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### ESEARCH ARTICLE

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## Vulnerability to HIV infection among female drug users in Kathmandu Valley, Nepal: a cross-sectional study

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#### Abstract

Background: Women who use drugs are extremely vulnerable to HIV and sexually transmitted infections (STIs), but studies on risk behaviours and HIV infection among female drug users are limited in Nepal.

Methods: In this cross-sectional study conducted between September 2010 and May 2011, HIV prevalence and risk factors for HIV infection were investigated among female drug users recruited in drop-in centres, parks and streets in the Kathmandu Valley. The participants completed face-to-face interviews for a structured questionnaire, HIV pre-test counselling, specimen collection for HIV test and they were provided with their results at post-test counselling.

Results: A total of 269 female drug users were recruited, of whom 28% (n = 77) were found HIV positive; the majority (78%, n = 211) being injecting drug users and aged below 25 years (57%, n = 155). Nearly half (n = 137) of the total participants had shared needles or syringes in the past month, and 131 and 102 participants were involved in commercial or casual sex respectively with only half or less of them having had used condoms in the last 12 months. In multivariate analysis the variables associated with HIV infection included: (a) older age; (b) history of school attendance; (c) frequency of sharing of injection instruments; and (d) unsafe sex with commercial or casual partners.

Conclusions: HIV was highly prevalent among female drug users in the Kathmandu Valley, with its risk being strongly associated not only with unsafe injection practice but also with unsafe sexual behaviours. Awareness raising programmes and preventive measures such as condom distribution, needle or syringe exchange or methadone maintenance therapy should be urgently introduced in this neglected subpopulation.

Keywords: HIV, Female drug user, Injecting drug use, Sexual behaviour, Nepal

#### Background

The World Drug Report 2013 estimated that in 2011 between 167 to 315 million people aged 15–64 (3.6% - 6.9% of the world's population in that age group) had used an illicit substance at least once in the previous year [1]. In the same report, the United Nations Office on Drugs and Crime (UNODC) estimated that about 14 million people inject drugs globally and of them 1.6 million (11.4%) are living with HIV. Countries with higher prevalence of HIV infection among people who inject drugs are located in

Western and Central Europe, Sub-Saharan Africa, and South and South-East Asia including Nepal [2]. In recent years, there has been a rapid increase in female injecting drug users, especially in Asia and Eastern Europe [3,4]. In Central Asia and the countries like China, India and Russia, drug use and sharing injection equipment is increasing rapidly among females, and in many regions more females are seeking harm reduction services and drug treatment [5,6].

In Nepal, the first case of HIV/AIDS was reported in 1988. As of 2011, national estimates indicated that approximately 50,200 adults and children were infected with HIV, with an estimated overall HIV prevalence of 0.30% in the adult population of 15 to 49 years. Out of

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the total infections, around one third is estimated to have among females [7]. Although estimated prevalence among Nepal's adult population is fairly low, the HIV epidemic in Nepal is extremely heterogeneous with respect to the most at risk populations and geographic distribution [8,9]. The epidemic is concentrated in key subpopulations such as commercial sex workers, injecting drug users (IDUs), men who have sex with men, and migrants. IDUs are the subpopulation most heavily affected by the epidemic [10,11]. The drug user population is concentrated in the Kathmandu Valley and in the locations along the Eastwest Highway, where 30% of all the people living with HIV are IDUs. According to a government report, 42,954 (92.8%) male and 3,356 (7.2%) female drug users were living in the Kathmandu Valley alone in 2007 where 34.8% of IDUs were estimated to be HIV positive [12,13].

Compared to male drug users, information has been limited for female drug users regarding HIV prevalence and their risk behaviours. Though smaller in number, the situation of female drug users could be more serious than that of male drug users for several reasons. Firstly, female drug users are known to trade sex for money or drugs. A study has shown that over half of the female IDUs in China have been involved in sex work [14]. Secondly, female drug users who exchange sex for drugs or cash may not identify themselves at risk of HIV infection be-cause they do not consider themselves as sex workers [15]. Thirdly, condom use can be infrequent among them because drug dependency and financial problems may im- pair their judgment and power to negotiate for condom use with their sex partners [16-19]. Fourthly, female drug users depend in many cases on male partners for drugs and injections, leading them to an elevated risk of equip- ment sharing practice [20,21]. Fifthly, female drug users are socially stigmatized more than male drug users, ma-king them hidden and thus it is difficult for them to access preventive services [21-23]. For these reasons, female drug users could expose themselves to exceptional risk of HIV infection and play a critical role in the local HIV epidemic by bridging infection to the broader population through their drug injection network as well as sexual network [18,24,25]. These situations, however, largely remain unknown in Nepal.

With these backgrounds, this study aims to investigate prevalence of HIV infection and social and behavioural correlates of HIV infection among female drug users in Kathmandu Valley, Nepal, with a hope that it may help to improve intervention programmes for female drug users in Nepal.

#### Methods

#### Setting and sampling procedures

This cross-sectional study was conducted between September 2010 and May 2011 among female drug users of Kathmandu Valley, in which the capital city is situated. Female drug users were recruited in drop-in centres (DICs) that were working for various drug-related harm reduction programmes for female drug users as well as in parks and on the street. Recruitment was carried out directly by ex-drug users and trained outreach workers and indirectly through personal networks. The outreach workers first mapped out the groups and areas where they expect to encounter the target population, and they then set out to actively recruit potential candidates there. The time of field observations varied to cover morning, afternoon, evening, and late night hours. They often made use of existing social networks within a population. As selection proceeds, suitable new candidates with appropriate characteristics or behaviour were sought within the social networks of respondents already included in the study (snowball sampling) [26]. The inclusion criteria for the study was that they were current drug users of at least 16 years old and willing to give informed consent for both questionnaire survey and HIV testing. Eligible respondents received an explanation about the survey, its purpose and types of the questions to be asked.

#### Interview

Trained outreach workers and peer educators of the HIV/AIDS programme who had already established trust with female drug users through their daily activities interviewed participants face to face using structured questionnaires. A small incentive was provided to each participant for travel and refreshment. The name of the participants or their addresses were not recorded anywhere. Instead, they were provided with a unique identification (ID) number written on a plastic-coated card that was used for both questionnaire and HIV testing. Same ID was used for preand post-counselling and for the provision of test results.

#### Instrument

The structured questionnaire was developed from a questionnaire recommended and produced by Family Health International for IDUs [27]. With modifications made following the findings of the preliminary qualitative study (conducted among 21 female drug users in May 2010), the final questionnaire included 90 questions. The topics in the questionnaire included the main socio-demographic characteristics, drug use practices, frequency and duration of injection drug use, sexual activities and a history of sexually transmitted infections (STIs), and knowledge and perception of HIV/AIDS. Questions on knowledge included: (1) Can people protect themselves from HIV by using condoms?; (2) Can a person get HIV from mosquito bites?; (3) Can people protect themselves from HIV by having one uninfected faithful sex partner?; (4) Can people protect themselves from HIV by abstaining from sexual intercourse?; (5) Can a person get HIV by sharing a meal

with someone who is infected?; (6) Can a person get HIV through injections with a needle that was already used by someone else?; (7) Can people who inject drugs protect themselves from HIV by switching to non-injecting drugs?; (8) Can a pregnant woman infected with HIV transmit the virus to her unborn child?; and (9) Can a woman with HIV transmit the virus to her newborn child through breastfeeding? All of these questions were given in a Likert scale with options of "yes", "no" and "do not know".

