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Suboptimal antiretroviral therapy adherence among HIV-infected adults in Guangzhou, China

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Abstract

Despite China“s free antiretroviral treatment (ART) program, there are high rates of treatment failure, large sociodemographic disparities in care outcomes and emerging medication resistance. Understanding patient medication adherence behaviors and challenges could inform adherence interventions to maximize the individual and prevention benefits of ART. This study assessed recent non-adherence and treatment interruption among 813 HIV-infected adult outpatients in Guangzhou, China. Participants completed a behavioral survey, underwent chart review, and were tested for syphilis, gonorrhea, and chlamydia. Factors associated with suboptimal adherence were identified using univariate and multivariate logistic regression. Among 721 HIV-infected adults receiving ART, 18.9% reported recent non-adherence (any missed ART in the past 4 weeks) and 6.8% reported treatment interruption (four or more weeks of missed ART in the past year). Lower education, living alone, alcohol use and being on ART one to three years were associated with recent non-adherence. Male gender, lower education and being on ART one to three years were associated with treatment interruption. ART medication adherence interventions are needed in China that include individualized, long-term adherence plans sensitive to patients“ educational and economic situations. These interventions should also consider possible gender disparities in treatment outcomes and address the use of alcohol during ART. Successful ART medication adherence interventions in China can inform other international settings that face similar adherence challenges and disparities.

Keywords

antiretroviral therapy; ART; ARV; adherence; alcohol; China

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INTRODUCTION

The HIV Prevention Trials Network 052 generated renewed urgency to optimize patient adherence to antiretroviral therapy (ART) in order to improve individual patient outcomes and reduce forward HIV transmission (Cohen et al., 2011). China embraced HIV treatment as prevention initiatives through its National Free Antiretroviral Treatment Program and a 2012 decision to promote earlier ART initiation (Zhao, Poundstone, Montaner, & Wu, 2012). Amidst rapid ART scale-up, poor medication adherence threatens these initiatives“ ability to achieve virologic suppression (Zhang et al., 2009) and reverse increasing medication resistance (Gardner, Burman, Steiner, Anderson, & Bangsberg, 2009) documented in China (Liao et al., 2012) and globally (Gupta et al., 2012).

In 2011, 126,448 of China“s estimated 780,000 persons living with HIV were receiving free ART (Ministry of Health People“s Republic of China, 2012), however wide disparities in adherence and treatment outcomes have been noted (Xing et al., 2013; Yan et al., 2013; Zhang et al., 2009). As ART expands, a better understanding of patient adherence is urgently needed. This study assessed factors associated with suboptimal adherence among a large sample of HIV-infected individuals in south China.

METHODS

The main study design has been reported in detail (X. B. Wang et al., 2012). Briefly, between April and June 2011, 813 HIV-infected outpatients 18 years of age and older were recruited at the largest HIV clinic in Guangzhou, China for a cross-sectional survey and sexually transmitted disease (STD) testing. Sample size calculation was based on a three month HIV patient population of 10,000 (hospital records), a 95% confidence level and 3.3 confidence interval, resulting in an estimated required sample size of 811. Among 813 eligible individuals recruited, three declined to participate, leaving a final sample of 810. Participants completed a self-administered survey covering sociodemographics, health behaviors and ART. Survey items were based on prior validated tools among HIV patients (Bunnell et al., 2006; Eisele et al., 2009). The questionnaire was field-tested and revised with input from Chinese clinic patients, six clinic physicians and three nurses. Participants provided 2 ml of blood for syphilis testing and 5 ml of urine for gonorrhea and chlamydia testing (see X.B. Wang et al., 2012 for laboratory procedures). Data on ART initiation and recent CD4 count were abstracted from chart reviews. Institutional review boards from the study hospital, Guangdong Provincial STD Control Center, and the University of North Carolina at Chapel Hill approved the study. Participants provided informed consent and received a small gift ($4 USD equivalent) as remuneration.

ANALYSIS

Two outcomes were assessed: recent non-adherence (missing any days of ART in the past four weeks), and treatment interruption (missing four weeks or more of ART during the past year). Univariate and multivariate associations with each adherence outcome were calculated using logistic regression. A backward elimination process was used to build multivariate models, and a p-value of <0.10 was required for retention in the final model.

