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# Antiretroviral Therapy Initiation Following Policy Changes: Observations From China

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## Abstract

China's HIV/AIDS treatment policies have been evolving over the preceding decade. This study describes patterns of antiretroviral therapy (ART) initiation for a sample of people living with HIV/AIDS (PLHIV) in rural Anhui, China, where most PLHIV were infected via paid plasma donation during the 1990s. A total of 481 PLHIV who were receiving ART were included in our analyses. Times between HIV diagnosis and the initiation of ART were examined relative to the time points when major ART-related policies changed in China. More than half (53%) of PLHIV who had been diagnosed by 2003 received ART within 6 months, whereas 93% of PLHIV who had been diagnosed in 2010 or later received ART within 6 months. The study results provide additional support that the “Four Frees and One Care” policy in 2003 and the relaxation of ART eligibility in 2010 have facilitated the initiation of treatment for PLHIV in China.

## Keywords

HIV, antiretroviral therapy, treatment outcome, China, policy

## Introduction

The HIV epidemic began in China during the prior century, after the first case of AIDS in China was identified in 1985.<sup>1</sup> By the end of 2014, there were 501,000 reported people living with HIV (PLHIV) in China.<sup>2</sup> China's responses to the HIV/AIDS epidemic have been evolving over time; in particular, treatment policies have changed. In 2002, China initiated and implemented a pilot community-based free HIV treatment, care, and prevention program named China CARES; this pilot program was subsequently expanded to the entire nation in 2003 and became the current National Free Antiretroviral Treatment Program (NFATP).<sup>3,4</sup> In 2003, the Chinese government implemented a national HIV/AIDS policy, “Four Frees and One Care,” to provide free antiretroviral drugs to PLHIV who are rural residents or uninsured urban residents.<sup>5–8</sup> The Four Frees and One Care program significantly expanded access to antiretroviral therapy (ART) in China, resulting in an increase of 23,000 in the number of PLHIV enrolled in this program between 2005 and 2007.<sup>3,9</sup>

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In 2005, ART services in China were again scaled up as the government began to provide provincial-level plans.<sup>10</sup> In 2006, China officially announced the first legislation directly aimed at controlling HIV/AIDS.<sup>11</sup> By December 2006, highly active ART (HAART) coverage for former plasma donors with AIDS had reached 70.5%, with an accompanying decrease in mortality.<sup>12</sup> In addition to improving the accessibility and reach of ART, the World Health Organization (WHO) issued new treatment guidelines for ART in 2011 that specified a cutoff point of a CD4 count of 350 cells/mm<sup>3</sup> for beginning ART.<sup>13</sup> This guidance led to a change in the national treatment guidelines for initiating ART in China, allowing an even greater number of PLHIV to obtain HIV-related treatment and care.<sup>14</sup>

However, the implications of China's policy changes regarding ART initiation remain understudied, particularly among rural subsamples. With the rapid scaling up of HIV treatment and care in recent years, it is imperative to understand the impact of HIV policies on the initiation of treatment for PLHIV. This study describes a sample of PLHIV living in rural Anhui, China, who are currently receiving ART, focusing on the initiation of treatment for these individuals during various timeframes involving policy changes.

## Methods

### Study Sample

This study used baseline data from a randomized controlled trial for HIV-affected families in Anhui Province, China. Most existing HIV infections in Anhui were caused by commercial plasma donations during the early 1990s.<sup>15</sup> Thousands of commercial plasma collection centers were established in rural China between 1990 and 1994,<sup>1</sup> and donating blood to earn money became an easy method by which rural farmers augmented their incomes. In particular, plasma donors were paid to donate blood; during blood donations, plasma was removed, and red blood cells were intravenously re injected into donors to prevent anemia caused by repeat blood donation. HIV-1 antibody testing was not required prior to 1995 and therefore was not performed at any local plasma collection center during the early 1990s.<sup>1</sup> The mixing during collection and reinfusion led to thousands of new HIV infections among commercial plasma donors in Anhui.<sup>16</sup> Although these practices were stopped long ago, the history of this HIV outbreak among former plasma donors continues to affect the region. In this area, new cases of HIV infection have been diagnosed among children and among adults with no history of plasma donation, suggesting that transmission to populations other than plasma donors via sex, mother-to-child transmission, and injection drug use has already occurred.<sup>16,17</sup>

### Data Collection

Data were collected between late 2011 and early 2013 from 32 villages within the 4 counties of Anhui. To recruit PLHIV, informational flyers regarding the study were posted in village clinics that were frequently visited by PLHIV for routine check-ups and care. Service providers at clinics also disseminated study information to potential participants verbally and via informational materials. PLHIV interested in participating in the study were referred to a project recruiter who subsequently met privately with each potential study subject in a room of the village clinic or at the subject's preferred location. During this meeting, the study recruiter screened the potential participant for eligibility, explained the study procedures, answered questions, emphasized the voluntary nature of participation, and obtained informed consent. A total of 522 PLHIV were included in this study.