#### HIV testina

After completing the interview, blood samples were collected from each study participant by finger prick blood sampler complying with the National HIV Testing Protocol. Considering the availability of limited human financial resources, the Ministry of Health and Population of Nepal has recommended the use of two or more rapid tests based on different test principles (antigens) as a minimum standard HIV test algorithm to be followed at all levels of the health care delivery system [28]. Two rapid test kits Determine HIV 1/2 and Uni-Gold HIV 1/2 were used for the purpose. The initial screening test was performed using Determine HIV 1/2 and then retested using the Uni-Gold HIV 1/2 when the first test result was positive for confirmation. A third test SD Bioline HIV 1/2 was performed for final confirmation when there was discrepancy in the first two tests. If the third test showed a reactive result, the tested sample was reported as "HIV positive" and if the third test showed a non-reactive result, it was reported as "HIV negative". Sensitivity and specifi- city of combined testing algorism of Determine and SD Bioline are reported to be both 100% [29,30]. The HIV test results were kept confidential. Pre-test counselling was provided as a part of informed consent and the partici- pants were informed of the testing result only at post-test counselling.

#### Ethical issues

This research protocol was approved by the Nepal Health Research Council and the Committee for Research on Human Subjects at Kyoto University in Japan. Separate written informed consents were obtained for the interview and HIV testing, and no personal identifier was recorded on the questionnaires. All the participants were advised to undertake free HIV testing for final clinical diagnosis.

#### Statistical analysis

Statistical analyses were carried out using SPSS software for Windows (version 19, IBM Inc., Chicago). Bivariate analyses were conducted to estimate the association of demographic or behavioural variables with HIV infection, calculating crude odds ratio (OR) with 95% confidence interval (CI). Multiple multivariate models were

run: (a) to compare the predictive powers of behavioural variables of different time frames; and (b) to show independent correlates to HIV infection. The significant variables from bivariate analyses, epidemiologically important variables and synthetic variables created by combining related variables were included in the models. Independent variables were assessed for multicollinearity, variance inflation factor and tolerance statistics were within acceptable limits for all variables [31]. From multivariate models adjusted odds ratio (AOR) and 95% CI were calculated. A p-value less than 0.05 (2-sided) was considered to be statistically significant. Answers to the HIV knowledge questions were transformed into scores by giving 1 for correct answer and 0 for otherwise.

#### Results

A total of 269 participants were included in the analysis, of whom 28.6% were HIV positive. The major sociodemographic characteristics of the participants are shown in Table 1.

More than half (52.0%) of the study participants were recruited in the streets. No association was detected between sites of recruitment and HIV status of the participants (p = 0.98). More than half of the participants (57.6%) were under 25 years old; the median age being 23 years. HIV infection was found to be associated with older age groups; the prevalence being 50.0% in the 30 years and above. The majority (76.2%) of the participants were married and/or cohabitating with their sexual partners, which is highly associated with HIV infection (p = 0.002 or p < 0.001). More than 80% of the participants had ever been to school, and the HIV prevalence (34.1%) is much higher in this group than those without school education (4.1%) (p = 0.001). Although 53.3% of the participants were unemployed, the job situation of the participants was unrelated to the HIV status (p = 0.307).

Table 2 shows the prevalence of risky behaviours in this population and the results of bivariate analyses between HIV status and HIV/STI knowledge score or behavioural variables. Risky behaviours are highly prevalent in this population. Injection practice in lifetime was reported from 78.4% (211/269); of them 24.2% (51/211) shared needles and/or syringes most times or always, and 86.7% (183/211) had shared a cooker or other utensils sometimes or more with other people in the past one month. Sex with regular, non-regular non-commercial partners (herein after "casual partners") and commercial partners were reported by 74.1% (166/224), 45.5% (102/224) and 58.5% (131/224) of sexually active participants respectively. Among them 79.5% (132/166), 75.5% (77/102) and 87.8% (115/131) reported that they are not always using condoms, respectively.

All these variables are significantly associated with increased risk of HIV infection except for HIV knowledge.

Table 1 Socio-demographic characteristics of female drug users with or without HIV infection recruited in the Kathmandu Valley, Nepal

	Positive HIV test (n = 77) n (%)	Total (n = 269)	Crude OR (95% CI)	p value
Place of recruitment				
Street/Park	40 (28.6)	140	1.00	
Drop in centre	37 (28.7)	129	1.01 (0.59-1.71)	0.984
Age (years)				
16 - 19	7 (25.9)	27	1.00	
20 - 24	25 (19.5)	128	0.69 (0.26-1.82)	0.457
25 - 29	28 (35.0)	80	1.54 (0.58-4.08)	0.387
30 - 38	17 (50.0)	34	2.86 (0.96-8.52)	0.060
Mean (SD)(Median)	26.3 (6.0) (25.0)	24.4 (4.8) (23.0)	1.12 (1.06-1.18)	<0.001
Marriage and live-in partnerships				
Not married, not living with sexual partner	6 (9.4)	64	1.00	
Not married, living with sexual partner	25 (32.5)	77	4.65 (1.77-12.22)	0.002
Currently married, not living with spouse or any other sexual partner	12 (36.4)	33	5.52 (1.84-16.59)	0.002
Currently married, living with spouse or other sexual partner	34 (35.8)	95	5.39 (2.11-13.79)	<0.001
_evel of education				
Never went to school	2 (4.1)	49	1.00	
Primary (1–5 years)	15 (48.4)	31	22.03 (4.54-107.04)	<0.001
Secondary (6–10 years)	26 (27.4)	95	8.86 (2.01-39.10)	0.004
Higher (11 years and higher)	34 (36.2)	94	13.32 (3.04-58.28)	0.001
Job situation				
Have a job	32 (25.6)	125	1.00	
Jobless	45 (31.3)	144	1.32 (0.77-2.25)	0.307

SD, standard deviation.

The prevalence of HIV is high among those who had ever injected (OR = 3.04, p = 0.006) as well as among those who ever used needle or syringes previously used by someone else (OR = 3.08, p < 0.001). Frequency of injection in the past one month is associated with positive HIV in a dose-dependent manner; the participants injecting once or more a day have the highest (39.2%) HIV prevalence (OR = 4.03, p = 0.001). Frequency of sharing injection instruments or other accessory utensils such as a cooker in the past one month is also associated with positive HIV status but not in a dose-dependent manner. Sexual experiences, both over a life time and in the last 12 months, are strongly associated with HIV status with equivalent magnitudes (OR = 10.82 and 9.13, p  $\leq 0.001$ ). Similarly, sexual experience with any type of partner in the past 12 months is strongly associated with the HIV status (OR = 3.50-5.91, p < 0.001) with the highest association being with casual partners. The majority of the participants used condoms inconsistently with any type of sexual partner. The frequency of condom use with a

regular partner or casual partner is associated with HIV status in a dose-dependent manner. The prevalence is highest among the participants who never or only sometimes used condoms with their regular partners (40.4%, OR = 3.97, p < 0.001) or casual partner (55.2%, OR = 6.99, p < 0.001). The frequency of condom use with commercial partners is also significantly associated with the HIV status but not in a dose-dependent manner.

Table 3 summarizes the results of multivariate analyses of factors associated with HIV infection. Multiple logis- tic regression analyses were carried out using behavioural variables with different time frames as well as synthetic variables with different risk specificities. This analytic strategy was adopted because although some questions were asked in an "ever" time frame for injection and sexual behaviours, the rest of the questions were asked in different time frames; "in the past one month" for drug use and "in the past 12 months" for sexual behaviours. It seemed therefore necessary to assess the effect of the time frame on the predictive power

OR, odds ratio.

Cl, confidence interval.