Collinearity was assessed using the variance inflation factor. SAS 9.2 (SAS Institute Inc., Cary NC, USA) was used to perform all data analysis.

RESULTS

89% of enrolled participants (721 out of 810) had started ART (Table 1). Participants taking ART ranged in age from 19 to 79 years old, 61.3% were male, 67.5% had education of middle school or lower, under a third were full-time employed, and 40.8% lived alone. Average length of ART was 827 days, but 34.4% had been on ART under one year. Median most recent CD4 count was 282 cells/μL. 89.5% of participants reported receiving sexual risk reduction counseling at the start of ART. 17% of participants had not used a condom at last intercourse, and prevalence of any STD was 9.3%. Overall, 20.6% (n=147) of participants reported drinking alcohol in the past month. Among these 79.6% (n=117) drank alcohol several times a month (moderate), while 20.4% (n=30) drank alcohol several times a week or more (heavy).

Recent non-adherence

18.9% (n=136) of participants reported recent non-adherence (Table 2). In the multivariate analysis, lower education, living alone, alcohol use and longer time on ART were associated with recent non-adherence. Lower education was associated with higher likelihood of recent non-adherence as compared to those with some post-secondary education (high school: adjusted odds ratio [aOR] 3.39; 95% confidence interval [CI], 1.32-8.71; middle school: aOR 3.31, 95% CI, 1.36-8.07; primary school: aOR 4.52, 95% CI 1.78-11.45). Those who lived alone were 1.49 times more likely to report recent non-adherence (95% CI, 1.00-2.21). Alcohol use was associated with recent non-adherence for both moderate (aOR 3.76, 95% CI, 1.65-8.55) and heavy (aOR 2.31, 95% CI, 1.44-3.71) consumption. Compared to patients on therapy for less than one year, those on ART for one to three years were more likely to report recent non-adherence (aOR 1.76, 95% CI, 1.10-2.84). This difference was not significant among participants who had been on ART over three years compared to those on therapy for under one year (aOR 1.26, 95% CI, 0.75-2.12).

Treatment interruption

6.8% (n=49) of participants reported treatment interruption in the past year (Table 3). In the multivariate analysis, being male, having lower education, and longer time on ART were associated with greater likelihood of treatment interruption. Men were 2.06 times more likely to report treatment interruption that women (95% CI, 1.07-3.96). Education below high school (middle school: aOR 6.55, 95% CI, 0.87-49.64; primary school aOR 14.31, 95% CI, 1.86-110.27) was associated with higher likelihood of treatment interruption. There was a non-significant trend between time on ART and treatment interruption. Participants who had been on ART for one to three years were 1.91 times more likely to report a treatment interruption compared to those who had been on therapy under one year (95% CI, 0.91-4.01).

DISCUSSION

Among 721 ART-experienced patients in Guangzhou, China we found frequent ART non-adherence and treatment interruptions. Recent non-adherence (18.9%) surpassed the median rate found in a 6-country study (13.3%) (Corless et al., 2012) and rates reported in comparable China-based samples (Corless et al., 2012; L. Li, Ji, Ding, Tian, & Lee, 2012; Sabin et al., 2010; Simoni et al., 2011).

We found a relationship between alcohol use and adherence consistent with the global literature (Azar, Springer, Meyer, & Altice, 2010; Braithwaite & Bryant, 2010) but not identified in earlier Chinese studies (H. Wang et al., 2008; X. Wang & Wu, 2007). Occasional, daily and binge drinking are significantly associated with worse adherence and decreased survival worldwide (Braithwaite et al., 2005; Hendershot, Stoner, Pantalone, & Simoni, 2009) – a serious concern given the portion of our participants who reported alcohol use in the past month (20.6%). China has high levels of binge drinking and alcohol use (Yang et al., 2012), yet prior adherence studies were not adequately powered to examine this relationship. Alcohol use is also associated with high-risk sexual behaviors internationally (Shuper, Joharchi, Irving, & Rehm, 2009) and in China (Q. Li, Li, & Stanton, 2010). Given the 9.3% prevalence of STDs found in our sample, addressing alcohol use among HIV-infected individuals could also improve prevention of STDs and forward HIV transmission.