Assessments were administered by computer-assisted personal interview (CAPI). Trained interviewers read the questions shown on a screen to the participant and entered their answers

directly into a computer database. The data collection process required approximately 45 to 60 minutes for each participant. Each participant received 50 yuan (US\$8) for completing the assessment. The study protocol was approved by the institutional review boards of the Anhui Provincial Center for Disease Control and Prevention and the University of California, Los Angeles.

## Measures

In this study, subjects' sociodemographic characteristics, including age, gender, years of education, and annual family income (in yuan) were collected. For PLHIV in China, CD4 counts and viral loads are routinely assessed every 6 months.<sup>18</sup> During this study, no additional biomedical tests were performed. With participants' consent, subjects' medical records were examined and various clinical data were obtained, including dates of HIV diagnoses, dates when ART was initiated, CD4 counts, CD4 testing dates, and viral loads. For each participant, project staff recorded a CD4 count, viral load test dates, and the results of tests conducted closest to the survey date. Continuous viral load data were dichotomized into the categories of undetectable and detectable viral RNA (with a threshold of 50 copies per mL of blood).<sup>19</sup> The year of HIV diagnosis was divided into 4 categories: 2003 and earlier, 2004-2005, 2006-2009, and 2010 and later. These categories reflect major changes in HIV policies and treatment guidelines in China. To measure adherence to ART, participants were asked whether they had ever forgotten to take their ART medication. Subjects who responded affirmatively were further questioned regarding the number of day(s) they had not taken their ART medication during the past 7 and 30 days. A dichotomous measure was constructed in which a score of 1 was assigned if a participant reported ever stopping their medicine and a score of 0 was assigned if a participant had not forgotten to take ART during the preceding 7- and 30-day periods.

## Data Analysis

Demographic and clinical characteristics of the HIV-positive participants who were enrolled in the study and currently receiving ART treatment were summarized using descriptive statistics (means and standard deviations) for continuous data and frequencies for categorical data. The frequencies of PLHIV who received their ART treatments within 6 months of HIV diagnosis across the 4 HIV-diagnosis intervals described above were graphically examined, and compared without and with accounting for the clustering at the village level using chi-square and Cochran-Mantel-Haenszel tests, respectively. All descriptive analyses were performed using SAS software (SAS Institute, Cary, NC, USA).

## Results

### *Demographic and ART-Related Characteristics*

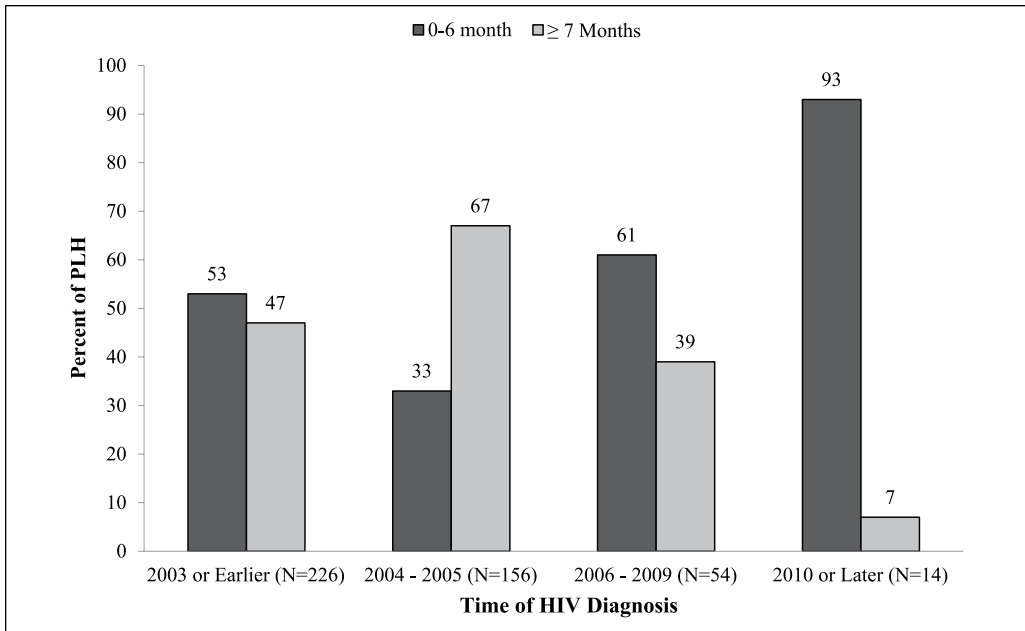
A total of 522 PLHIV participated in this trial, and 481 of these participants were receiving ART when they enrolled in the study. Participants' demographic and ART-related characteristics are presented in Table 1. Subjects' average age was 48.6 years, with 68% of participants between 36 and 55 years of age. Less than half of the study sample (45%) was male. Participants' average annual family income was 14,598 yuan (US\$2383), which was lower than the average family income in Anhui Province in 2013 (25,006 yuan or US\$4,024).<sup>20</sup> More than 40% of subjects were illiterate, and 13% of participants had received more than 6 years of education (Table 1).