Table 2 Bivariate association of behavioural factors with HIV infection among female drug users recruited in the Kathmandu Valley, Nepal

Kathmandu Valley, Nepal				
	Positive HIV test (n = 77) n (%)	Total (n = 269)	Crude OR (95% CI)	p value
HIV Knowledge scores				
6 - 9	66 (27.8)	237	1.00	
0 - 5	11 (34.4)	32	1.36 (0.62-2.97)	0.445
Drug use behaviour				
Ever injected illegal/non-medical drugs				
No	8 (13.8)	58	1.00	
Yes	69 (32.7)	211	3.04 (1.37-6.76)	0.006
Ever used a needle or syringe previously used by someone else				
No/Non-IDU	23 (17.4)	132	1.00	
Yes	54 (39.4)	137	3.08 (1.75-5.43)	<0.001
Frequency of injecting with a needle or syringe previously used by someone else in the past one month				
Non-IDU/Never	24 (17.5)	137	1.00	
Occasionally/About half the time	36 (44.4)	81	3.77 (2.02-7.01)	<0.001
Always/Most times	17 (33.3)	51	2.35 (1.13-4.89)	0.022
Frequency of sharing cooker/vial/container, cotton/filter, or rinse water when injecting in the past one month				
Never/Non-IDU	19 (22.1)	86	1.00	
Sometimes	17 (21.8)	78	0.98 (0.47-2.06)	0.963
Always/Often	41 (39.0)	105	2.26 (1.19-4.30)	0.013
Frequency of injecting drugs in the past one month				
Non-IDU	8 (13.8)	58	1.00	
6 times a week or LESS	9 (15.5)	58	1.15 (0.41-3.22)	0.793
1 time a day or MORE	60 (39.2)	153	4.03 (1.79-9.10)	0.001
Sexual behaviour				
Ever had sexual intercourse				
No	2 (4.4)	45	1.00	
Yes	75 (33.5)	224	10.82 (2.55-45.89)	0.001
Sexual intercourse in the last 12 months with any type of partner				
No/Never had sex	4 (5.9)	68	1.00	
Yes	73 (36.3)	201	9.13 (3.19-26.08)	<0.001
Sexual intercourse with regular partner in the last 12 months				
No/Never had sex	15 (14.6)	103	1.00	
Yes	62 (37.3)	166	3.50 (1.86-6.58)	<0.001
Sexual intercourse with commercial partner in the last 12 months				
No/Never had sex	19 (13.8)	138	1.00	
Yes	58 (44.3)	131	4.98 (2.75-9.02)	<0.001
Sexual intercourse with non-regular non-commercial partner in the last 12 months				
No/Never had sex	25 (15.0)	167	1.00	
Yes	52 (51.0)	102	5.91 (3.32-10.51)	<0.001

Table 2 Bivariate association of behavioural factors with HIV infection among female drug users recruited in the Kathmandu Valley, Nepal (Continued)

Frequency of condom use in the last 12 months with all regular partners				
Never had sex/No sex with regular partner in the last 12 months	15 (14.6)	103	1.00	
Always/Often	20 (32.3)	62	2.79 (1.30-6.00)	0.008
Sometimes/Never	42 (40.4)	104	3.97 (2.03-7.79)	<0.001
Frequency of condom use in the last 12 months with all commercial partners				
Never had sex/No sex with commercial partner in the last 12 months	19 (13.8)	138	1.00	
Always/Often	36 (54.5)	66	7.52 (3.79-14.91)	<0.001
Sometimes/Never	22 (33.8)	65	3.20 (1.58-6.49)	0.001
Frequency of condom use in the last 12 months with all non-regular non-commercial partners				
Never had sex/No sex with casual partner in the last 12 months	25 (15.0)	167	1.00	
Always/Often	20 (45.5)	44	4.73 (2.28-9.82)	<0.001
Sometimes/Never	32 (55.2)	58	6.99 (3.58-13.66)	<0.001

Non-IDU, non-injecting drug user.

OR, odds ratio.

CI, confidence interval.

of the variables. It was also expected that the predictive power of the variables would be enhanced by creating synthetic variables to represent more directly the risk of behaviours.

Models 1 to 6 include all drug users but model 7 includes only injecting drug users. "Ever injected illegal/ non-medical drugs" and "Ever had sexual intercourse" were entered in model 1, while the latter was replaced with "Had sexual intercourse in the last 12 months" in model 2 showing that association of sexual behaviour is more prominent "in the last 12 months" than "ever". In models 3 and 4, on the other hand, a variable "Ever injected illegal/non-medical drugs" was replaced with a variable "Ever used needles or syringes previously used by someone else" (model 3) or a synthetic variable "Used needles or syringes previously used by someone else in the past one month" (model 4), while keeping the variable "Ever had sexual intercourse" the same as in model 1. From the comparison of models 1 to 4, it was shown that all injection variables had equivalent predictive power (AOR = 2.5) irrespective of time frame or the presence/absence of sharing practice, and that sexual variables had predictive powers that were equivalent to or more potent than the injection variables among the participants.

Model 5 is an extension of model 2 where the risks of sexual intercourses with different types of partners in the past 12 months with HIV infection were compared. While significant association was detected for sexual intercourses with commercial and casual partners, it was not significant with regular partners. Model 6 is the extension of model 4 using a synthetic variable where "Used needles or syringes previously used by someone

else in the past one month" was combined with the frequency of injection in the past month. It was shown that frequent unsafe injection practice (sharing needles and syringes once a day or more) and frequent unsafe sex (intercourses with 'sometimes or never' condom use) with casual partners were significantly associated with HIV infection, while with commercial sexual partners intercourses with 'always or often' rather than infrequent condom use showed significant association. Such an association pattern was maintained when analysis was confined to female injecting drug users (model 7). Throughout these models, age and "Ever attended school" but not "Marital status" were significantly associated with HIV infection. "Ever attended school" was the most potent predictor of HIV infection, while its association nearly halved when sexual behaviour variables were switched from the general ones to those specific to sexual partners. Behavioural and injecting practice variables were introduced in the order of all possible combinations into models 5 through 7, yielding similar results.

#### Discussion

Overall, HIV prevalence in this population was revealed to be 28.6%; 33% in those who practised injecting drug use and 14% even among those who reportedly never experienced injecting drug use. In Nepal, the Integrated Biological and Behavioral Surveillance (IBBS) surveys are conducted at regular intervals among male IDUs. The latest round of IBBS showed a significant decline in HIV prevalence among male IDUs in Kathmandu Valley, from 51.7% in 2005 to 6.3% in 2009 [10], which is much lower than the HIV prevalence we found among female IDUs. This study strongly suggests that female drug users are

Table 3 Multivariate association of behavioural factors with HIV infection among female drug users in the Kathmandu Valley, Nepal

