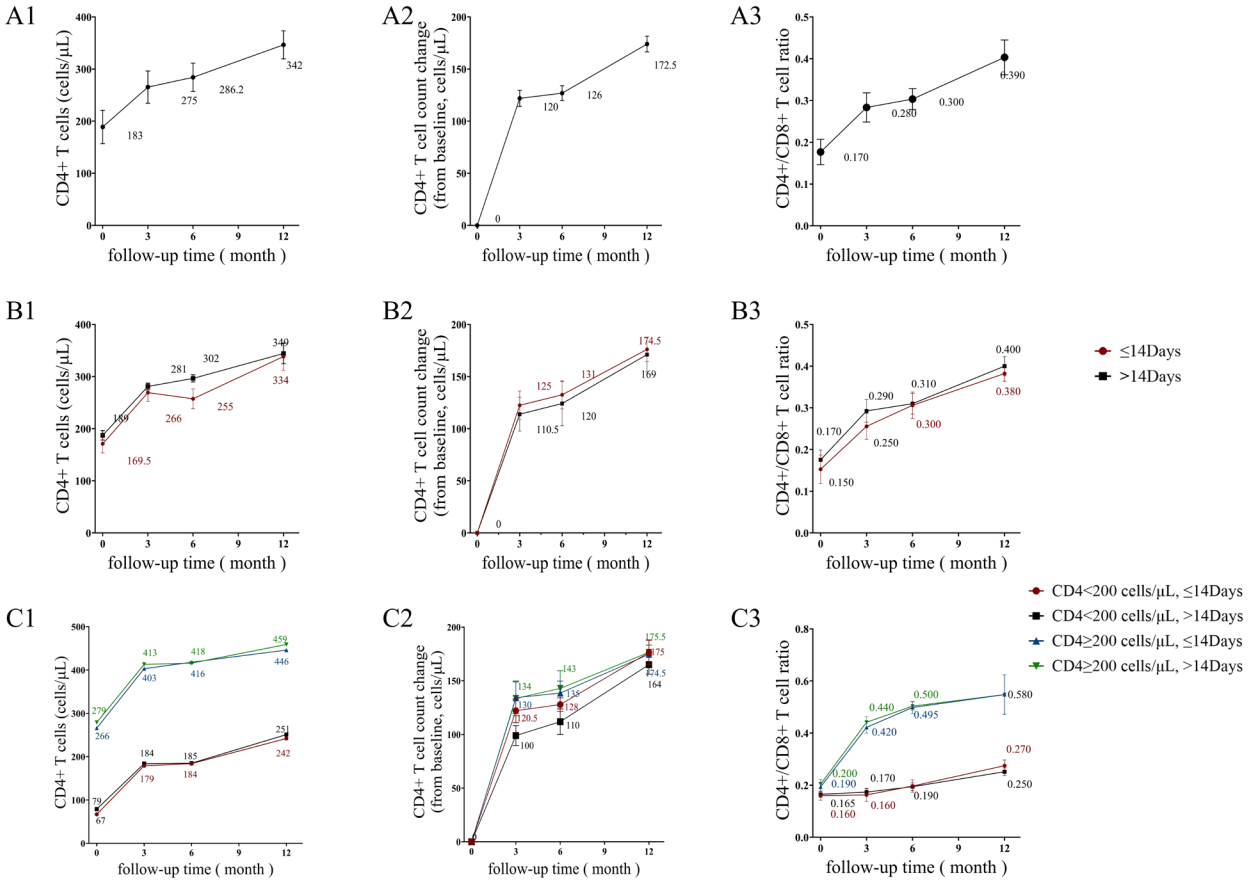


**Figure 3. Immune reconstitution in late-presenting PLWH within one year of treatment.** (**A1**) $CD4^+$ T cell recovery in late-presenting PLWH within one year of treatment. (**A2**) Increase in $CD4^+$ T cells from baseline in late-presenting PLWH within one year of treatment. (**A3**) CD4/CD8 ratio recovery in late-presenting PLWH within one year of treatment. (**B1**) Changes in $CD4^+$ T cell count in late-presenting PLWH within one year after treatment. (**B2**) Increase in $CD4^+$ T cells in late-presenting PLWH within one year after treatment. (**B3**) Changes in the CD4/CD8 ratio in late-presenting PLWH within one year after treatment. (**C1**) Changes in $CD4^+$ T cell count in late-presenting PLWH with baseline $CD4^+$ T cells < 200/μL, and $CD4^+$ T cells 200-350/μL under different treatment initiation groups within one year of treatment. (**C2**) Increase in $CD4^+$ T cells in late-presenting PLWH with baseline $CD4^+$ T cells < 200/μL, and $CD4^+$ T cells 200-350/μL under different treatment initiation groups within one year of treatment. (**C3**) Changes in CD4/CD8 ratio in late-presenting PLWH with baseline CD4+ T cells < 200/μL, and $CD4^+$ T cells 200-350/μL under different treatment initiation groups within one year of treatment.

