

BMJ Open HIV virological failure and drug resistance among injecting drug users receiving first-line ART in China

Xuebing Leng,¹ Shujia Liang,² Yanling Ma,³ Yonghui Dong,⁴ Wei Kan,¹ Daniel Goan,⁵ Jenny H Hsi,¹ Lingjie Liao,¹ Jing Wang,¹ Cui He,¹ Heng Zhang,¹ Hui Xing,¹ Yuhua Ruan,¹ Yiming Shao¹

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XL, SL, YM, YD and WK contributed equally to this work.

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For numbered affiliations see end of article.

Correspondence to
Hui Xing;
xingh@chinaaids.cn

ABSTRACT

Objective: To explore HIV virological failure and drug resistance among injecting drug users (IDUs) receiving first-line antiretroviral treatment (ART) in China.

Design: A series of cross-sectional surveys from 2003 to 2012 from the Chinese National HIV Drug Resistance (HIVDR) Surveillance and Monitoring Network.

Setting: China.

Participants: Data were analysed by the Chinese National (HIVDR) Surveillance and Monitoring Network from 2003 to 2012. Demographic, ART and laboratory data (CD4+ cell count, viral load and drug resistance) were included. Factors associated with virological failure were identified by logistic regression analysis.

Results: 929 of the 8556 individuals in the Chinese HIVDR database were IDUs receiving first-line ART. For these 929 IDUs, the median duration of treatment was 14 months (IQR 6.0–17.8). 193 of the 929 IDUs (20.8%) experienced virological failure (HIV viral load ≥ 1000 copies/mL). The prevalence of HIVDR among patients with virological failure was 38.9% (68/175). The proportion of patients with drug resistance to non-nucleoside reverse transcriptase inhibitor (NNRTIs), nucleoside reverse transcriptase inhibitor (NRTIs) and protease inhibitors (PIs) was 52.9%, 76.5% and 4.4%, respectively. Factors independently associated with virological failure include: ethnic minorities, junior high school education or less, farmers, self-reported missing doses in the past month, CD4 cell count at survey from 200 to 349 cells/mm³ or from 0 to 199 cells/mm³, and residence of Guangxi and Yunnan provinces.

Conclusions: The proportion of virological failure was high among IDUs receiving first-line ART in China. However, better treatment outcomes were observed in Guangxi and Yunnan, which indicates the importance of ART education and adherence to intervention, especially for patients who are farmers, minorities or have a poor educational background.

INTRODUCTION

Since the early 1990s, highly active antiretroviral therapy (HAART) has been used to treat

Strengths and limitations of this study

- This study is a large sample from the Chinese National HIV Drug Resistance (HIVDR) Surveillance and Monitoring Database that was obtained from a series of cross-sectional surveys from 2003 to 2012.
- The prevalence of injecting drug users (IDUs) in southwest China is serious; however, IDUs in Guangxi and Yunnan showed promising results from antiretroviral treatment and had fewer virological failures.
- The outcomes of this study may not fully represent all IDUs in China.
- Owing to the long time span covered by the data in our study, changes to prevention policies and treatment programmes may have influenced the effectiveness of the treatment.
- Our study can only provide a reference for the diverse localities studied, with each having different epidemic and intervention situations.

HIV-infected patients worldwide, improving immune reconstitution and decreasing AIDS-related mortality.^{1–3} Unfortunately, incomplete viral suppression may lead to the development of HIV drug resistance, which not only compromises therapeutic effects for an individual, but also endangers the population as a whole.⁴

In 2012, UNAIDS reported that injecting drug users (IDUs) worldwide were the population most at risk to be affected by HIV. Based on data from 49 countries, the rate of HIV infection of IDUs was 22 times that of the general population.⁵ In China, where sex has become the main route of HIV transmission, HIV prevalence in IDUs is higher for female sex workers and men who have sex with men.^{6 7} In 2003, the ‘four free one care’ policy was introduced, which provided free antiretroviral treatment for all eligible HIV patients in China. According to the analysis of the 2013 HIV/STD epidemic in

China, more than 278 000 patients had received the free antiretroviral treatment.⁸ Since 2004, methadone maintenance treatment (MMT), needle exchange and harm reduction have gradually expanded in China; this has improved the adherence of IDUs to treatment and reduced HIV transmission. However, a previous smaller study showed that when compared to other patients, the proportion of virological failure among IDUs was higher.⁹ Taking into consideration the conditions of IDUs in China, a large sample from the Chinese National HIV Drug Resistance (HIVDR) Surveillance and Monitoring Database was used to analyse and determine the prevalence of virological failure and drug resistance among IDUs receiving the first-line ART in China.