			All dru	g users			Only IDUs
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
			Adj	usted odds r	ratio		
			(95% (	confidence in	nterval)		
Age	1.10*	1.10*	1.11*	1.11*	1.07*	1.07	1.08*
	(1.04-1.17)	(1.03-1.17)	(1.04-1.18)	(1.04-1.19)	(1.01-1.15)	(1.00-1.15)	(1.00-1.17)
Ever attended school (ref. No)	10.85*	9.03*	10.83*	10.52*	6.14*	6.21*	4.85
	(2.46-47.79)	(2.05-39.73)	(2.44-48.13)	(2.38-46.56)	(1.34-28.06)	(1.31-29.49)	(0.96-24.55)
Currently married, or currently not married but	2.33	2.15	1.84	1.85	2.01	1.62	1.69
living with sex partner (ref. Not married, not living with sexual partner)	(0.72-7.53)	(0.78-5.94)	(0.57-5.96)	(0.57-6.01)	(0.72-5.66)	(0.57-4.62)	(0.52-5.47)
Ever injected illegal/non-medical drugs (ref. No)	2.48*	2.41*			2.65*		
	(1.05-5.84)	(1.02-5.73)			(1.08-6.49)		
Ever used a needle or syringe previously used			2.50*				
by someone else (ref. No/Non-IDU)			(1.35-4.63)				
Used needles or syringes previously used by someone				2.60*			
else in the past one month (ref. Never/non-IDU)				(1.40-4.81)			
Used needles or syringes previously used by someone						0.93	0.78
else, injecting 6 times a week or less in the past month (ref. Non-IDU/Never)						(0.24-3.64)	(0.19-3.26)
Used needles or syringes previously used by someone						2.53*	2.19
else, injecting 1 time a day or more in the past month (ref. Non-IDU/Never)						(1.28-4.99)	(0.99-4.84)
Ever had sexual intercourse (ref. No)	2.52		2.72	2.57			
	(0.40-15.96)		(0.43-17.20)	(0.41-16.26)			
Had sexual intercourse in the last 12 months		3.77*					
(ref. No/Never had sex)		(1.19-11.97)					
Had sexual intercourse with regular partner in the last					1.24		
12 months (ref. No/Never had sex)					(0.57-2.70)		
Had sexual intercourse with commercial partner in the					2.20*		
last 12 months (ref. No/Never had sex)					(1.09-4.48)		
Had sexual intercourse with non-regular non-commercial					2.49*		
partner in the last 12 months (ref. No/Never had sex)					(1.25-4.95)		
Frequency of condom use in the last 12 months with all regular partner(s) <sup>a</sup>							
Always/Often						1.15	1.13
·						(0.45-2.93)	(0.40-3.20)
Sometimes/Never						1.33	1.19
						(0.57-3.11)	(0.47-3.04)
Frequency of condom use in the last 12 months with all commercial partner(s) <sup>a</sup>						(6.67 6,71)	(0.11 0.01)
Always/Often						3.35*	3.41*
,						(1.47-7.61)	(1.39-8.40)
Sometimes/Never						1.45	1.66
Sometimes/Nevel							
						(0.63-3.35)	(0.67-4.08)

Table 3 Multivariate association of behavioural factors with HIV infection among female drug users in the Kathmandu Valley, Nepal (Continued)

Frequency of condom use in the last 12 months with all non-regular non-commercial partner(s) <sup>a</sup>	
Always/Often	1.71 2.13
	(0.72-4.07) (0.82-5.53)
Sometimes/Never	3.11* 3.11*
	(1.36-7.13) (1.28-7.56)

IDUs, injecting drug users.

now one of the most vulnerable populations with regard to HIV infection in Nepal.

Consistent with previous studies, injection behaviour showed a strong association with HIV infection in this population. This association could be causal because the sharing of injection instruments was associated strongly with HIV infection and in a dose-dependent manner. A study in Montreal among active drug users found that increasing injection frequency is highly correlated with HIV transmission, as it may reduce the chances of sterile injecting equipment being used each time [32]. Also, where group injecting is common, women may be the last to use the needles/syringes [33]; this may have strong implications with regard to the spread of HIV.

Unprotected sexual behaviour was also of great risk in this study. Risk significantly increased for sex with com- mercial or casual sex partners. The association of HIV infection and sex with commercial partners was not dose-dependent, where the people who reported more condom use were more likely to be HIV positive. The reason for this association could be multiple. It may be that partici-pants who were involved in commercial sex and knew their HIV infection before the study might have provided socially desirable answers to our interview, or they were really using condoms to either prevent HIV transmission to their clients or as self-protection from re-infection. A recent study by UNODC among female drug users in Nepal has reported nearly 90% of condom use in last sex act with commercial sex partners [34]. In addition, pre-vious studies among drug users have found safer sex prac- tices strongly associated with HIV infection. A study in the United States found that self-reporting of being HIV- infected was the strongest factor associated with con-sistent condom use in the past 6 months [35]. Another study in Puerto Rico found that HIV-positive drug users were nearly five times more likely to use condoms during vaginal sex [36]. In contrast, HIV infection risk of the sex with casual partners was dose-dependent on condom use, where the people who have less condom use are more likely to be HIV positive. Studies in other countries have observed the association between sex with casual partners

and HIV infection among IDUs [37]. These women may not have skills to negotiate for condom use, and even if the woman is aware of her HIV status, in casual relationships she may not feel responsible for preventing further transmission of HIV to this type of partner.

Injection or sexual behaviours at high risk of HIV infection were shared by around 70% or more participants with HIV infection and even one third to half of participants without HIV infection in this study. This strongly suggests that if left uncontrolled the HIV epidemic could expand in this population and that this population could continue to be a source of HIV infection through its networks of injection and/or behavioural practices.

It is increasingly being recognized that women who use drugs are generally different from men who use drugs, and thus have different needs [6,38-40]. Targeted HIV prevention and treatment programmes should be urgently developed and implemented for this population. Provision of clean needles and syringes or methadone maintenance therapy (MMT) will be useful for the prevention of HIV transmission through injecting network. Several studies have shown that drug users who used needle and syringe exchange programs were less likely to share needles and syringes [41,42]. Programs such as needle and syringe exchange and MMT can achieve high coverage of IDUs in some settings [42]. A study in Amsterdam showed the benefits of the combined availability of needle exchange and MMT, and argued that involvement with both services, compared to only one, was associated with a lower incidence of HIV infections among IDUs [43]. Additionally, free STI diagnosis and treatment and condom distribution will be suitable for the prevention of HIV infection through sexual network [44]. Despite mixed evidence from three large community-based randomized controlled trials in sub-Saharan Africa, syndromic and mass treatment of STIs may contribute to HIV infection prevention [44]. Finally, problems of drug use and commercial/casual sex are frequently intertwined in female drug users as they often engage in commercial/casual sex to get drugs or money [45,46]. An overlap of sex and drug networks among IDUs enhances their vulnerability to HIV infection

aref. Never had sex/No sex with this type of sexual partner in the last 12 months.

and promotes HIV transmission among their sexual partners. MMT, the most widely available treatment for opiate addiction, is of particular importance since it can prevent infection through both injecting drug use and commercial/casual sex for drugs at the same time. MMT has shown to reduce both injection drug use and the risk of infection with HIV [47,48]. Since the size of this subpopulation has been unknown, these measures should be accompanied with studies to estimate the size of this population.

In this study, most of the behavioural questions were taken from the standard questions of Family Health International [27]. In this set of questions drug use and sexual behaviours are asked, though in part covering the participant's lifetime, but mostly in different time frames; one month and one year for drug use and sexual behaviours, respectively. Since such a difference in time frames could influence the predictive power of the variables, we compared their predictive powers and found that predictive powers were largely independent of time frame for both types of behaviours, suggesting that once initiated, the same behavioural pattern will be maintained over a long period of time in this population.

Older age and having education remained as strong predictors of HIV infection even in the presence of all behavioural variables that could affect HIV infection. Since HIV infection other than through injecting drug use and sexual intercourse is unlikely in this population, this may suggest the uncertainty of behavioural variables or that the behavioural variables we used could reflect the risk for HIV infection only partially. The uncertainty of information could come from self-reported nature of the information which could be affected by recall bias, the psychotic effect of drugs or by socially desirable answers to the sensitive and/or illegal behaviours.