> 0.05), the increase from baseline (174.5 cells/μL *vs.* 169 cells/μL; $P > 0.05$), or the CD4/CD8 ratio (0.40 *vs.* 0.38; $P > 0.05$). Similar to the overall trend, both groups experienced the most rapid increase in $CD4^+$ T cell counts at 3 months post-treatment, with increases of 125 cells/μL and 110.5 cells/μL, respectively, although the differences between the groups were not statistically significant (Figures 3B).

We compared $CD4^+$ T cell recovery between rapid and delayed ART initiation groups stratified by baseline CD4+ levels (< 200 *vs.* 200-350 cells/μL) in late-stage PLWH. In the < 200 cells/μL subgroup, the rapid initiation group showed numerically higher but statistically non-significant improvements in $CD4^+$ counts (251 *vs.* 242 cells/μL) and CD4/CD8 ratio (0.27 *vs.* 0.25) at one year ($P > 0.05$). Similarly, in the 200-350 cells/μL subgroup, no significant differences were observed in final $CD4^+$ counts (446 *vs.* 459 cells/μL), absolute increases (174.5 *vs.* 175.5 cells/μL), or CD4/CD8 ratio (0.58 *vs.* 0.58) between initiation strategies ($P > 0.05$). Both subgroups demonstrated comparable immune reconstitution regardless of treatment initiation timing (Figures 3C).

### 3.3. Viral suppression rates, treatment retention rates, and immune recovery within 5 years of ART

The follow-up period for this study extended up to five years, with a decreasing number of participants over time. Specifically, the number of patients followed up at 1 year, 2 years, 3 years, 4 years, and 5 years were 1,402, 1,143, 837, 601, and 337, respectively.

#### 3.3.1. Viral suppression rates

This five-year longitudinal study of late-stage PLWH revealed progressive viral suppression improvements, with rates rising from first-year levels to 88.2% by year five. The rapid initiation group demonstrated significantly higher 1-year suppression rates (81.6% *vs.* 72.1%, $P = 0.001$), with subsequent annual rates of

84.4% (*vs.* 83.6%, $P > 0.05$) at year 2, 89.3% (*vs.* 88.7%, $P > 0.05$) at year 3, and 90.8% (*vs.* 87.4%, $P > 0.05$) at year 5 (Table 5). Stratified analyses showed consistent temporal patterns: for $CD4^+ < 200$ cells/μL patients, rapid initiation achieved 77.3% *vs.* 66.6% ($P = 0.005$) at year 1, 81.6% *vs.* 78.2% at year 2, 85.9% *vs.* 85.0% at year 3, 86.7% *vs.* 86.5% at year 4, and 88.9% *vs.* 85.5% at year 5 (all $P > 0.05$ beyond year 1); while the $CD4^+$ 200-350 cells/μL cohort showed 86.0% *vs.* 77.6% ($P = 0.021$) at year 1, 95.3% *vs.* 92.6% at year 3, and 95.2% *vs.* 92.4% at year 5 (all $P > 0.05$ post-year 1). These results demonstrate that rapid ART initiation's early virological advantage (particularly during the first year) gradually converges with delayed initiation outcomes across all $CD4^+$ strata by year 2-5.

3.3.2. Treatment retention rates

Our study evaluated ART retention rates among late-stage PLWH, finding an overall 5-year retention rate of 75.64% with declining adherence over time. While rapid ART initiation showed significantly higher retention only at year 2 (97.7% *vs.* 92.5%, $P = 0.011$), trends favored this approach across all years (96.8% *vs.* 93.6% at year 1; 96.4% *vs.* 91.5% at year 3; 96.2% *vs.* 91.4% at year 4; 96.4% *vs.* 91.9% at year 5; all $P > 0.05$ except year 2) (Table 6). Stratified analysis revealed distinct patterns: in the $CD4^+ < 200$ cells/μL subgroup, retention gradually declined from 97.3% (rapid) *vs.* 92.4% (delayed) at year 1 to 94.0% *vs.* 93.3% at year 5 (all $P > 0.05$), while the $CD4^+$ 200-350 cells/μL subgroup showed significantly better 1-year retention with rapid initiation (96.2% *vs.* 95.1%, $P = 0.009$) but comparable subsequent rates. These findings suggest that while rapid initiation may offer early retention benefits, particularly in less immunocompromised patients, long-term adherence challenges persist across all subgroups.

