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## Original Article

## Self reported adherence to antiretroviral treatment and correlates in Hunan province, the Peoples Republic of China

John Kipsang<sup>a</sup>, Jia Chen<sup>b</sup>, Chulei Tang<sup>a</sup>, Xianhong Li<sup>b</sup>, Honghong Wang<sup>b,\*</sup><sup>a</sup> Xiangya School of Nursing, Central South University, Hunan, China<sup>b</sup> School of Nursing of Central South University, Hunan, China

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## ABSTRACT

**Aims:** This study aimed to describe the adherence level to antiretroviral therapy and its associated factors among people living with HIV in Hunan province, China.

**Methods:** Across-sectional survey study was done at two major HIV treatment sites within Hunan province in China from July 2011 to Oct 2012 through face-to-face interviews. Adherence measures were captured using a 30-day visual analog scale (VAS).

**Results:** A total of 418 participants consented and completed the questionnaires with the mean age being 38 years old. Based on VAS, 28% of the participants had lower than 90% ART adherence level. The main reasons for missing drugs were; forgetting, being away from home, being busy and feeling worse after taking drugs. Logistic regression results showed that drug use ( $B = 0.68$ ,  $OR = 2.11$ ), time on ART ( $B = -0.31$ ,  $OR = 0.72$ ) and side effects ( $B = 0.64$ ,  $OR = 1.82$ ) were significantly associated with adherence to ART.

**Conclusion:** Patients on ARVs in Hunan province are faced with adherence challenges notably drug abuse, drug regime scheduling challenges at the initial stages of therapy and drug side effects. It is therefore necessary to institute specific adherence interventions that target those who abuse drugs, ART naïve patients, and those experiencing side effects in order to achieve optimal ART adherence.

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## 1. Introduction

Human immunodeficiency virus (HIV) infection continues to exert a heavy burden on the health care systems globally. The devastating clinical picture of acquired immunodeficiency syndrome (AIDS) epidemic that was seen during the first two decades of the epidemic changed dramatically with the introduction of antiretroviral therapy (ART). People living with HIV (PLWH) are now living longer productively so long as they remain adherent to the prescribed ART regimen [1]. Research has demonstrated that patients ART programs experienced adherence challenges that have the potential of not only reversing the achievements made in combating spread of the virus, reducing HIV-related morbidity and mortality and the emergence of mutant viral strains that are resistant to the available antiretroviral drugs [2]. A study in British

Columbia demonstrated that the development of viral drug resistance has reduced significantly over the years but still poses the greatest risk to the gains made in the management of the HIV epidemic [3]. Studies that have been done to determine ART adherence based on self-reports have shown mixed results, with a majority of the studies reporting optimum adherence to therapy by a majority of those participating, but other studies have reported that a significant portion of those on ART were not meeting the minimum accepted adherence levels [4,5]. The above-cited studies and other similar studies have identified factors that hinder optimum adherence to therapy. Current ART regimes involve the administration of a combination of antiretroviral agents that require high levels of fidelity to therapy by those on treatment for a lifetime [6].

According to the Center for Disease Control (CDC) in China, the cumulative reported number of HIV infection was 746,644 in China at the end of September 2017 [7]. The epidemic in China has yet to stabilize and it was feared that the number of those infected could be more than twice the aforementioned figure. This was attributed to HIV-associated stigma that discourages many from coming out

\* Corresponding author.

E-mail addresses: [kipsang@gmail.com](mailto:kipsang@gmail.com) (J. Kipsang), [cjia65215@163.com](mailto:cjia65215@163.com) (J. Chen), [honghong\\_wang@csu.edu.cn](mailto:honghong_wang@csu.edu.cn) (H. Wang).

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voluntarily to be tested or failing to disclose their sero-positive status once they test positive [7]. New HIV infections in China have almost reached a plateau phase nationally but the dynamics differ from region to region. By the end of 2015 there were over 448,000 PLWH on ART in China [8]. In recent years, due to the scaling up of ART services, more PLWH are getting into the treatment bracket and the success of ART roll-out programs globally depends on effective monitoring of individual client's drug adherence.