One of the limitations of this study is the sampling procedure because it was not random; the participants may not be a true representative to the female drug user population in the study region. Participants were recruited through a snowballing process. Though efforts were made to recruit the initial respondents in many locations and opportunities to ensure variability, our sampling procedure could still introduce the bias into the participants in a way that people who have larger social connections and have similar characteristics to initial respondents are overrepresented. To get an unbiased prevalence of HIV infection and risky behaviours, more sophisticated sampling methods, such as respondent driven sampling [49-51] should be considered. Finally, cross-sectional design of this study limits the causal inference in association detected in this study.

#### Conclusions

HIV was highly prevalent among female drug users in Kathmandu Valley, with its risk being strongly associated not only with unsafe injection practice but also with unsafe sexual behaviours. Awareness raising programmes and preventive measures such as condom distribution, needle or syringe exchange or methadone maintenance therapy should be urgently introduced in this neglected subpopulation.

#### Abbreviations

IDUs: Injecting drug users; DICs: Drop-in centres; ID: Identification; STIs: Sexually transmitted infections; OR: Odds ratio; CI: Confidence interval; AOR: Adjusted odds ratio; IBSS: Integrated bio-behavioural surveillance survey; NCASC: National Center for AIDS and STD Control; MMT: Methadone maintenance therapy.

#### Competing interests

The authors declare that they have no competing interests.

#### Authors' contributions

BG, SZ, MOK, and MK participated in the conception and design of the study. BG supervised the data collection. BG, SPS and MK performed the statistical analysis and interpretation of results. BG and MK drafted the manuscript. All authors revised, read and approved the final manuscript.

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# Food Insecurity Is Associated with Increased Risk of Non-Adherence to Antiretroviral Therapy among HIV-Infected Adults in the Democratic Republic of Congo: A Cross-Sectional Study

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#### **Abstract**

Background: Food insecurity is increasingly reported as an important barrier of patient adherence to antiretroviral therapy (ART) in both resource-poor and rich settings. However, unlike in resource rich-settings, very few quantitative studies to date have investigated the association of food insecurity with patient adherence to ART in Sub-Saharan Africa. The current study examines the association between food insecurity and adherence to ART among HIV-infected adults in the Democratic Republic of Congo (DRC).

Methods and Findings: This is a cross-sectional quantitative study of patients receiving ART at three private and one public health facilities in Kinshasa, DRC. Participants were consecutively recruited into the study between April and November 2012. Adherence was measured using a combined method coupling pharmacy refill and self-reported adherence. Food insecurity was the primary predictor, and was assessed using the Household Food Insecurity Access Scale (HFIAS). Of the 898 participants recruited into the study, 512 (57%) were food insecure, and 188 (20.9%) were not adherent to ART. Food insecurity was significantly associated with non-adherence to ART (AOR, 2.06; CI, 1.38–3.09). We also found that perceived harmfulness of ART and psychological distress were associated respectively with increased (AOR, 1.95; CI, 1.15–3.32) and decreased (AOR, 0.31; CI, 0.11–0.83) odds of non-adherence to ART.

Conclusion: Food insecurity is prevalent and a significant risk factor for non-adherence to ART among HIV-infected individuals in the DRC. Our findings highlight the urgent need for strategies to improve food access among HIV-infected on ART in order to ensure patient adherence to ART and ultimately the long-term success of HIV treatment in Sub-Saharan Africa.

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#### Introduction

The benefits of antiretroviral therapy (ART) in reducing HIV/AIDS related-morbidity and mortality are extensively documented [1–3]. Recent evidence indicates that early initiation of ART substantially reduces sexual transmission of HIV at individual [4,5] and population levels [6]; conferring ART a crucial place in both treatment and prevention of HIV/AIDS.

Prior studies have shown that, without high and sustained adherence levels, both therapeutic and public health benefits of ART cannot be secured, and that individuals with sub-optimal levels of adherence have higher risk of incomplete viral

suppression, disease progression, and development of drug resistance [7–9].

Our understanding of adherence to ART has substantially increased over the past years with a wide documented range of factors influencing ART adherence across differing settings in developed and developing countries [10–17]. Recently, food insecurity has emerged as a key structural barrier that affects adherence to ART in both resource-rich and constrained settings. Studies from British Columbia [18], San Francisco [19], Atlanta [20,21], and France [22] have found lower levels of medication adherence among food insecure individuals on ART. Similarly, a number of, predominantly qualitative, studies from Sub-Saharan

Africa (SSA) have documented food insecurity as an important barrier to ART adherence [12,23–26]. Furthermore, food insecurity was shown to be independently related to poor virologic response and mortality even when adjusting for patient adherence to ART [19,27,28].

Food insecurity parallels, and is viciously intertwined with the AIDS epidemic in SSA, both having a damaging impact in the region [29]. SSA accounts for 69% of the people infected with HIV worldwide, and is home to 234 million (26.8%) people classified as undernourished [1,30]. In the Democratic Republic of Congo (DRC), the research setting of the current study, the Multi Indicator Cluster Survey (MICS) revealed that approximately 33% of the households were experiencing food insecurity in 2010, with figures ranging from 5% in the Kinshasa City to nearly 60% in some eastern provinces of the DRC [31]. The national HIV program reports a HIV prevalence of 2.57% among the general population, with only 12.3% of eligible patients having access to ART [32].

A review of the literature revealed that, unlike in resource-rich settings, very few quantitative studies to date, using a validated measure of food insecurity, have documented the association between food insecurity and patient adherence to ART in SSA and the developing world at large [26,33]. Additionally, literature on patient adherence to ART in the DRC, the second largest country in Africa, remains exceptionally scarce. In our preliminary qualitative study, we found that food insecurity, financial constraints, forgetfulness, and fear of disclosure/stigma were common barriers to ART adherence; while religious beliefs were both a barrier and facilitator of ART adherence among HIV-positive adults in the DRC [23].

The current study, grounded in the results of our qualitative study [23], aims at quantitatively assessing factors associated with adherence and more specifically, documenting the prevalence of food insecurity, and its effect on ART adherence among HIV-positive adults receiving ART in the DRC. Such information is crucial for guiding context-specific interventions to promote patient adherence to ART.

#### Methods

#### **Ethics Statement**

This study was granted ethical approval from the Committee for Research on Human Subjects at Kyoto University and the Kinshasa University School of Public Health Ethics Review Committee in the DRC. All the participants provided written informed consents before being interviewed.

#### Study Design, Participants and Setting

This is a cross-sectional study conducted in Kinshasa, DRC, between April and November 2012. Participants were consecutively recruited into the study from one public health facility: Hopital Provincial General de Référence de Kinshasa (HGPRK) and three private health institutions which included one treatment site of the NGO Actions Communautaires Sida/Avenir Meilleur pour les Orphelins (ACS/Amo-Congo), three treatment sites of the Armée du salut (Salvation Army), and two treatment sites of the Centre Hospitalier Monkole (CHM). Recruitment sites were in geographically dispersed locations and served patients coming from all the townships of Kinshasa. At the time the study was conducted, around 1,000, 2,900, 2,300, and 1,100 patients were receiving free ART respectively at the HGPRK, ACS/Amo-Congo, Armée du salut, and the CHM, and none of the facilities provided food or any kind of nutrition aid to patients. We collected data using an interviewer-administered questionnaire, which we

designed based on the findings from our prior qualitative study [23] supplemented with other relevant questions obtained from the available literature [34–38]. The questionnaire was piloted in a sample of 20 respondents (not included in the final sample) to ensure clarity prior to conducting interviews, and it showed an overall good test-retest reliability performed within a one month interval. The interviews were conducted in French or Lingala, the most commonly used languages in Kinshasa, and the interviewers were provided guidance on questionnaire administration over two training sessions organized by the research team. Participants were included in the study provided that they were at least 18 years old, on ART for at least 6 months, and had given written informed consent. Participants were compensated for their time and transportation with an amount of 3 US dollars.