3.3.3. Immune recovery

Five-year immunological monitoring of late-stage PLWH demonstrated progressive immune recovery under ART, with both $CD4^+$ T cell counts and CD4/CD8 ratio showing sustained improvement. $CD4^+$ counts increased from 342 cells/μL at year 1 to 442 cells/μL at year 5, representing median gains of 172 cells/μL (year 1), 213 (year 2), 241 (year 3), 257 (year 4), and 373 (year 5) above baseline. Parallel improvements occurred in CD4/CD8 ratio, rising from 0.39 (year 1) to 0.57 (year 5), with median annual increases of 0.22, 0.28, 0.32, 0.38, and 0.40 respectively above the baseline ratio of 0.17. These quantitative and functional immune parameters showed consistent year-over-year enhancement throughout the observation period (Figure 4A).

Comparative analysis of immune recovery between ART initiation strategies revealed that while both groups showed progressive improvements in $CD4^+$ counts and CD4/CD8 ratio over five years, the rapid initiation group maintained consistently lower absolute $CD4^+$ counts at all annual follow-ups despite starting with lower baseline values. Notably, the magnitude of $CD4^+$ count increases from baseline showed no statistically significant differences between groups. By year 5, the rapid initiation group achieved a marginally higher CD4/CD8 ratio (0.706 *vs.* 0.674), though intergroup differences remained non-significant at all timepoints (Figure 4B),

**Table 5. Changes in virological suppression rates within five years after antiviral treatment**

| Population group | Total Population | | | Baseline $CD4^+$ T cell count < 200 cells/μL | | | Baseline CD4+ T cell count: 200-350 cells/μL | | |
|---|---|---|---|---|---|---|---|---|---|
| Time Point | ≤ 14 Days | > 14 Days | *P* | ≤ 14 Days | > 14 Days | *P* | ≤ 14 Days | > 14 Days | *P* |
| 1 Year | 81.60% | 72.10% | 0.001*** | 77.30% | 66.60% | 0.005** | 86.00% | 77.60% | 0.021* |
| 2 Years | 84.40% | 83.60% | 0.733 | 81.60% | 78.20% | 0.342 | 88.50% | 89.70% | 0.727 |
| 3 Years | 89.30% | 88.70% | 0.818 | 85.90% | 85.00% | 0.801 | 95.30% | 92.60% | 0.377 |
| 4 Years | 87.80% | 88.70% | 0.74 | 86.70% | 86.50% | 0.976 | 90.50% | 91.80% | 0.796 |
| 5 Years | 90.80% | 87.40% | 0.499 | 88.90% | 85.50% | 0.564 | 95.20% | 89.70% | 0.424 |

*: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$.

**Table 6. Treatment maintenance rates within five years after ART**

| Population group | Total Population | | | Baseline $CD4^+$ T cell count < 200 cells/μL | | | Baseline CD4+ T cell count: 200-350 cells/μL | | |
|---|---|---|---|---|---|---|---|---|---|
| Time Point | ≤ 14 Days | > 14 Days | *P* | ≤ 14 Days | > 14 Days | *P* | ≤ 14 Days | > 14 Days | *P* |
| 1 Year | 96.80% | 93.60% | 0.510 | 97.30% | 92.40% | 0.160 | 96.20% | 95.10% | 0.009** |
| 2 Years | 97.70% | 92.50% | 0.011* | 96.10% | 94.60% | 0.299 | 96.40% | 97.00% | 0.916 |
| 3 Years | 96.40% | 91.50% | 0.056 | 95.70% | 93.60% | 0.266 | 94.40% | 95.90% | 0.593 |
| 4 Years | 96.20% | 91.40% | 0.155 | 95.00% | 93.40% | 0.715 | 92.70% | 95.80% | 0.307 |
| 5 Years | 96.40% | 91.90% | 0.380 | 94.00% | 93.30% | 1.000 | 89.30% | 95.10% | 0.204 |

*: $P < 0.05$; **: $P < 0.01$.