The adherence threshold for ART historically has been set at 95% for the prescribed doses based on older ART regimes [9]. A study done in California reported that an 80%–90% medication adherence rate based on current regimes is sufficient in suppressing viral replication [10]. ART adherence levels in China are based on uptake of at least 90% of the prescribed doses [11]. Taking into consideration that first-line ART drug regimes globally have not changed much, the 90% adherence threshold is still used when assessing ART adherence in China.

Previous studies have identified the following factors as being the major impediments to optimal ART adherence: substance use, depressive symptoms, traveling, being busy, ART-associated side effects, failure to go for ART drug refills, stigma/discrimination, and lack of family or partner support [12–14]. Non-adherence to therapy is not an option for PLWH because of the limited options available in case of ART drug resistance or drug failure. This study used a self-reported approach as it was the most effective and feasible method based on the resources available at the time the study was done. There are other more effective ways to monitor adherence that come at a cost, are invasive, and that require skilled manpower to operate the associated technology, making them challenging during implementation [15]. The purpose of this study was to determine HIV clients' ART adherence levels as well as learning about context-specific factors that hinder adherence to therapy in Hunan province, China.

## 2. Methodology

### 2.1. Setting and samples

We adopted a descriptive study design. Clients on ART were recruited at two major HIV treatment sites in Hunan province. The two sites were chosen primarily because they were the main care sites for HIV management in the province. Hunan province is in the central southern region of China. The first reported cases of HIV in China were diagnosed in the southern Yunnan province, the virus then spread to the neighboring south eastern and to the central regions of China. The national average HIV prevalence rate is less than 0.1% but the rate is slightly higher in the central and southern regions of China [8]. This explains why the region has a relatively higher HIV prevalence rates when compared to the other regions of China. This called for close surveillance in order to contain the spread of the epidemic and treat those who were infected.

Data were collected through direct face-to-face interviews over a period of 10 months from October 2011 to July 2012. The two treatment sites provide ARTs and HIV-associated care to all those affected by HIV within the town and the surrounding villages. Potential participants were approached on an individual basis during routine visits they made to the facility for diagnostic tests, counseling, drug refills, and other routine clinic assessment schedules. Study participants were selected based on the following criteria: being at least 18 years of age and receiving ART drugs from the two HIV treatment sites; they had to be psychologically fit to give an informed consent and physically fit to answer interview questions independently.

### 2.2. Measures and instruments

Raw data were captured using a questionnaire administered by the primary investigators with assistance from the other co-authors. The first part of the questionnaire captured socio-demographic data, age, residence, education, occupation, income, marital status, drug use status, time of HIV status diagnosis, and length of time on ART. Part two captured data on ART adherence measures that included patients reporting their adherence over the past 30 days on a 100-point visual analog scale (VAS), where 0 indicated complete non-adherence and 100 indicating perfect adherence. The threshold for optimal adherence was defined at 90% and above [16]. This part also asked about the number of doses taken or missed during the last 7 days prior to the interview and included questions on reasons for missing the dose(s), use of reminders (if any), family support, and side effects experienced. The questionnaire was tested and validated in the previous study, with a content validity of 0.84 and test-retest reliability of 0.91 [17].

### 2.3. Statistical analysis

Data were analyzed using Statistical Program for Social Sciences version 18.0 from IBM Company of the United States of America. Descriptive statistics provided general information concerning participant characteristics including ART adherence levels and reasons for missing medication. The chi-square test was used to compare participants who met optimal ART adherence levels (those who took 90% of prescribed ART doses in the past month) to those who were deemed to be non-adherent (took less than 90% of prescribed doses in the past month) based on demographic characteristics and health status variables. Multivariate associations among the two adherence categories (adherent and non-adherent) and all related factors of adherence were subjected to logistic regression analysis. A backward elimination process was used to build multivariate models with a *P*-value of <0.05, which was required for retention in the final model.

### 2.4. Ethical considerations

The study targeted adult participants at least 18 years old. We sought ethical approval for the study and the Institutional Review Board firstly approved it in 2009 and reapproved it in the beginning of 2011. The approval protocol number was Protocol 2009–12, and data collection was done over a period of 10 months from late 2011 to mid 2012. The two respective hospitals and the CDC in the region were approached and gave approval for the study to be conducted. Prospective participants were given explanations orally and in writing for comprehension of the study objectives. Those who agreed to participate in the study gave oral consent indicating that they had voluntarily consented to participate. To ensure confidentiality, participants' codes instead of names were used for identification purposes in the questionnaires. Interviews were conducted in private rooms with the participant and interviewer being alone during the interview. The clinic staff provided logistical support and did not participate in the actual interviews. A package of food (milk powder or cookies) was given to each participant as a gift for their participation in the survey.