METHODS

Study design and study participants

We collected data through the Chinese National HIVDR Surveillance and Monitoring Network, which consists of four core laboratories (National Center for AIDS/STD Control and Prevention (NCAIDS), Shanghai Municipal Center for Disease Control and Prevention (CDC), Chinese Medical University Center for AIDS Research, and Institute of Microbiology and Epidemiology of the Chinese Academy of Military Medical Sciences) and laboratories from 30 provincial CDCs.¹⁰ IDUs were defined as patients who had a history of self-reported drug injection. Samples were obtained from a series of cross-sectional surveys from 2003 to 2012 on HIV drug resistance in adult patients at nationally representative ART clinics. The inclusion criteria were: (1) HIV infected IDU; (2) age ≥ 18 years; (3) onset of HAART between 1 January 2003 and 31 December 2011; (4) received free national first-line ART treatment; (5) consent and willingness to participate in the study.

Data collection

Data were collected through an interviewer-administered questionnaire. All participants provided written informed consent before participation in the study. Each participant was assigned a confidential identification number used to identify questionnaires and blood specimens. The questionnaire was administered face to face by a trained interviewer in a private room. Questionnaire questions included sociodemographic characteristics, HIV risk factors, HAART regimens and self-reported adherence measures. Demographic variables included sex, ethnicity, education level, occupation, marital status and HIV transmission route. Self-reported adherence variables included missed ART doses in the past month.

Laboratory analysis

Blood specimens were collected from all participants to test CD4 cell count, HIV viral load (VL) and HIV drug resistance mutations at the baseline survey. CD4 cell counts were determined by flow cytometry in the

provincial CDC offices within 24 h of collection. Plasma HIV RNA was quantified with real-time NASBA (NucliSense Easy Q, bioMerieux, France) or COBAS (Roche Applied Biosystems, Germany) according to the manufacturer's recommendations. Samples with VL ≥ 1000 copies/mL were selected for HIV drug resistance testing by using an in-house PCR.^{9 10} In order to perform HIV drug resistance mutations, HIV-1 *pol* gene (protease 1–99 amino acids and part of the reverse transcriptase 1–252 amino acids) were amplified and analysed using the Stanford HIV Drug Resistance Database (<http://hivdb.stanford.edu/>). We included mutation results that conferred low-level, intermediate-level and high-level resistance.^{11 12}

Data analysis

All questionnaire data were double-entered using Epidata 3.1 (The Epidata Association Odense, Denmark). Statistical Analysis System (SAS V.9.2, SAS Institute Inc, Cary, North Carolina, USA) was then used for data cleaning and analysis. Univariate logistic regression models were constructed to explore associations between virological failure, demographic characteristics, HAART regimens, adherence and CD4 data. OR and 95% CIs were calculated as well. Variables that were significant ($p < 0.05$) in the univariate models were used in stepwise multivariate logistic regression models and presented with AOR and 95% CIs. Owing to the large sample and according to some previous studies,^{9 10 13 14} $p < 0.05$ was defined as statistically significant, and all tests were two sided.

RESULTS

Demographic characteristics

Of the 8556 patients in the National HIVDR Database who began treatment between 1 January 2003 and 31 December 2011, 929 IDUs matched the inclusion criteria. The demographic characteristics of the participants were shown in [table 1](#). In total, 90.8% were men; the mean age was 35.7 ± 6 years; 55.1% were ethnically Han; 60.8% had an education level of junior high school or higher; 23.4% were farmers; and more than half (65.2%) were married.

HAART regimens and virological profiles

Initial HAART regimens were AZT+3TC+EFV (9.5%), AZT+3TC+NVP (34.8%), D4T+3TC+EFV (9.3%), D4T+3TC+NVP (32.8%), and DDI-based regimens (didanosine (DDI)+nevirapine (NVP) or efavirenz (EFV)) (13.6%). HAART regimens at survey were AZT+3TC+NVP/EFV (52.3%), D4T+3TC+NVP/EFV (34.8%), DDI-based regimens (9.7%) and second-line regimens (3.2%). At the time of the survey, 193 (20.8%) patients had a VL ≥ 1000 copies/mL. Among these participants, 175 were successfully genotyped. CRF07_BC was the most common HIV viral subtype (41.7%), followed by CRF01_AE (27.4%). Of these, 68 had detectable HIVDR mutations.