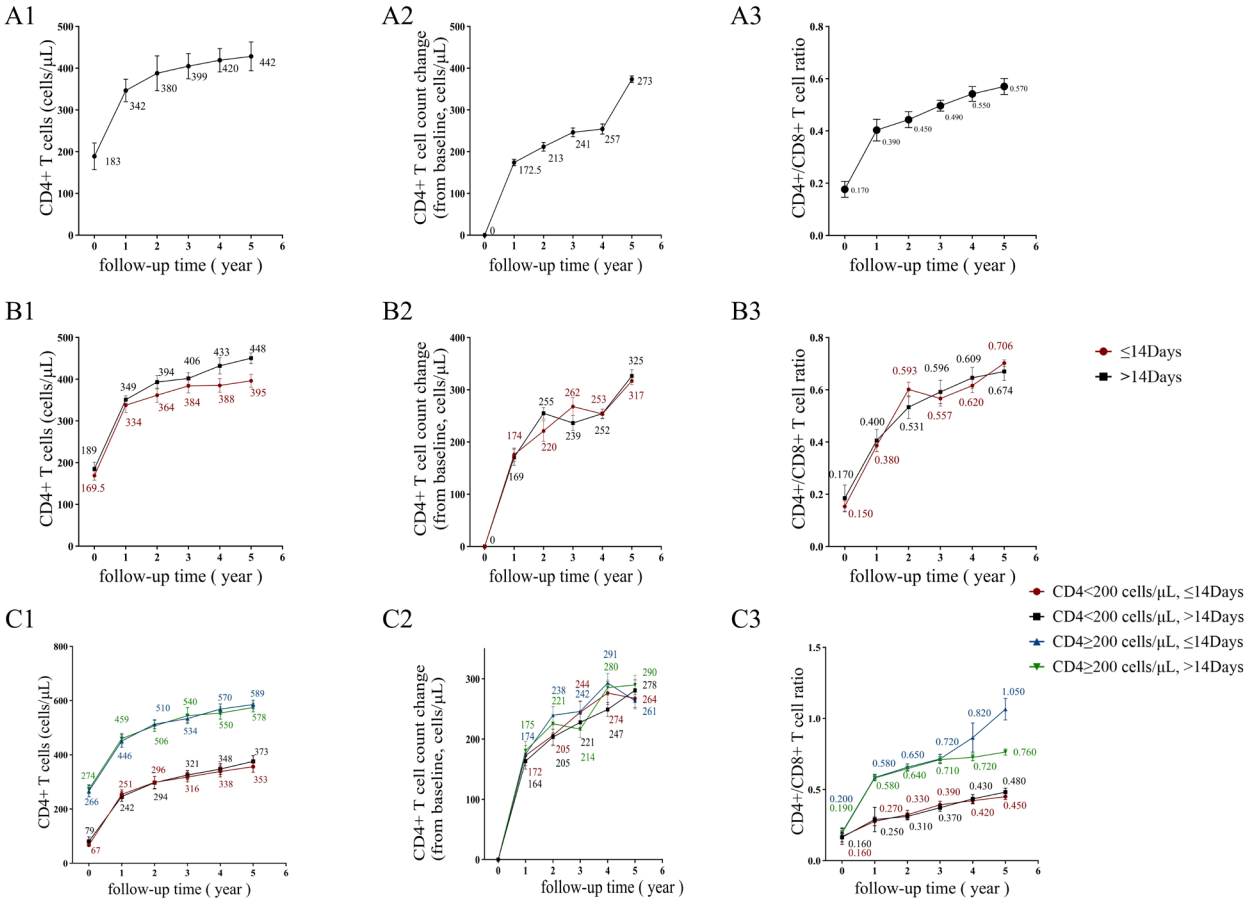


**Figure 4. Immune reconstitution in late-presenting PLWH within five year of treatment.** (**A1**) Changes in CD4$^+$ T cell count in late-presenting PLWH within five years of ART. (**A2**) Change in CD4$^+$ T cell count from baseline in late-presenting PLWH within five years of ART. (**A3**) Changes in CD4/CD8 ratio in late-presenting PLWH within five years of ART. (**B1**) CD4$^+$ T cell recovery in late-presenting HIV patients in the rapid start and delayed treatment groups within five years of treatment. (**B2**) Increase in CD4$^+$ T cells in late-presenting HIV patients in the rapid start and delayed treatment groups within five years of treatment. (**B3**) CD4/CD8 ratio recovery in late-presenting HIV patients in the rapid start and delayed treatment groups within five years of treatment. (**C1**) CD4$^+$ T cell recovery in late-presenting HIV patients with different CD4$^+$ T cell stratifications in the rapid start and delayed treatment groups within five years of treatment. (**C2**) Increase in CD4$^+$ T cells in late-presenting HIV patients with different CD4$^+$ T cell stratifications in the rapid start and delayed treatment groups within five years of treatment. (**C3**) CD4/CD8 ratio recovery in late-presenting HIV patients with different CD4$^+$ T cell stratifications in the rapid start and delayed treatment groups after five years of treatment.

suggesting comparable long-term immune reconstitution regardless of initiation timing.