#### Measures

Primary outcome. The primary outcome of interest was adherence to ART, and was assessed using a composite measure coupling both pharmacy refill and self-reported adherence. Pharmacy refill adherence measures were shown to be reliable in assessing adherence, and to correlate well with virological and clinical outcomes in resource limited settings [39–42], and the combination with self-reported adherence performed better in predicting virological failure than other singular methods [43].

The pharmacy refill adherence in this study is based on a variation of the medication possession ratio (MPR), a measure of the proportion of days a patient has his/her medication on hand, and was calculated by dividing the number of days late for pharmacy refills by the total days on ART, and then subtracting this proportion from 100% [40,44]. We calculated the average pharmacy refill rate of adherence for each patient over the preceding six months. When applicable, the number of days being late for pharmacy refills was adjusted to account for cases where patients were provided with more medication than needed. Patients with pharmacy adherence levels  $_{>}95\%$  were categorized as non-adherent to ART [8].

To measure self-reported adherence, we adopted a validated tool that assesses adherence over the previous seven days [34]. The tool contains questions that first measure adherence over shorter time frames (yesterday and the day before yesterday), and an aided-recall question for situations that can potentially lead to missed ART doses with the intent to facilitate a more accurate reporting of the number of pills skipped during the previous seven days, and to limit the influence of forgetfulness. Self-reported non-adherence was defined as taking  $_{>}95\%$  of the prescribed pills over the previous seven days [8].

In this study, participants were categorized as non-adherent to ART when they were non-adherent to either one or both of the measures of adherence described above; otherwise, they were considered to be adherent.

Primary independent variable. Food insecurity was the primary independent variable of this study, and was measured by the Household Food Insecurity Access Scale (HFIAS) [35]. The HFIAS is a validated instrument and has been shown to distinguish food insecure from food secure households across different cultural contexts. It is a set of nine questions designed to reflect universal domains of the experience of food insecurity including 1) anxiety and uncertainty about the household food supply, 2) insufficient quality (includes variety and preferences of the type of food), and 3) insufficient food intake and its physical consequences. We presented results in a categorical format including 1) food secure, 2) mildly food insecure 3) moderately food insecure, and 4) severely food insecure, which we dichotomized into food insecure versus food secure. The Cronbach's

alpha was 0.97, demonstrating a high internal consistency of the scale in our sample.

Other covariates. Internalized AIDS stigma: The Internalized AIDS-Related Stigma Scale was used to assess the internalized AIDS stigma [36]. The items were administered on a 5-point Likert-scale ranging from strongly disagree to strongly agree. Strongly disagree, disagree, and neutral were converted to 0 and agree and strongly agree to 1. Scale score ranged 0–6; participants who obtained relatively high scores on the scale (\_2) were compared to those who had low scores (#2) [45]. The scale showed a moderate degree of internal consistency with Cronbach's alpha = 0.60.

Psychological distress (Depression, anxiety disorders): Mental health status was assessed using the Kessler-6 scale, a standardized and validated screening tool for non-specific psychological distress including depression and anxiety disorders [37]. Participants were asked on a 5-points Likert scale ranging from 0 (none of the time) to 4 (all of the time) how often they felt 1) nervous, 2) hopeless, 3) restless or fidgety, 4) so depressed that nothing could cheer you up, 5) that everything was an effort, and 6) worthless. Scores equal to or higher than 13 indicate higher probability of psychological distress. There was a high internal consistency of the scale in our sample with Cronbach's alpha = 0.89.

Other variables: other covariates included the household wealth index [46], socio-demographic characteristics (10 items), HIV/AIDS disease-related variables (4 items) and HIV/AIDS knowledge (8 items), ART-related variables (8 items), perceptions about HIV/AIDS and ART (12 items), alcohol and drug use (2 items), social support [47], and perceived quality of health care (6 items) [38]. (See Text S1 for additional information on variables).

#### Statistical Analysis

Data was analyzed using SPSS (PASW) for Windows 17.0 (SPSS Inc., Chicago, Illinoi, USA). Univariate analysis was conducted to obtain descriptive statistics of all the variables. Bivariate analyses were performed using Chi-square tests for categorical variables and Mann Whitney U-test for continuous variables. We included in the analysis nonresponse cases on items related to perceptions about HIV/AIDS and ART; their exclusion did not affect the results of our analysis (See Table S1, which shows frequency of nonresponse for perception items). We grouped nonresponses with participants whose answers were "disagree" and "don't know" since they were similar with respect to their odds ratios when compared to participants who agreed to the assertions. Factors associated with non-adherence by bivariate analysis with P value #0.10 and those considered epidemiologically important were entered into a multivariate logistic regression model to obtain adjusted odds ratios (AOR) and 95% confidence intervals (CI). "Frequency of ART" and "regimen drugs" were not included in the multivariate model, even though both variables had each a category with P value #0.10, overall the two variables did not meet the inclusion criteria, and we excluded "duration of HIV infection" from the model because of its multicollinearity with "duration of ART".

#### Results

#### Participant Characteristics

A total of 898 participants completed the study and 25 declined participation, giving a response rate of 97.3%. The median age was 44 years [Interquartile range (IQR): 38–51]. The majority of participants were female (72.2%), without standard employment (76.4%), had completed at least secondary school (75.3%), and

Christians (87.9%) by religion (Table 1). The median treatment duration was 41 months (IQR: 18–64); most participants were on first line regimens (97.9%), and on a twice a day dosing schedule (92.3%). (Table 2).

#### Food Insecurity and Adherence Assessment

Based on the HFIAS, 386 participants (43.0%) were classified as food secure, 9 (1.0%) as mildly food insecure, 46 (5.1%) as moderately food insecure and 457 (50.9%) as severely food insecure (See Table S2, which shows details of participants' food security status). The overall prevalence of food insecurity among our participants was 57% (Table 2). 188 (20.9%) participants were categorized as non-adherent to ART in respect to the definition of adherence described above (See Table S3, which shows details of participants' adherence status).

## Bivariate Associations between Independent Variables and ART Adherence

Factors significantly associated with non-adherence in the bivariate analysis included food insecurity [odds ratio (OR), 2.25; CI, 1.58–3.19; P=0.000)], psychological distress (OR, 0.38; CI, 0.15–0.98; P=0.039), presence of (an)other HIV-infected individual(s) in the household (OR, 0.62; CI, 0.40–0.96; P=0.042), alcohol intake (OR, 1.65; CI, 1.13–2.40; P=0.012), duration of ART [\$48 months] (OR, 1.45; CI, 1.05–2.01; P=0.027), perceived ART harmfulness (OR, 1.68; CI, 1.10–2.55; P=0.042), and the beliefs that God or prayers could cure HIV (OR, 2.10; CI, 1.45–3.04; P=0.000), or that ART worked better when associated with prayers (OR, 1.73; CI, 1.23–2.43; P=0.002), and receiving treatment from ACS/Amo-Congo (OR, 2.99; CI, 1.58–5.62; P=0.001). (Table 2 & Table 3).

Table 4 shows reasons reported by participants for skipping ART doses during the previous seven days. 36 (39.5%) participants cited forgetfulness, 17 (18.6%) were unable to pay for the medical consultation or for transport, 13 (14.2%) ran out of pills, 11 (12.0%) reported lack of food, 7 (7.6%) had travelled, and other reasons were reported in much lower proportions.