Among the 481 PLHIV who were receiving ART at enrollment, the earliest HIV diagnosis was in 1996 and the latest HIV diagnosis was in 2013. Among these PLHIV, 239 subjects (50%) had been diagnosed by 2003, and 152 PLHIV (34%) had begun ART by 2003. More than 70% of

**Table 1.** Demographic and Antiretroviral Therapy (ART)-Related Characteristics of Study Participants.<sup>a</sup>

Characteristics	n	%
No. of participants (n = 522)		
On ART	481	92.1
Not on ART	41	7.9
Demographic characteristics (n = 481)		
Age (years)		
18-35	26	5.41
36-45	164	34.1
46-55	165	34.3
>55	126	26.2
Male	216	44.9
Education (years)		
None	197	41.0
0-6	222	46.2
>6	62	12.9
Family income (yuan)		
<5000	68	14.2
5001-10 000	108	22.6
10 000-20 000	161	33.6
>20 000	142	29.6
ART-related characteristics (n = 481)		
Viral load		
Mean (SD)	10,185	(69,051)
<50	325	71.1
≥50	132	28.9
CD4		
Mean (SD)	409	(210)
<200	72	15.4
200-350	129	27.6
350-500	131	28.1
≥500	135	28.9
HIV diagnosis (year)		
2003 or earlier	239	49.9
2004-2005	166	34.7
2006-2009	57	11.9
2010 or later	17	3.5
ART initiation (year)		
2003 or earlier	152	33.8
2004-2005	114	25.3
2006-2009	134	29.8
2010 or later	50	11.1
Months between diagnosis and ART, mean (SD)	22.2	(28.8)
ART adherence (n = 481)		
Never forgotten to take ART medication	295	61.3
Never missed a day of ART in the past 7 days	451	93.8
Never missed a day of ART in the past 30 days	402	83.6

<sup>a</sup>Number of missing values varied across demographic and clinical characteristics.



**Figure 1.** Interval between HIV diagnosis and antiretroviral therapy (ART) initiation stratified by the time of HIV diagnosis.

PLHIV had undetectable viral loads, and 57% of PLHIV had CD4 counts greater than 350 cells/mm<sup>3</sup>. More than 60% of PLHIV reported that they had never forgotten to take their ART medication, and about 84% of PLHIV had always remembered to take their ART medication during the preceding 30 days. Figure 1 presents the distribution of time intervals between HIV diagnosis and ART initiation across four HIV-diagnosis intervals. Thirty-one (6%) PLHIV had either missing HIV diagnosis or ART initiation dates. More than half (53%) of PLHIV who had been diagnosed by 2003 began receiving ART within 6 months, whereas 93% of PLHIV who had been diagnosed in 2010 or later began receiving ART within 6 months. Differences in the distributions of PLHIV who had their ART initiation within 6 months of HIV diagnosis across the four policy-related intervals were statistically significant without and with accounting for the village-level of clustering ( $p < .001$  and  $p = .022$ , respectively).

## Discussion

This study described the condition of PLHIV receiving ART by examining their treatment initiation patterns in rural Anhui, China. We observed that the pattern of individual treatment initiation was associated with the time of HIV diagnosis, suggesting there might be a connection with changes in HIV treatment policies. Globally, recommendations regarding initiating therapy for asymptomatic HIV-infected patients have undergone major alterations over time.<sup>21</sup> It appears that China's decision to adhere to WHO treatment guidelines resulted in an increase in the early initiation of treatment among PLHIV. In addition, this increase could also be attributed to the implementation of the "Four Frees and One Care" program, which provides free ART to rural and poor urban residents,<sup>3</sup> including PLHIV enrolled in this study. This study provided further evidence illustrating the impact of ART expansion at the policy level on the treatment experiences of individual PLHIV. In 2014,

China again updated its national ART guidelines to a threshold CD4 count of 500 cells/mm<sup>3</sup> to further ease ART initiation eligibility.<sup>22,23</sup> Based on the findings of our study, we predict that this change will further facilitate the initiation of ART for more PLHIV in China.

Our findings should be interpreted in light of several limitations. First, the single group cross-sectional design was a major limitation of the study, which restricted the ability to make between-group comparisons and causality inferences. Second, most existing HIV infections in the examined region were caused by commercial plasma donations during the early 1990s; this situation may not be representative of conditions in other areas of China. Another limitation of this study was that no blood samples were collected to perform CD4/viral load testing. Instead, these data were obtained from patients' medical records; therefore, there could be a lag between the collection of biomedical data and the time when our survey was conducted. Last, the sample size was limited, that is, the sample sizes for the later intervals (2010 and after) were relatively small. Nevertheless, the study findings indicate the impact of HIV policies on the early initiation of treatment. China is one of the few low- and middle-income countries in which domestic funds are the major source of HIV/AIDS program funding,<sup>24</sup> and policy makers can use these findings to prioritize HIV-related health services and ensure that sufficient resources are committed to HIV care to curb the HIV epidemic in China.

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### Declaration of Conflicting Interests

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