Stratified by baseline CD4$^+$ levels (< 200 *vs.* 200-350 cells/μL), both rapid and delayed ART initiation groups demonstrated similar five-year immune recovery trajectories, with comparable improvements in CD4$^+$ T cell counts, absolute increases from baseline, and CD4/CD8 ratio (Figure 4C). While all immunological parameters showed sustained upward trends regardless of initiation timing, no statistically significant differences emerged between the treatment strategies in either CD4$^+$ stratum, indicating equivalent long-term immune reconstitution across different baseline immunological statuses (Figure 4C).

## 4. Discussion

Our study highlights several clinical benefits of initiating ART rapidly, including a reduction in time to achieve virological suppression, increased virological suppression rates, and higher treatment adherence rates.

Our findings indicate that rapid ART initiation significantly shortens the time to achieve virological suppression for late-presenting individuals with HIV, regardless of their baseline HIV RNA levels. The time to suppression is positively correlated with baseline viral load. These results corroborate previous studies. For example, research by Christopher D Pilcher *et al.* in the United States demonstrated that initiating ART on the same day of diagnosis reduced the median time to virological suppression (defined as HIV RNA < 200 copies/mL) to 56 days, compared to 79 days for standard ART (*18*). A similar retrospective study in Taiwan showed that starting ART within 7 days of diagnosis decreased the median time to virological suppression from 138 days to 47 days (*30*).

Moreover, our study found that the rapid ART initiation group had significantly higher virological

suppression rates at both 6 months and 1 year compared to the delayed initiation group. This supports previous findings. For instance, Serena P Koenig *et al.* in Haiti reported that among individuals aged 18 and older, those who started ART on the same day of diagnosis had a 1-year virological suppression rate (HIV-1 RNA < 50 copies/mL) of 53%, while those starting ART 3 weeks after diagnosis had a rate of 44% (*13*). In our study, despite a rapid initiation period within 14 days, the 1-year virological suppression rate was 81.6% for the rapid initiation group, compared to 72.1% for the delayed initiation group. Although both rates exceeded those reported in Haiti, they underscore that rapid ART initiation can achieve higher 1-year suppression rates. Similarly, a study in Lesotho found that initiating ART on the same day of an HIV-positive diagnosis resulted in a 1-year virological suppression rate of 50.4%, compared to 34.3% for standard ART (*31*). Additional studies support these findings, such as a multicenter retrospective study in Taiwan showing that 88% of late-presenting HIV patients (with a baseline CD4 count < 200 cells/μL) who started ART within 14 days had a 48-week virological suppression rate of 84% (*32*). The Rainbow study in Italy, which included 30 late-presenting HIV patients (with a baseline CD4 count < 200 cells/μL) who began ART within 7 days, reported a 48-week virological suppression rate of 90% (*33*). Rapid ART initiation not only accelerates HIV suppression but also enhances virological suppression rates. Compared to standard ART, same-day initiation can increase the virological suppression rate by 9.2-16% by months 10-12 (*13,17,34,35*).

Although our study did not examine HIV transmission risks at different time points for the rapid and delayed initiation groups, existing research indicates that lower HIV viral loads correlate with reduced transmission risk. Therefore, rapid ART initiation, by shortening the time to virological suppression and achieving higher suppression rates, likely reduces the risk of HIV transmission to others.

Treatment adherence is crucial for achieving sustained virological suppression and immune recovery in HIV-infected individuals. Our study found that the 1-year treatment adherence rate was 96.8% in the rapid initiation group, compared to 93.6% in the delayed initiation group. Although this difference was not statistically significant, subgroup analysis based on baseline $CD4^+$ T cell counts revealed that for individuals with a baseline $CD4^+$ count < 200 cells/μL, the rapid initiation group had a significantly higher treatment adherence rate at 6 months (97.3% *vs.* 92.4%). For individuals with a baseline $CD4^+$ count between 200 and 350 cells/μL, the 1-year treatment adherence rate was 96.2% in the rapid initiation group, compared to 95.1% in the delayed initiation group. A retrospective study in Taiwan also analyzed treatment adherence, finding that the 7-day rapid ART group had an adherence rate of 88.3%, significantly higher than the 79.0% for the standard initiation group (*30*). Jason Halperin's prospective study in the United States found that patients who initiated ART within 3 days of diagnosis had a 12-month adherence rate of 92%, compared to 80% for those starting ART after 3 days (*36*). Although the grouping methods differed, these studies suggest that earlier ART initiation may be associated with higher adherence rates, potentially due to improved patient compliance. At Nanjing Second Hospital, both rapid and delayed initiation groups had high treatment adherence rates, likely attributable to both patient compliance and high-quality HIV chronic disease management.