#### Multivariate Analysis

In the multivariate analysis (Table 5), food insecurity was strongly associated with non-adherence. Food insecure participants were two times more likely to be non-adherent to ART compared to those who were food secure (AOR, 1.99; CI, 1.36—2.90, P=0.000). Other factors significantly associated with non-adherence to ART included alcohol intake (AOR, 1.55; CI, 1.02—2.34, P=0.037), and perceived ART harmfulness (AOR, 2.06; CI, 1.30—3.27, P=0.002). Paradoxically, we found that participants who had psychological distress (depression, anxiety) as measured by the K6-scale, had lower odds of non-adherence (AOR, 0.34; CI, 0.12—0.90, P=0.030), as well as those who reported that skipping ART doses could worsen the disease (AOR, 0.58; CI, 0.38—0.88, P=0.012).

#### Discussion

Designed based on the findings of our preceding qualitative study that food insecurity is a prominent structural barrier to ART adherence [23], this study is one of the first to quantitatively demonstrate the association of food insecurity with ART nonadherence in a Sub-Saharan African country. Our findings corroborate previous qualitative studies from SSA [12,23–25], quantitative studies in resource rich settings [18–22], and recent findings from a longitudinal cohort study in rural Uganda [26].

Table 1. Sociodemographic characteristics of non-adherent and adherent participants on ART recruited in Kinshasa, DRC.

	Non-Adherent (n = 188)	Adherent (n = 710)	Total (n=898)	Crude OR (95% CI)	P value
	n (%)	n (%)	n (%)		
Gender					
Male	49 (26.1)	201 (28.3)	250 (27.8)	1.00	
Female	139 (73.9)	509 (71.7)	648 (72.2)	1.12 (0.77-1.61)	0.603
Educational level					
Primary school or less	46 (24.5)	176 (24.8)	222 (24.7)	1.00	
Secondary school	110 (58.5)	420 (59.2)	530 (59.0)	1.00 (0.68-1.47)	1.000
University	32 (17.0)	114 (16.0)	146 (16.3)	1.07 (0.64-1.78)	0.885
Marital status					
Married/cohabitating	63 (33.5)	261 (36.8)	324 (36.1)	1.00	
Single	43 (22.9)	164 (23.1)	207 (23.1)	1.08 (0.70-1.67)	0.793
Divorced/Separated	29 (15.4)	83 (11.7)	112 (12.5)	1.44 (0.87-2.39)	0.191
Widowed	53 (28.2)	202 (28.4)	255 (28.4)	1.08 (0.72-1.63)	0.768
Religion					
Catholic Christian	54 (28.7)	194 (27.3)	248 (27.6)	1.00	
Protestant Christian	22 (11.7)	125 (17.6)	147 (16.4)	0.63 (0.36-1.09)	0.127
Revival churches Christian	85 (45.2)	309 (43.5)	394 (43.9)	0.98 (0.67-1.45)	1.000
Others*	27 (14.4)	82 (11.5)	109 (12.1)	1.18 (0.69-2.00)	0.627
Employment status					
Employed	37 (19.7)	175 (24.6)	212 (23.6)	1.00	
Unemployed	151 (80.3)	535 (75.4)	686 (76.4)	1.33 (0.89-1.98)	0.184
IGA					
Yes	136 (72.3)	478 (67.3)	614 (68.4)	1.00	
No	52 (27.7)	232 (32.7)	284 (31.6)	0.78 (0.55-1.12)	0.220
	Median (IQR)	Median (IQR)	Median (IQR)		
Age (years)	43 (36. 25-50)	44 (38-51)	44 (38-51)		0.150
Household size	5 (4–7)	5 (3-7)	5 (3-7)		0.426
Financial dependents <sup>†</sup>	3 (1.25-5)	3 (1-5)	3 (1-5)		0.820
Household wealth index	0.08 (-2.29 to 2.55)	0.16 (-2.44 to 2.42)	0.16 (-2.43 to 2.42)		0.823

\*Other: Muslim, Kimbaguist, None:

†number of financial dependents; ART, antiretroviral therapy; IGA, income generating activity; OR, odds ratio; IQR, inter-quartile range; DRC, Democratic Republic of Congo.

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Because of the cross-sectional nature of this study, interpretation of the results could be multiple. Firstly the observed association could be confounded by a third factor that was associated with both ART non-adherence and food insecurity. Secondly, we could assume that ART non-adherence was causal to food insecurity. Lastly, food insecurity could be causal to ART non-adherence.

The first possibility could be the case with poverty as a most likely confounder since prior studies have shown that trade-offs between subsistence needs and health care needs resulted in participants missing clinic visits or giving up ART for food in financially constrained individuals [24,48]. However, our results failed to support this possibility because household wealth index and employment status were not associated with ART non-adherence in bivariate analyses and our multivariate analysis was adjusted for these variables. Residual confounding of poverty due to insufficient sensitivities of these measures to rate poverty seemed unlikely because both variables were strongly associated with food insecurity (P<sub>></sub>0.001). The second possibility seemed also unlikely because such a narrative had never been documented in

qualitative studies including our study [12,23–25] and because ART non-adherence was not associated with any financial measures such as household wealth index and employment status. The third possibility is therefore most likely the case. This is strongly supported by the recent findings from a study in rural Uganda showing that food insecurity is longitudinally associated with non-adherence to ART [26] and preliminary experimental studies that showed that food supplementation improved the adherence to ART among food-insecure adults in Zambia [49,50].

However, possible mechanisms through which food insecurity could lead to ART non-adherence remained unclear. Our qualitative study identified two perceptions held by the participants as potential mechanisms including ART can be harmful or is not effective when taken without food [23]. In this study, we tested these hypotheses including the questions on participants' perception on the harmfulness or effectiveness of ART when taken without food but failed to show any association of these perceptions with ART non-adherence. Possible mechanisms may include forgetfulness. Although our study was not designed to

Table 2. Bivariate analysis of factors associated with Non-adherence to ART.