Participants with lower education had worse ART adherence. Lower education is consistently associated with lower HIV medication adherence across geographic and economic settings (Fogarty et al., 2002; Rachlis, Mills, & Cole, 2011). This relationship is not well-quantified in China though qualitative studies have explored complex economic, employment and education-based barriers to adherence (L. Li et al., 2012; Sabin et al., 2008; Starks et al., 2008). HIV-infected men were more likely than women to report treatment interruptions. This differs from the global literature (Ammassari et al., 2002), but is consistent with Chinese national data (Dou et al., 2011; Zhang et al., 2009) and may be even more pronounced in rural areas (L. Li et al., 2012).

This study has several limitations. First, all recruitment took place in one outpatient setting. This focused recruitment is a result of the centralized HIV care system in Guangzhou. However, our sample has similar sociodemographic and HIV-transmission characteristics as national samples of HIV-infected individuals on ART (Dou et al., 2011; Sabin et al., 2010; Simoni et al., 2011; Zhang et al., 2009). Secondly, we lacked patient profile data on certain factors found to be associated with non-adherence in previous studies, such as medication tolerance, mental health status, and social support (L. Li et al., 2012; Sabin et al., 2008; Starks et al., 2008). As a possible proxy for social support, our finding that participants who lived alone were more likely to report recent non-adherence suggests that more nuanced measures of social support should be included in future adherence studies in China.

Numerous behavioral, pharmacologic and technology-based interventions to improve adherence demonstrate that high levels of patient adherence are difficult to achieve and maintain over time (Bae, Guyer, Grimm, & Altice, 2011; Mills et al., 2006). As ART adherence interventions are being adapted and tested among Chinese patient populations

(e.g. electronic drug monitoring (Sabin et al., 2010), nurse-delivered (Simoni et al., 2011), cognitive behavioral therapy (Shiu et al., 2013)), we urge greater attention to developing individualized, long-term medication adherence plans that are sensitive to patient educational and economic factors, consider possible gender disparities in treatment outcomes, and address alcohol use. Such plans should also address medication persistence for ART-experienced patients, emphasizing the importance of continued treatment support beyond the first year of therapy. These strategic adherence intervention components could support expanded ART for improved clinical outcomes and reduced forward HIV transmission.

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Table 1

Demographic and clinical characteristics of 721 HIV-infected patients on antiretroviral therapy in Guangzhou, China

Characteristic	n (%)
Age	
≤ 30 years	127 (17.6)
31 to 40 years	295 (40.9)
41 to 60 years	259 (35.9)
≥ 61 years	40 (5.6)
Sex	
Male	442 (61.3)
Female	279 (38.7)
Residence	
Guangzhou	269 (37.8)
Other, Guangdong Province	443 (62.2)
Education	
≤ Primary school	153 (21.2)
Middle school	334 (46.3)
High school	144 (20.0)
Vocational school	56 (7.8)
≥ College	34 (4.7)
Employment	
Full-time	223 (31.1)
Part-time or temporary	180 (25.1)
Retired	43 (6.0)
No employment	271 (37.8)
Marital status	
Single, live alone	127 (17.6)
Cohabitating/married	451 (62.6)
Separated/divorced	80 (11.1)
Widowed	62 (8.6)
Alcohol	
Several times a week	30 (4.2)
Several times a month	117 (16.4)
Do not drink	567 (79.4)
Intravenous drug use in the past month	
Yes	26 (3.9)
No	638 (96.1)
Most recent sex partner, last three months	
Casual partner	22 (2.7)
Steady partner	328 (80.4)
No partner	69 (16.9)

Characteristic	n (%)
Condoms at last intercourse	
Yes	343 (83.1)
No	70 (17.0)
HIV transmission route	
Homosexual sex	70 (9.7)
Heterosexual sex	272 (37.8)
Intravenous drug use	138 (19.2)
Transfusion	81 (11.3)
Not sure/other	158 (22.0)
Received risk reduction counseling at ART initiation	
Yes	638 (89.5)
No	75 (10.5)
Most recent CD4 count	
≤ 200 cells/mm^3	216 (30.0)
≥ 200 cells/mm^3	505 (70.0)
Time on ART	
< 1 year	248 (34.4)
1 to 3 years	270 (37.5)
> 3 years	203 (28.2)
Tested positive, any STD	
Yes	67 (9.3)
No	654 (90.7)