Table 1 Characteristics of IDU patients receiving antiretroviral treatment in China

Characteristics	Number	Percentage
Total	929	
Age (years): mean±SD	35.7±6.0	
Sex		
Male	844	90.8
Female	85	9.2
Ethnicity		
Han	512	55.1
Minorities	417	44.9
Education		
Illiterate	101	10.9
Primary school	263	28.3
Junior high school	410	44.1
High school or more	155	16.7
Occupation		
Farmer	217	23.4
Others	712	76.6
Married		
Yes	606	65.2
No	323	34.8
Initial ART regimen		
AZT+3TC+EFV	88	9.5
AZT+3TC+NVP	323	34.8
D4T+3TC+EFV	86	9.3
D4T+3TC+NVP	305	32.8
DDI-based regimens	127	13.6
ART regimen at survey		
AZT+3TC+NVP/EFV	486	52.3
D4T+3TC+NVP/EFV	323	34.8
DDI-based regimen	90	9.7
Second-line regimens	30	3.2
Duration of ART (months): median, IQR	14.0, 6.0–17.8	
Province		
Xinjiang	306	32.9
Yunnan	184	19.8
Hunan	174	18.7
Guangxi	122	13.1
Sichuan	42	4.5
Guizhou	25	2.7
Guangdong	19	2.1
Shandong	12	1.3
Gansu	12	1.3
Jiangxi	10	1.1
Others	23	2.5

ART, antiretroviral treatment; IDU, injecting drug users.

HIV drug resistance mutations

Among the participants with HIVDR mutations, 36/68 (52.9%) patients were resistant to non-nucleoside reverse transcriptase inhibitor (NNRTIs) drugs. Fifty two of sixty eight (76.5%) patients had drug resistance to nucleoside reverse transcriptase inhibitor (NRTIs) drugs. Three of sixty eight (4.4%) patients were identified to have drug resistance to protease inhibitors (PIs). In addition, 21/68 (30.9%) patients had multidrug resistance to NNRTIs and NRTIs. The most frequent

NNRTIs mutations occurred at position 103 in the RT (reverse transcriptase) region and NRTIs mutations occurred at position 184 in the RT region. PI mutations were also found at positions 47 and 46 in the PR (protease) region (table 2).

Predictors for HIV virological failure

The factors associated with HIV virological failure were examined in univariate logistic regression models; those found to be statistically significant were included in the multivariate logistic regression model. There were six

Table 2 HIV drug resistance mutations among IDU patients with drug resistance

Antiretroviral drug	N (%)	HIV drug resistance mutations, N (%)
Total	68 (100.0)	
<i>Non-nucleoside reverse transcriptase inhibitors (NNRTI, any)</i>	36 (52.9)	K103N/R, 18 (26.5) Y181C, 8 (11.8) K101E/P/Q, 5 (7.4)
Efavirenz (EFV)*	36 (52.9)	
Nevirapine (NVP)*	36 (52.9)	
Delavirdine (DLV)	34 (50.0)	G190A/Q/S, 4 (5.9)
Etravirine (ETV)	8 (11.8)	
Rilpivirine (RPV)	2 (2.9)	V106A/M, 3 (4.4) E138A/Q, 2 (2.9) A98G, 1 (1.5) M230L, 1 (1.5) P225H, 1 (1.5) V179D, 1 (1.5) Y188H, 1 (1.5)
<i>Nucleoside reverse transcriptase inhibitors (NRTI, any)</i>	52 (76.5)	M184I/V, 38(55.9) D67G/N, 6 (8.8) V75I/L/T, 4 (5.9)
Emtricitabine (FTC)	50 (73.5)	K65R, 3 (4.4)
Lamivudine (3TC)*	50 (73.5)	Y115F, 2 (2.9)
Abacavir (ABC)	19 (27.9)	K70E, 1 (1.5)
Didanosine (DDI)*	17 (25.0)	L74V, 1 (1.5)
Stavudine (D4T)*	12 (17.6)	M41L, 1 (1.5)
Tenofovir (TDF)*	9 (13.2)	N41L, 1 (1.5)
Azidothymidine (AZT)*	7 (10.3)	T69IN, 1 (1.5)
<i>Protease inhibitors (PI, any)</i>	3 (4.4)	
Tipranavir (TPV)	3 (4.4)	
Fosamprenavir (FPV)	2 (2.9)	
Lopinavir (LPV)*	2 (2.9)	I47V, 1 (33.3)
Nelfinavir (NFV)	2 (2.9)	M46I, 1 (33.3)
Atazanavir (ATV)	1 (1.5)	
Darunavir (DRV)	1 (1.5)	
Indinavir (IDV)	1 (1.5)	
Saquinavir (SQV)	1 (1.5)	
<i>Multi-drug resistance to NNRTI and NRTI</i>	21 (30.9)	