Theoretically, rapid ART initiation should facilitate faster and better immune recovery, given its ability to shorten the time to virological suppression and achieve higher suppression rates. We assessed immune recovery using changes in $CD4^+$ T cell counts and CD4/CD8 ratio. Our results show that while $CD4^+$ T cell counts increased over time with ART, there were no statistically significant differences in absolute $CD4^+$ T cell counts between the rapid and delayed initiation groups at various follow-up points. This suggests that late-presenting PLWH, particularly those receiving long-term treatment, experience the most rapid recovery of $CD4^+$ T cell counts and CD4/CD8 ratio within the first or second year of treatment, with stabilization occurring after more than four years. Recent research indicates that from baseline to week 48, the average $CD4^+$ T cell count increased from 133 to 309 cells/μL, and the average CD4/CD8 ratio increased from 0.18 to 0.44 ($P < 0.001$) (*33*). Previous studies have reported that 28% of patients achieved normalization of the CD4/CD8 ratio during a median follow-up of 2.6 years, with a 5-year probability of normalization at 0.44 (*37*). The lack of significant differences in $CD4^+$ T cell counts and CD4/CD8 ratio between the rapid and delayed initiation groups may be attributed to various influencing factors, such as thymic regeneration, microbiome shifts, cellular apoptosis, age, and comorbidities, which were not examined in our study. However, rapid ART initiation at least mitigates the impact of HIV infection, a key factor influencing immune recovery. Our study also found that the rapid initiation group had lower $CD4^+$ T cell counts compared to the delayed initiation group over the 5-year follow-up period, possibly due to higher baseline $CD4^+$ T cell counts in the delayed initiation group.

In summary, our study confirms that rapid ART initiation can shorten the time to virological suppression and achieve higher suppression and adherence rates. These outcomes are critical for evaluating ART efficacy, benefiting HIV-infected individuals, and reducing the risk of HIV transmission in the population. Although rapid ART did not show clear advantages in immune recovery metrics such as $CD4^+$ T cell counts and CD4/CD8 ratio, the numerous influencing factors warrant further investigation into additional factors affecting

immune recovery in both groups.

**Limitations and future directions**

As a single-center study, our results may not be generalizable to other settings with different HIV care practices and ART regimens. The retrospective nature of this study and missing follow-up data limit the sample size. Future studies with larger sample sizes are needed. The study did not analyze comorbidities in late-presenting PLWH. This single-center study did not track HIV transmission rates, so the benefits of rapid ART initiation in reducing population-level HIV transmission cannot be directly confirmed.

**Acknowledgements**

We thank Dr. Zhilang Hu for his insightful and guiding comments on this paper.

*Funding*: This work was supported by a grant from 2022 Annual Key Project supported by Medical Science and Technology Development Foundation, Nanjing Department of Health, (Grant number: ZKX 22040) and Phase I Reserve Talent of The Second Hospital of Nanjing (Grant number: HBRCYL01)

*Conflict of Interest*: The authors have no conflicts of interest to disclose.