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Table 2

Factors associated with self-reported missed ART in the past month

Characteristic	Missed ART, past 4 weeks (N=136) n (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age					
≤ 30 years	20 (14.7)	1.00			
31 to 40 years	60 (44.1)	1.36 (0.78 –2.38)	0.276		
≥ 41 years	56 (41.2)	1.22 (0.70 –2.13)	0.490		
Sex					
Female	48 (35.3)	1.00			
Male	88 (64.7)	1.21 (0.82 – 1.78)	0.345		
Residence					
Guangzhou	52 (38.8)	1.00			
Other, Guangdong	82 (61.2)	0.95 (0.64 – 1.39)	0.783		
Education					
≥ Post-secondary	6 (4.4)	1.00		1.00	
High school	28 (20.6)	3.25 (1.29 –8.20)*	0.013	3.39 (1.32 –8.71)*	0.011
Middle school	65 (47.8)	3.30 (1.38 –7.89)*	0.007	3.31 (1.36 –8.07)*	0.008
≤ Primary school	37 (27.2)	4.33 (1.74–10.74)*	0.002	4.52 (1.78 –11.45)*	0.002
Employment					
Full-time	34 (25.4)	1.00			
Part-time or temporary	42 (31.3)	1.69 (1.02 –2.79)*	0.042		
Retired	3 (2.2)	0.40 (0.12 – 1.38)	0.148		
No employment	55 (41.0)	1.39 (0.87 –2.23)	0.171		
Cohabitating/married					
Yes	77 (56.6)	1.00		1.00	
No	59 (43.4)	1.40 (0.96 –2.05)*	0.083	1.49 (1.00 –2.21)*	0.049
Alcohol					
None	90 (66.7)	1.00		1.00	
Several times a month	34 (25.2)	2.16 (1.36 –3.41)*	0.001	3.76 (1.65 –8.55)*	0.002

Characteristic	Missed ART, past 4 weeks (N=136) n (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Several times a week	11 (8.2)	3.58 (1.61 –7.96)*	0.002	2.31 (1.44 –3.71)*	0.001
IV drug use past month					
No	117 (94.4)	1.00			
Yes	7(5.7)	1.81 (0.73 –4.46)	0.198		
Most recent sex partner, past 3 months					
No partner	16 (19.3)	1.00			
Steady partner	65 (78.3)	0.79 (0.42 – 1.47)	0.453		
Casual partner	2 (2.4)	0.69 (0.14 –3.55)	0.874		
Condoms at last intercourse					
Yes	69 (81.2)	1.00			
No	16 (18.8)	1.17 (0.63 –2.17)	0.622		
HIV transmission route					
Heterosexual sex	48 (35.6)	1.00			
Homosexual sex	13 (9.6)	1.05 (0.53 –2.07)	0.889		
Intravenous drug use	32 (23.7)	1.39 (0.84 –2.30)	0.200		
Transfusion	16 (11.9)	1.11 (0.59 –2.09)	0.740		
Not sure/other	26 (19.3)	0.91 (0.54 – 1.54)	0.728		
Received risk reduction counseling at ART initiation					
Yes	123 (91.1)	1.00			
No	12 (8.9)	0.87 (0.56 – 1.35)	0.519		
Most recent CD4 count					
≥ 200 cells/mm^3	93 (68.4)	1.00			
≤ 200 cells/mm^3	43 (31.6)	1.11 (0.74 – 1.67)	0.607		
Time on ART					
< 1 year	35 (25.7)	1.00		1.00	
1 to 3 years	63 (46.3)	1.82 (1.15 –2.87)*	0.010	1.76 (1.10 – 2.84)*	0.020
> 3 years	38 (27.9)	1.38 (0.84 –2.28)	0.209	1.26 (0.75 – 2.12)*	0.384
Tested positive, any STD					

Characteristic	Missed ART, past 4 weeks (N=136) n (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
No	122 (89.7)	1.00			
Yes	14 (10.3)	1.17 (0.63 –2.19)	0.617		

*Statistically significant at the p<0.1 level.