## 3. Results

### 3.1. Demographic data

A total of 418 (*N* = 418) participants consented and were interviewed during the study. The average age of the participants was 38 years (*SD* = 9.72), 90.2% (*n* = 377) were below the age of 50, 70.1%

( $n = 293$ ) were male, 73.0% (305) were living in a city, 58.4% ( $n = 244$ ) had been educated up to middle high school, 51.0% ( $n = 214$ ) were married, and 67.2% ( $n = 281$ ) were either jobless or had unstable jobs. In regard to income, 72.0% ( $n = 301$ ) earned less than 20,000 ¥ annually, with 50% of these earning less than 5000 ¥ annually. In regard to the length of time since they were diagnosed with HIV, 81.6% ( $n = 341$ ) of the respondents had lived with the virus for two years or more since being diagnosed. Almost a third, 28.0% ( $n = 117$ ), of the respondents reported having used or were using drugs at the time the study was done. The average time of participants on ART was 18 months (range = 1–73 months), with more than half of the participants (232/418) having been on therapy for 12 months or less. The sample characteristics are presented in Table 1.

### 3.2. ART adherence

Based on a 30-day VAS, 72.0% ( $n = 301$ ) of the study participants attained an ART adherence score  $\geq 90\%$ , the minimum ART adherence level required for viral suppression. The remaining 28.0% ( $n = 117$ ) had an adherence score  $< 90.0\%$ , which is considered inadequate for viral suppression. These results are presented in Table 2. The results indicate that 4.1% ( $n = 17$ ) of the non-adherent participants took less than 50.0% of the prescribed doses, 7.0% ( $n = 29$ ) took between 51.0% and 80.0% of the prescribed doses, and 17.0% ( $n = 71$ ) took 81.0%–89.0% of the prescribed doses.

### 3.3. Reasons for missing doses

Out of 418 participants, 90 gave the reasons for missing a dose or doses in the seven days prior to the interview. The top five reasons for missing doses were: forgetting to take drugs 42.2% ( $n = 38$ ), being away from home at the time when they were required to take drugs 28.9% ( $n = 26$ ), being busy with other activities 16.7% ( $n = 15$ ), felt worse after taking drugs 12.2% ( $n = 11$ ), and 12.2% ( $n = 11$ ) did not want others to know that they were taking ARTs. The reasons for missing drugs are presented in Table 3.

**Table 1**  
Sample Characteristics (N = 418).

Characteristics	Categories	No.	%
Gender	Male	293	70.1
	Female	125	29.9
Age (yr)	18–30	112	26.8
	31–50	265	63.4
	51–70	41	9.8
Marital status	Single	204	49.0
	Married/have stable partner	214	51.0
Employment	Unemployed	199	47.6
	Employed occasionally	82	19.6
Residence	Rural	113	27.0
	Town/city	305	73.0
Education level	Primary education or less	65	15.6
	Middle school	179	42.8
	High school or above	174	41.6
Annual income RMB	0–4999	154	36.8
	5000–19999	147	35.2
	$\geq 20000$	116	27.8
Drug use	No	301	72.0
	Yes	117	28.0
Time on ART	$\leq 1$ yr or less	232	55.5
	1 yr up to 2yrs	64	15.3
	>2yrs	122	29.2

Note: ART = Antiretroviral therapy; RMB = Renminbi; (yr) = age or time in years.

### 3.4. Time adherence

Table 4 presents time adherence to ART (the ability to take the prescribed drugs within 2 h of the required time). The results showed that 57.9% (242/418) reported taking nearly all the doses at the required time, with 92.8% (388/418) reporting that they took more than half of the doses within the 2-h upper limit within which a dose must be taken.