**References**

1. World Health Organization. HIV/AIDS. Available at *https://www.who.int/data/gho/data/themes/hiv-aids.* 2022.
2. Han M. Analysis of the HIV/AIDS Epidemic Situation in China and Prospects for Prevention and Control. Zhongguo Ai Zi Bing Xing Bing. 2023; 29:247-250 (in Chinese).
3. WHO Guidelines Approved by the Guidelines Review Committee. Guidelines for Managing Advanced HIV Disease and Rapid Initiation of Antiretroviral Therapy. World Health Organization. 2017.
4. UNAIDS_Global HIV & AIDS Statistics-2019 Fact Sheet: Latest Statistics on the Status of the AIDS Epidemic, World Aids Day. *https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf.* 2020.
5. WHO Guidelines Approved by the Guidelines Review Committee, Guideline on When to Start Antiretroviral Therapy and on Pre-Exposure Prophylaxis for HIV. Geneva, 2015.
6. Yang X, Li X, Qiao S, Zhang Q, Shen Z, Zhou Y. Immunological and virologic outcomes of people living with HIV in Guangxi, China: 2012-2017. PLoS One. 2019; 14:e0213205.
7. Zhang F-G, Ma Y. Progress and challenges in China's free ART programme. Lancet HIV. 2019; 6:e8-e9.
8. Ford N, Migone C, Calmy A, Kerschberger B, Kanters S, Nsanzimana S, Mills EJ, Meintjes G, Vitoria M, Doherty M, Shubber Z. Benefits and risks of rapid initiation of antiretroviral therapy. AIDS. 2018; 32:17-23.
9. Jiao J, Dai L, Chen X. Research progress on rapid antiviral treatment strategies for HIV/AIDS. Zhongguo Ai Zi Bing Xing Bing. 2020; 26:660-663.
10. Zhao Y, Wu Z, McGoogan JM, Shi CX, Li A, Dou Z, Ma Y, Qin Q, Brookmeyer R, Detels R, Montaner JSG. Immediate antiretroviral therapy decreases mortality among patients with high CD4 counts in China: A nationwide, retrospective cohort study. Clin Infect Dis. 2018; 66:727-734.
11. Girometti N, Nwokolo N, McOwan A, Whitlock G. Outcomes of acutely HIV-1-infected individuals following rapid antiretroviral therapy initiation. Antivir Ther. 2017; 22:77-80.
12. Hoenigl M, Chaillon A, Moore DJ, Morris SR, Mehta SR, Gianella S, Amico KR, Little SJ. Rapid HIV viral load suppression in those initiating antiretroviral therapy at first visit after HIV diagnosis. Sci Rep. 2016; 6:32947.
13. Koenig SP, Dorvil N, Dévieux JG*, et al.* Same-day HIV testing with initiation of antiretroviral therapy versus standard care for persons living with HIV: A randomized unblinded trial. PLoS Med. 2017; 14:e1002357.
14. Bacon O, Chin J, L. H. The Rapid ART Program Initiative for HIV Diagnoses (RAPID) in San Francisco. In: Conference on Retroviruses and Opportunistic Infections; 2018 Mar 4-7; Boston, MA.
15. Dijkstra M, van Rooijen MS, Hillebregt MM, *et al.* Decreased time to viral suppression after implementation of targeted testing and immediate initiation of treatment of acute human immunodeficiency virus infection among men who have sex with men in Amsterdam. Clin Infect Dis. 2021; 72:1952-1960.
16. Halperin J, Butler I, Conner K, Myers L, Holm P, Bartram L, Van Sickels N. Linkage and antiretroviral therapy within 72 hours at a federally qualified health center in New Orleans. AIDS Patient Care STDS. 2018; 32:39-41.
17. Labhardt ND, Ringera I, Lejone TI, Klimkait T, Muhairwe J, Amstutz A, Glass TR. Effect of offering same-day ART vs usual health facility referral during home-based HIV testing on linkage to care and viral suppression among adults with HIV in Lesotho: The CASCADE randomized clinical trial. JAMA. 2018; 319:1103-1112.
18. Pilcher CD, Ospina-Norvell C, Dasgupta A, Jones D, Hartogensis W, Torres S, Calderon F, Demicco E, Geng E, Gandhi M, Havlir DV, Hatano H. The effect of same-day observed initiation of antiretroviral therapy on HIV viral load and treatment outcomes in a US public health setting. J Acquir Immune Defic Syndr. 2017; 74:44-51.
19. Wu Z, Zhao Y, Ge X*, et al.* Simplified HIV testing and treatment in China: Analysis of mortality rates before and after a structural intervention. PLoS Med. 2015; 12:e1001874.
20. Colasanti J, Sumitani J, Mehta CC, Zhang Y, Nguyen ML, Del Rio C, Armstrong WS. Implementation of a rapid entry program decreases time to viral suppression among vulnerable persons living with HIV in the Southern United States. Open Forum Infect Dis. 2018; 5:ofy104.
21. Sun J, Liu L, Shen J, Chen P, Lu H. Trends in baseline CD4 cell counts and risk factors for late antiretroviral therapy initiation among HIV-positive patients in Shanghai, a retrospective cross-sectional study. BMC Infect Dis. 2017; 17:285.
22. Lin KY, Cheng CY, Li CW, *et al.* Trends and outcomes of late initiation of combination antiretroviral therapy driven by late presentation among HIV-positive Taiwanese patients in the era of treatment scale-up. PloS One. 2017;