*Provided through the National Free Antiretroviral Treatment Program (NFATP).

factors that remained in the final multivariate models (table 3). Factors positively associated with virological failure include: Ethnicity (compared to Han ethnicity: minorities AOR 1.8, 95% CI 1.3 to 2.6), education (compared to high school or greater: junior high school or

less AOR 1.6, 95% CI 1.0 to 2.7), occupation (compared to other jobs: farmer AOR 1.6, 95% CI 1.1 to 2.3), self-reported missing doses in the past month (compared to not missing doses in the past month: AOR 1.6, 95% CI 1.0 to 2.5), CD4± cell count at survey (compared to CD4

Table 3 Factors associated with HIV viral suppression failure (viral load ≥ 1000 copies/mL) among IDU patients receiving antiretroviral treatment in China

Variable	Number	Viral suppression Failure N (%)	Crude OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
Total	929	193 (20.8)				
Age (years)						
<35	436	95 (21.8)				
≥ 35	493	98 (19.9)	0.9 (0.6 to 1.2)	0.47		
Sex						
Male	844	174 (20.6)				
Female	85	19 (22.4)	1.1 (0.6 to 1.9)	0.71		
Ethnicity						
Han	512	85 (16.6)				
Minorities	417	108 (25.9)	1.8 (1.3 to 2.4)	<0.01	1.8 (1.3 to 2.6)	<0.01
Education						
High school or more	155	23 (14.8)				
Junior high school or less	774	170 (22.0)	1.6 (1.0 to 2.6)	0.04	1.6 (1.0 to 2.7)	0.04
Occupation						
Others	712	133 (18.7)				
Farmer	217	60 (27.6)	1.7 (1.2 to 2.4)	<0.01	1.6 (1.1 to 2.3)	0.02
Married						
No	323	70 (21.7)				
Yes	606	123 (20.3)	0.9 (0.7 to 1.3)	0.62		
CD4 cell counts before ART						
0–199	642	123 (19.2)				
200–349	266	63 (23.7)	1.3 (0.9 to 1.8)	0.12		
≥ 350	21	7 (33.3)	2.1 (0.8 to 5.3)	0.12		
Duration of ART (months)						
0–12	413	77 (18.6)				
>12	516	116 (22.5)	1.3 (0.9 to 1.7)	0.15		
Initial ART regimen						
AZT+3TC+NVP/EFV	411	97 (23.6)				
D4T+3TC+NVP/EFV	391	70 (17.9)	0.7 (0.5 to 1.0)	0.05		
DDI-based regimen	127	26 (20.5)	0.8 (0.5 to 1.4)	0.46		
ART regimen at survey						
AZT+3TC+NVP/EFV	486	116 (23.9)				
D4T+3TC+NVP/EFV	323	49 (15.2)	<0.01			
DDI-based regimen	90	20 (22.2)	0.74			
Second-line regimens	30	8 (26.7)	0.73			
Missed doses in the past month						
No	794	153 (19.3)				
Yes	135	40 (29.6)	1.8 (1.2 to 2.7)	<0.01	1.6 (1.0 to 2.5)	0.03
CD4 cell counts at survey						
≥ 500	140	16 (11.4)				
350–499	176	34 (19.3)	1.9 (1.0 to 3.5)	0.06	1.7 (0.9 to 3.3)	0.11
200–349	285	66 (23.2)	2.3 (1.3 to 4.2)	<0.01	2.2 (1.2 to 4.1)	<0.01
0–199	328	77 (23.5)	2.4 (1.3 to 4.2)	<0.01	2.9 (1.6 to 5.2)	<0.01
Time of starting ART (year)						
2003–2007	528	103 (19.5)				
2008–2011	401	90 (22.4)	1.2 (0.9 to 1.6)	0.27		
Province						
Others	623	158 (25.4)				
Guangxi and Yunnan	306	35 (11.4)	0.4 (0.3 to 0.6)	<0.01	0.4 (0.2 to 0.6)	<0.01

ART, antiretroviral treatment.