### 3.5. Factors associated with adherence

#### 3.5.1. Bivariate analysis

Inferential statistical analysis was done to determine factors associated with ART adherence. The dependent variable adherence to ART was dichotomized as suboptimal adherence (VAS score  $< 90\%$ , value = 1) versus optimal adherence (VAS score  $\geq 90\%$ , value = 0). CD4<sup>+</sup> T cell count were not associated with adherence ( $P = 0.76$ ). The following factors were found to be significantly associated with adherence drug abuse ( $P = 0.003$ ), perceived side effects of ARTs ( $P = 0.043$ ), and time on ART ( $P = 0.01$ ) as presented in Table 2. These factors were then entered as independent variables for multivariate regression analysis.

#### 3.5.2. Logistic regression analysis

Logistic regression results (Table 5) indicated that participants who were using or had used drugs previously ( $B = 0.68$ ,  $OR = 2.1$  (1.3–3.3)), were ART naïve ( $B = -0.31$ ,  $OR = 0.72$  (0.6–0.9)), and those were experiencing side effects ( $B = 0.64$ ,  $OR = 1.8$  (1.1–2.8)) were more likely to be non-adherent to therapy.

## 4. Discussion

This study found that 72.0% of the study participants were adherent to ART with the remaining 28.0% being deemed to be non-adherent. These findings are comparable with previous study findings in China, other parts of Asia, and the rest of the world that have found non-adherence levels ranging from 15% to 40% [17–22]. Adherence studies based on self-reports in sub-Saharan Africa and the developing world have shown similar results and in some instances produced near-perfect adherence results [5,23]. This study identified the following reasons to be associated with non-adherence to therapy: forgetting, being too busy working, traveling, and feeling worse after taking medication. These barrier reason(s) were either responsible as standalone reasons for non-adherence or in combination.

This study identified three key factors that were associated with non-adherence: drug use, time on ART, and ART side effects. Drug use was the most highly correlated factor to non-adherence to therapy. Previous studies have not only identified the close link between drug use and suboptimal adherence, but also its role in HIV infection. This result is in agreement with previous study findings in India that found that 53% of those who abused drugs were non-adherent [21,24]. However, another large study that incorporated the use of electronic data monitoring (EDM) in the United States of America done to determine the association between adherence and the use various substances, demonstrated that those who used cocaine or heroin were more likely to be non-adherent when compared to those who used alcohol or cannabis [25]. The study participants in the above-cited studies were either actively abusing drugs or were on drug replacement therapy.

Time on ART (being naïve) was the second most significant factor associated with non-adherence. A majority of the participants in this study had been on therapy for a period of one year or less (55.5%). This finding is attributable to naïveté on the part of the participants (sero-positive status and starting ARTs). Many of them

**Table 2**  
Factors Associated with Adherence to ART.

Variables	Optimal adherence ( $\geq 90\%$ , $n = 301$ )	Suboptimal adherence ( $< 90\%$ , $n = 117$ )	<i>P</i>	OR (95% CI)
Gender				
Male	211	82		
Female	90	35	0.991	1.00 (0.6–1.6)
Age (yr)				
18–30	76	36		
31–50	192	73		
51–70	33	8	0.313	
Marital status				
Single	139	65		
Married/have stable partner	162	52	0.092	0.70 (0.4–1.1)
Employment				
Unemployed	218	90		
Employed	83	27	0.346	0.80 (0.5–1.3)
Residence				
Rural	82	31		
Town/city	219	86	0.877	1.00 (0.6–1.7)
Education				
Primary school or less	44	21		
Middle school	123	56		
High school or above	134	40	0.203	
Income per year (RMB) 0–4999	107	47		
5000–19999	102	45		
$\geq 20000$	92	25	0.214	
Drug use	229	72		
No				
Yes	72	45	0.003**	2.00 (1.3–3.1)
ART time	156	76		
$\leq 1$ yr				
>1 yr to 2yrs	51	13		
>2 yrs	94	28	0.043*	
Perceived side effect	231	76		
No				
Yes	70	41	0.011*	1.80 (1.1–2.8)
CD4+T cell counts				
<200 cells/mm <sup>3</sup>	116	72		
200–500 cells/mm <sup>3</sup>	110	90		
>500 cells/mm <sup>3</sup>	14	16	0.076	

Note: ART = Antiretroviral therapy; RMB = Renminbi; (yr) = age or time in years; \* $P < 0.05$ , \*\* $P < 0.001$ .