[1]Includes those previously married then separated, divorced or widowed.

Table 3

Factors associated with missing at least four weeks of ART in the past year

Characteristic	Missed ≥4 weeks of ART, past year(N=49) n (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age					
≤ 30 years	7 (14.3)	1.00			
31 to 40 years	15 (30.6)	0.91 (0.36–2.30)	0.844		
≥ 41 years	27 (55.1)	1.78 (0.75–4.22)	0.188		
Sex					
Female	14 (28.6)	1.00		1.00	
Male	35 (71.4)	1.70 (0.90–3.23)	0.103	2.06 (1.07–3.96)*	0.031
Residence					
Guangzhou	17 (36.2)	1.00			
Other, Guangdong	30 (63.8)	1.06 (0.57– 1.97)	0.854		
Education					
≥ Post-secondary	1 (2.0)	1.00		1.00	
High school	5 (10.2)	2.94 (0.34–25.58)	0.329	3.03 (0.35–26.57)*	0.318
Middle school	23 (46.9)	6.23 (0.83–46.83)	0.076	6.55 (0.87–49.64)*	0.069
≤ Primary school	20 (40.8)	12.82 (1.69–97.42)	0.014	14.31 (1.86–110.27)*	0.011
Employment					
Full-time	8 (16.3)	1.00			
Part-time or temporary	16 (32.7)	2.57 (1.07–6.16)*	0.035		
Retired	2 (4.1)	1.28 (0.26–6.25)	0.763		
No employment	23 (46.9)	2.47 (1.08–5.64)*	0.032		
Cohabitating					
Yes	29 (59.2)	1.00			
No	20 (40.8)	1.15 (0.64-2.08)	0.643		
Alcohol					
None	34 (70.8)	1.00			

Characteristic	Missed ≥4 weeks of ART, past year(N=49) n (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Several times a month	11 (22.9)	1.60 (0.78–3.26)	0.200		
Several times a week	3(6.3)	2.05 (0.58–7.22)	0.264		
IV drug use, past month					
No	43 (95.6)	1.00			
Yes	2 (4.4)	1.21 (0.28–5.34)	0.800		
Most recent sex partner, past 3 months					
No partner	4 (16.0)	1.00			
Steady partner	20 (80.0)	1.05 (0.35–3.20)	0.929		
Casual partner	1 (4.0)	1.58 (0.19– 13.08)	0.673		
Condoms at last intercourse					
Yes	21 (84.0)	1.00			
No	4 (16.0)	0.91 (0.30–2.74)	0.865		
HIV transmission route					
Heterosexual sex	18 (37.5)	1.00			
Homosexual sex	7 (14.6)	1.59 (0.63–3.99)	0.323		
Intravenous drug use	9 (18.8)	1.00 (0.43–2.28)	0.992		
Transfusion	5 (10.4)	0.94 (0.34–2.62)	0.903		
Not sure/other	9 (18.8)	0.86 (0.38– 1.98)	0.727		
Received risk reduction counseling at ART initiation					
Yes	46 (93.9)	1.00			
No	3 (6.1)	0.58 (0.17–1.91)	0.369		
Most recent CD4 count					
≥ 200 cells/mm^3	34 (69.4)	1.00			
< 200 cells/mm^3	15 (30.6)	1.03 (0.55– 1.93)	0.936		
Time on ART					
< 1 year	11 (22.5)	1.00		1.00	
1 to 3 years	26 (53.1)	2.14 (1.03–4.43)*	0.042	1.91 (0.91–4.01)*	0.088
> 3 years	12 (24.5)	1.26 (0.54–2.93)	0.588	1.15 (0.49–2.72)	0.742
Tested positive, any STD					

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Characteristic	Missed ≥4 weeks of ART, past year(N=49) n (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
No	44 (89.8)	1.00			
Yes	5 (10.2)	1.15 (0.44–3.02)	0.776		

*Statistically significant at the p<0.1 level