≥ 500 cells/mm³: CD4 350–499 AOR 1.7, 95% CI 0.9 to 3.3, CD4 200–349 AOR 2.2, 95% CI 1.2 to 4.1, CD4 0–199 AOR 2.9, 95% CI 1.6 to 5.2). Compared to other provinces, residence in Guangxi and Yunnan provinces was negatively associated with virological failure (AOR 0.4, 95% CI 0.2 to 0.6).

Sensitivity analysis

Table 4 presents factors associated with HIV viral suppression failure at the time of starting ART from 2003 to 2007 and from 2008 to 2011, respectively. Only residence of Guangxi and Yunnan provinces was observed to be at lower risk than that in other provinces during 2003 and 2007 (OR=0.4, 95% CI 0.2 to 0.6, $p < 0.01$) after adjusting for the initial ART regimen, ART regimen at survey, self-reported missing doses in the past month, and CD4 cell counts before ART. During 2008 and 2011, four factors were associated with virological failure, including province. Patients who were more likely to be virological failure were minorities (OR=2.3, 95% CI 1.3 to 4.0, $p < 0.01$), farmers (OR=2.1, 95% CI 1.2 to 3.8, $p = 0.01$), CD4 200–349 or 0–199 (OR=3.2, 95% CI 1.3 to 7.9, $p = 0.01$ and OR=4.1, 95% CI 1.6 to 10.3, $p < 0.01$) and residence of Guangxi and Yunnan provinces was a protective factor (OR=0.3, 95% CI 0.1 to 0.8, $p = 0.01$).

DISCUSSION

In this study, we analysed HIVDR data to evaluate the prevalence and risk factors of virological failure among IDUs at the national level. Our findings show that among 929 IDUs receiving free first-line ART, 20.8% had virological failure (VL ≥ 1000 copies/mL), which is higher than the outcomes of previous surveillance

studies among other patient populations in China.^{9 13 14} This suggests that treatment among IDUs has been less effective than in other high-risk populations, indicating a need for improved interventions.

Of the 193 patients who experienced failed viral suppression, 175 were successfully genotyped and 68 were identified as having drug resistance mutations. The prevalence of HIVDR among patients with virological failure was 38.9% (68/175), which suggested that HIVDR was one of the most important factors associated with virological failure, and further researches should be focused on other potential factors. 36 (52.9%) had NNRTI mutations, 52 (76.5%) had NRTI mutations and 3 (4.4%) had PI mutations. In addition, 21 (30.9%) were resistant to dual-class drugs. Similar to other studies in China, K103N/R and M184I/V were the most common NNRTI and NRTI mutations, respectively.^{9 13} Since three patients had detectable drug resistance to PIs, drugs such as second-line regimens should be used judiciously.

Our study found that minorities, people with junior high school or lower education levels and farmers were the three sociodemographic factors associated with virological failure. IDUs are more commonly found in southwest China, where there is an abundant multi-ethnic presence. Owing to sparser population distributions and lower income levels province-wide, these people generally received lower levels of education.¹⁵ In addition, traditional cultures and religions may pose obstacles to efficient implementation of CDC-based interventions.¹⁶ Similarly, most HIV-infected farmers live in rural areas, where income levels were low and healthcare infrastructure is poor, which compromises ART administration; this is corroborated by another research study conducted at three sentinel surveillance sites in China.¹⁴ Thus, efforts should be carried out in order to raise awareness, strengthen health education and train doctors at villages and townships regularly; supplemental policies should aim to improve income and healthcare infrastructure in rural areas.

Poor ART adherence was another risk factor in our study, with 135 (14.5%) patients having reported missing doses in the past month, which was higher than that of other studies in China.^{9 10 13} Except for one study from Indonesia which showed that adherence to ART was no different between IDUs and non-IDUs,¹⁷ some international studies have found that IDUs tend to have lower ART adherence rates than non-IDUs.^{18 19} Non-adherence is associated with depression, a lack of stable relationships and active drug injection.^{20–22} Good adherence can promise suppression of plasma HIV RNA and utilise the optimum effectiveness of the ART therapy.²³ Several international studies have focused on strategies to improve adherence, including behavioural interventions, social support,²⁴ directly administered antiretroviral therapy (DAART)²⁵ and MMT.^{26–28} These studies have found that drug adherence education should be part of the rehabilitation treatment

Table 4 Multivariate analysis of factors associated with HIV viral suppression failure among IDU patients receiving antiretroviral treatment in China from 2003 to 2007 and 2008 to 2011

Variable	Adjusted OR (95% CI)	
	2003–2007	2008–2011
Ethnicity		
Han	–	–
Minorities	–	2.3 (1.3 to 4.0)
Occupation		
Others	–	–
Farmer	–	2.1 (1.2 to 3.8)
CD4 cell counts at survey		
≥ 500	–	–
350–499	–	–
200–349	–	3.2 (1.3 to 7.9)
0–199	–	4.1 (1.6 to 10.3)
Province		
Others	–	–
Guangxi and Yunnan	0.4 (0.2 to 0.6)	0.3 (0.1 to 0.8)

IDU, injecting drug users.

programme for IDUs as well as a further expansion of health services.