12:e0179870.
23. Antinori A, Coenen T, Costagiola D, *et al.* Late presentation of HIV infection: a consensus definition. HIV Med. 2011; 12:61-64.
24. Sobrino-Vegas P, Moreno S, Rubio R, Viciana P, Bernardino JI, Blanco JR, Bernal E, Asensi V, Pulido F, del Amo J, Hernando V. Impact of late presentation of HIV infection on short-, mid- and long-term mortality and causes of death in a multicenter national cohort: 2004-2013. J Infect. 2016; 72:587-596.
25. Sabin CA, Smith CJ, Gumley H, Murphy G, Lampe FC, Phillips AN, Prinz B, Youle M, Johnson MA. Late presenters in the era of highly active antiretroviral therapy: uptake of and responses to antiretroviral therapy. AIDS. 2004; 18:2145-2151.
26. Kelley CF, Kitchen CM, Hunt PW, Rodriguez B, Hecht FM, Kitahata M, Crane HM, Willig J, Mugavero M, Saag M, Martin JN, Deeks SG. Incomplete peripheral CD4+ cell count restoration in HIV-infected patients receiving long-term antiretroviral treatment. Clin Infect Dis. 2009; 48:787-794.
27. Jevtović D, Vanovac V, Veselinović M, Salemović D, Ranin J, Stefanova E. The incidence of and risk factors for HIV-associated cognitive-motor complex among patients on HAART. Biomed Pharmacother. 2009; 63:561-565.
28. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS. 2006; 20:1447-1450.
29. van Opstal SEM, van der Zwan JS, Wagener MN, Been SK, Miedema HS, Roelofs P, van Gorp ECM. Late presentation of HIV infection in the Netherlands: Reasons for late diagnoses and impact on vocational functioning. AIDS Behav. 2018; 22:2593-2603.
30. Huang YC, Sun HY, Chuang YC, Huang YS, Lin KY, Huang SH, Chen GJ, Luo YZ, Wu PY, Liu WC, Hung CC, Chang SC. Short-term outcomes of rapid initiation of antiretroviral therapy among HIV-positive patients: real-world experience from a single-centre retrospective cohort in Taiwan. BMJ Open. 2019; 9:e033246.
31. Labhardt ND, Ringera I, Lejone TI, Klimkait T, Muhairwe J, Amstutz A, Glass TR. Effect of offering same-day ART vs usual health facility referral during home-based HIV testing on linkage to care and viral suppression among adults with HIV in Lesotho: The CASCADE randomized clinical trial. JAMA. 2018; 319:1103-1112.
32. Lee CY, Lee CH, Tang HJ, Tsai HC, Yang CH, Lin YP, Wang SF, Lu PL. Comparison of Virological Efficacy of DTG/ABC/3TG and B/F/TAF Regimens and Discontinuation Patterns in Persons Living with Advanced HIV in the Era of Rapid ART: A Retrospective Multicenter Cohort Study. Infect Dis Ther. 2023; 12:843-861.
33. Camici M, Gagliardini R, Lanini S, *et al.* Rapid ART initiation with bictegravir/emtricitabine/tenofovir alafenamide in individuals presenting with advanced HIV disease (Rainbow study). Int J Antimicrob Agents. 2024; 63:107049.
34. Rosen S, Maskew M, Fox MP, Nyoni C, Mongwenyana C, Malete G, Sanne I, Bokaba D, Sauls C, Rohr J, Long L. Initiating antiretroviral therapy for HIV at a patient's first clinic visit: The RapIT randomized controlled trial. PLoS Med. 2016; 13:e1002015.
35. Seekaew P, Phanuphak N, Teeratakulpisarn N, Amatavete S, Lujintanon S, Teeratakulpisarn S, Pankam T, Nampaisan O, Jomja P, Prabjunteuk C, Plodgratoke P, Ramautarsing R, Phanuphak P. Same-day antiretroviral therapy initiation hub model at the Thai Red Cross Anonymous Clinic in Bangkok, Thailand: An observational cohort study. J Int AIDS Soc. 2021; 24:e25869.
36. Halperin J, Conner K, Butler I, Zeng P, Myers L, Clark R, Van Sickels N. A care continuum of immediate ART for newly diagnosed patients and patients presenting later to care at a federally qualified health center in New Orleans. Open Forum Infect Dis. 2019; 6:ofz161.
37. Zhabokritsky A, Szadkowski L, Cooper C, Loutfy M, Wong A, McClean A, Hogg RS, Walmsley SL. Increased CD4:CD8 ratio normalization with implementation of current ART management guidelines. J Antimicrob Chemother. 2021; 76:729-737.

Received February 18, 2025; Revised April 24, 2025; Accepted April 25, 2025.

[§]These authors contributed equally to this work.

**Address correspondence to:*
Hongxia Wei and Rentian Cai, Department of Infectious Disease, The Second Hospital of Nanjing, Affiliated to Nanjing University of Chinese Medicine, 210000, No. 1-1, Kangfu road, Nanjing, China.
E-mail: njyy019@njucm.edu.cn (HW); cairentian@163.com (RC)