**Table 3**  
Reasons for missing doses ( $n = 90$ ).

Reasons	No.	%
Forgot to take drugs	38	42.2
Was away from home	26	28.9
Too busy	15	16.7
Felt worse after taking drugs	11	12.2
Didn't want others to notice	11	12.2
Difficulty with times	5	5.6
Confused about directions	4	4.4
Don't think I need the drugs	2	2.2
Too many drugs to take	1	1.1

**Table 4**  
Percentage of Doses Taken Within 2 h as Required ( $N = 418$ ).

Doses taken	No.	<i>n</i> (%)
Nearly all	243	58.1
More than half	145	34.7
About half	9	2.2
Less than half	2	0.5
Very little	5	1.2
None	14	3.4

were still trying to come to terms with their HIV status and the associated stigma and at the same time trying to fit the drug regime to their daily schedules. Previous studies have shown that ART-naïve patients were more likely to experience challenges with

**Table 5**  
Logistic regression analysis of adherence to antiretroviral therapy ( $N = 418$ ).

Independent Variables <sup>a</sup>	<i>B</i>	<i>SE</i>	Wald $\chi^2$	OR (95% CI)	<i>P</i>
Drug use	0.68	0.20	8.77	2.11 (1.3 - 3.3)	0.003**
Perceived side effects	0.64	0.18	5.61	1.82 (1.1 - 2.8)	0.009**
Time on ART	- 0.31	0.13	6.72	0.72 (0.6 - 0.9)	0.011*

Note: ART = Antiretroviral therapy; *B*: unstandardized regression coefficients; *SE*: Standardized error; Wald  $\chi^2$  = Wald Chi-square test; \* $P < 0.05$ , \*\* $P < 0.001$ .

<sup>a</sup> This table includes only the terminal model as determined by logistic regression analysis to build multivariate model.

adherence at the initial stages of therapy but improved as time progressed [26–28].

The third factor that was associated with non-adherence in the study was ART-related side effects. Drug side effects have generally been blamed for being a major impediment towards adherence to ART [5,21]. A study in Cameroon found a close association between ART side effects and suboptimal adherence and that men were more likely to miss doses if they experienced side effects when compared with women [29].

The five main reasons for missing a dose(s) identified in this study included: forgetting to take drugs, being away from home, a busy schedule, feeling worse after taking drugs, and not wanting others to know that they were on therapy. The same reasons have been identified by other studies for contributing to non-adherence. A study done in Rwanda identified non-disclosure (not wanting others to know they were on therapy), being busy, and drug side

effects as being the major reasons for missing a dose or doses [5]. Another study associated missing dose(s) to not wanting others to notice they were on drugs, being busy, and pills running out [21]. It is therefore important to identify interventions that can reverse the effects of these reasons in order to optimize adherence to therapy.

Finally, it is important to note that optimal adherence to therapy is now acknowledged as a preventive measure in HIV transmission; those who are adherent to therapy are less likely to spread the virus [30]. This demonstrates the added benefits that ART adherence provides, keeping PLWH healthy, preventing them from re-infection, and at the same time preventing the spread of HIV to those who are not infected.

In conclusion, this study found ART adherence levels above 70% in two HIV care sites in Hunan province. The three key factors that were identified to be associated with non-adherence are drug abuse, time on ART, and ART side effects, in that order. The reasons identified in this study for missing a dose or doses were similar to those that have been identified in previous studies that adopted the same methodology. We recommend that behavioral interventions as prescribed by UNAIDS be implemented in order to improve ART adherence. Being HIV-positive and drug use in China are highly stigmatizing attributes. Failing to address them at the onset will mean that a person living with the virus will be isolated from the very people that are expected to support them in a society/nation that is deeply anchored in family cohesion.

There were several limitations in this study. This was a follow-up study on ART adherence in Hunan province in China. The study site choice and sample size was large enough and reflects sample characteristics of PLWH in the South Central region of China. The findings can be generalized to the region and areas with similar demographics in China. However, this study adopted a cross-sectional descriptive design that only takes a snapshot of the events at one particular point in time; it does not provide data on adaptation and change that a prospective design can give. The data collected was subjective and therefore reflects a participant's self-appraisal, which is subject to self-overrating. The study tool was developed and has been utilized in three previous studies within China and one out of China.

## Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.ijnss.2018.04.008>.

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