Finally, when compared to other provinces, a lower proportion of IDUs in Guangxi and Yunnan experienced virological failure. IDUs are the main high-risk population for HIV infection in Guangxi, Yunnan and Xinjiang; however, in our study of 306 patients from Xinjiang, 87 (28.4%) had virological failure, of which 85 were successfully genotyped and 28 were found to have drug resistance. This finding indicated that Xinjiang had worse effectiveness of treatment, which was corroborated by a previous study showing that patients from Xinjiang were 12.6 times more likely to develop virological failure when compared to those from Guangxi and Yunnan.¹³ Of the 306 patients from Guangxi and Yunnan, 28 (9.2%) had missed doses in the past month, compared to 107 (17.2%) in other provinces. This supports the hypothesis that achieving good adherence is one of the most effective means to viral suppression. Similarly, a study in Guangxi reported that of the 120 patients receiving antiretroviral treatment, 113 (94.2%) took their medicine on time. The Guangxi CDC has a series of standard measurement protocols to supervise patient adherence: strict regulation of HIV drugs, regular follow-ups, treatment of opportunistic infections and strongly prioritised use of first-line regimens.²⁹ Large-scale ART treatment was implemented in Yunnan province in 2004; patients receiving free antiretroviral treatment in Yunnan had better survival effects.³⁰ In our study, the prevalence of virological failure among IDUs in Yunnan was low, which was supported by the results of local research.³¹

After MMT was implemented nationwide in 2004, the prevalence of HIV infection among IDUs was better controlled.⁶ Many studies have shown that MMT is a cost-effective intervention to scale up acceptance and adherence to HAART and improve the effectiveness of therapy among IDUs.^{16 26 27} However, adherence to MMT is itself associated with age, stable employment, alcohol abuse and coverage of ART.^{32 33} Hence, more strategies are needed to examine improving MMT retention.

Through the sensitivity analysis, some details would be presented. Before 2008, province was the only factor associated with virological failure; however, in addition to province, three more factors were found to be significantly associated with virological failure after 2008: ethnicity, occupation and CD4 cell counts at survey. Enlarging the sample size is an effective way to reduce biases and after combining the several cross-sectional surveys, education and self-reported missing doses in the past month were included into the final multivariate logistic regression models.

This study has several limitations. First, the data in our study was from the Chinese National HIVDR Surveillance and Monitoring Network, which may or may not fully represent all IDUs in China. Second, the study sample included patients starting antiretroviral

treatment from 2003 to 2011, during which period prevention policies and treatment programmes have undergone many significant changes that have most likely influenced treatment efficacy. Lastly, our study provided a systematic examination of the treatment outcomes of IDUs in China. However, as the epidemic and intervention situations differ across diverse localities, intervention and prevention measures should be tailored differently as well.

It has been more than 10 years since the China's National Free Antiretroviral Treatment Program (NFATP) was put into effect in 2003. During this time span, this programme has matured and improved and, as a result, more and more HIV-infected patients have gained access to antiretroviral therapy; this has brought the HIV/AIDS epidemic under control. The implementation of NFATP has had some successful examples, such as Guangxi and Yunnan, with success in dealing with antiretroviral treatment among IDUs; however, poor adherence to treatment is still a key problem, which has led to the high rate of failure of viral suppression among IDUs. More research is needed in order to explore how to improve the adherence of IDUs.

Author affiliations

¹State Key Laboratory for Infectious Disease Prevention and Control, National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Beijing, China

²Guangxi Center for Disease Control and Prevention, Nanning, Guangxi, China

³Yunnan Center for Disease Control and Prevention, Kunming, Yunnan, China

⁴Xinjiang Autonomous Region Center for Disease Control and Prevention, Urumqi, Xinjiang, China

⁵University of North Texas Health Science Center Graduate School of Biomedical Sciences, Fort Worth, Texas, USA

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