	Non-Adherent (n = 188)		Total (n = 898)	Crude OR (95% CI)	p value
	n (%)	n (%)	n (%)		
Food insecurity					
No	53 (28.2)	333 (46.9)	386 (43.0)	1.00	
Yes	135 (71.8)	377 (53.1)	512 (57.0)	2.25 (1.58-3.19)	0000
Disdozure					
No	36 (19.1)	170 (24.0)	206 (22.9)	1.00	
re	152 (80.9)	540 (76.0)	692 (77.1)	1.32 (0.88-1.98)	0.196
Psychological distress					
No (Score:0-12)	183 (97.3)	663 (93.4)	846 (94.2)	1.00	
(es (Score:13-24)	5 (2.7)	47 (6.6)	52 (5.8)	0.38 (0.15-0.98)	0.039
nternalized stigma					
icoret)-2	123 (65.4)	483 (68.0)	606 (67.5)	1.00	
core3-6	65 (34.6)	227 (32.0)	292 (32.5)	1.12 (0.80-1.57)	0.555
Social support from family					
No	96 (51.1)	417 (58.7)	513 (57.1)	1.00	
/es	92 (48.9)	293 (41.3)	385 (42.9)	1.36 (0.98-1.88)	0.071
Social support from non-family members					
No	137 (72.9)	544 (76.6)	681 (75.8)	1.00	
(es	51 (27.1)	166 (23.4)	217 (24.2)	1.22 (0.84-1.75)	0.331
Opportunistic infection					
Vo.	181 (96.3)	683 (96.2)	864 (96.2)	1.00	
(es	7 (3.7)	27 (3.8)	34 (3.8)	0.97 (0.41-2.28)	1,000
HIV-infected individual(s) in the household					
No	160 (85.1)	554 (78.0)	714 (79.5)	1.00	
res	28 (14.9)	156 (22.0)	184 (20.5)	0.62 (0.40-0.96)	0.042
Alcohol intake*					
No	139 (73.9)	585 (82.4)	724 (80.6)	1.00	
(es	49 (26.1)	125 (17.6)	174 (19.4)	1.65 (1.13-2.40)	0.012
l'obacco smoking					
No.	179 (95.2)	680 (95.8)	859 (95.7)	1.00	
res .	9 (4.8)	30 (4.2)	39 (43)	1.14 (0.53-2.44)	0.893
Knowledge of HIV/AIDS					
Good (≥5)	164 (87.2)	622 (87.6)	786 (87.5)	1.00	
Poor (≤4)	24 (12.8)	88 (12.4)	112 (12.5)	1.03 (0.63-1.67)	0.990
Regimen					
st line	184 (97.9)	695 (97.9)	879 (97.9)	1.00	
2nd line	4 (2.1)	15 (2.1)	19 (2.1)	1.00 (0.33-3.07)	1,000
Regimen drugs					
STC+TDF+EFV or NVP	10 (5.3)	67 (9.4)	77 (8.6)	1.00	
BTC+AZT+EFV or NVP or LPV/rit	165 (87.8)	575 (81.0)	740 (82.4)	1.92 (0.96-3.82)	0.080
TIC+D4T+EFV or NVP	9 (4.8)	53 (7.5)	62 (69)	1.13 (0.43-3.00)	0.990
ABC+DOI+LPV/r	4 (2.1)	15 (2.1)	19 (2.1)	1.78 (0.49-6.47)	0.597
Pill burden					
	169 (89.9)	650 (91.5)	819 (91.2)	1.00	
≥5	19 (10.1)	60 (8.5)	79 (8.8)	1.21 (0.70-209)	0,570
Frequency of ART					
Once/day	5 (2.7)	45 (6.3)	50 (5.6)	1.00	
[wice/day	179 (95.2)	650 (91.5)	829 (92.3)	2.47 (0.96-6,33)	0.075

Table 2. Cont.

	Non-Adherent (n = 188)	Adherent (n=710)	Total (n = 898)	Crude OR (95% CI)	p value
	n (%)	n (%)	n (%)		
Thrice/day	4 (2.1)	15 (2.1)	19 (2.1)	2.40 (0.56-10.11)	0.247
Refill Schedule					
Every 2 or 3 months	43 (22.9)	204 (28.7)	247 (27.5)	1.00	
Every month	145 (77.1)	506 (71.3)	651 (72.5)	1.35 (0.93-1.98)	0.132
Duration of HIV infection					
<48 months	76 (40.4)	342 (48.2)	418 (46.5)	1.00	
≥48 months	112 (59.6)	368 (51.8)	480 (53.5)	1.37 (0.98-1.89)	0.070
Median (IQR)	48 (24-72)	48 (24-72)	48 (24-72)		
Duration of ART					
<48 months	94 (50.0)	421 (59.3)	515 (57.3)	1.00	
≥48 months	94 (50.0)	289 (40.7)	383 (42.7)	1.45 (1.05-2.01)	0.027
Median (IQR)	48.5(24-72)	40 (18-62)	41 (18-64)		
Perceived quality of care					
Not satisfied (0-2)	10 (5.3)	23 (3.2)	33 (3.7)	1.00	
Moderately satisfied (3-4)	22 (11.7)	86 (12.1)	108 (12.0)	0.58 (0.24-1.41)	0.340
Highly satisfied (5–6)	156 (83.0)	601 (84.6)	757 (84.3)	0.59 (0.27-1.28)	0.263
Treatment sites					
HPGRK	13 (6.9)	86 (12.1)	99 (11.0)	1.00	
ACS/AMO CONGO	94 (50.0)	208 (29.3)	302 (33.6)	2.99 (1.58-5.62)	0.001
MONKOLE	35 (18.6)	165 (23.2)	200 (22.3)	1.40 (0.70-2.79)	0.423
ARMEE DU SALUT	46 (24.5)	251 (35.4)	297 (33.1)	1.21 (0.62-2.35)	0.684
Travel time (in hours)†					
<1	103 (54.8)	398 (56.1)	501 (55.8)	1.00	
1-<2	66 (35.1)	251 (35.3)	317 (35.3)	1.01 (0.71-1.43)	0.999
≥2	19 (10.1)	61 (8.6)	80 (8.9)	1.20 (0.68-2.10)	0.615

\*Defined as alcohol consumption at least once a month;

†travel time from home to health facility expressed in hour(s); ART, antiretroviral therapy; OR, odds ratio; CI, confidence interval; 3TC=Lamivudine; TDF=Tenofovir; EFV=Efavirenz; NVP=Nevirapine; AZT=Zidovudine; LPV/r=Lopinavir/Ritonavir, D4T=Stavudine, ABC=Abacavir; DDI=Didanosine; IQR, inter-quartile range; HPGRK, Hopital Provincial General de Référence de Kinshasa; ACS/AMO Congo, Actions Communautaires Sida/Avenir meilleur pour les orphelins. doi:10.1371/journal.pone.0085327.t002

compare participants' forgetfulness between the non-adherent and adherent groups as it was asked only as a branch question to the participants who reported ART non-adherence, forgetfulness was cited as one of the most frequent reasons for skipping ART doses in this study. In a qualitative study in Uganda, participants reported forgetting their daily ART doses as a result of spending most of their time working to obtain food [24], suggesting that food insecure individuals may particularly be prone to forgetfulness. In future studies, this hypothesis should be tested by introducing the question on general forgetfulness on daily ART doses for both groups as well as the question on food insecurity and creating an interaction term between the two.

Whatever the exact mechanism, however, the implications of the results of this study could be far-reaching, considering the vast number of people suffering from food insecurity and the estimated 6 million of people living with HIV on ART treatment in SSA [1,31], and the fact that food insecurity disproportionately affects HIV-infected individuals [51–54]. In our study, over half (57%) of our participants were food insecure and alarmingly, most of them were severely insecure, a rate much higher than that previously reported in the general population in Kinshasa City [32]. In view

of the threat of food insecurity to the long-term success of HIV/AIDS treatment programs in SSA, which hosts the largest number of people on and in need of ART, with a very restricted access to second or third line therapy [1], it is crucial to integrate food security strategies into HIV treatment programs [55,56]. Though, clinic-based short-term intervention studies in SSA have shown promising results for improving patient adherence to ART using food assistance [49,50]; in order to be sustainable over time, such intervention should be built on a clear understanding of context-specific determinants of food insecurity, and packaged into a holistic approach that takes into account local socio-cultural and structural correlates of ART adherence.

Besides food insecurity our study identified a number of factors associated with ART non-adherence. Consistent with prior studies [57,58], participants who perceived that ART was harmful had higher odds of non-adherence. Most of them believed so because of ART-related side effects, or the fact that ART was a life-long medication. We observed an association between alcohol use and non-adherence to ART. Participants who reported consuming alcohol at least once a month had a 50% increased odds of being non-adherent to ART. This is consistent with previous studies

Table 3. Perceptions about HIV/AIDS and ART.

	Non-Adherent (n = 188)	Adherent (n = 710)	Total (n = 898)	Crude OR (95% CI)	P value
	n (%)	n (%)	n (%)		
Sociocultura l/Religious beliefs					
God/prayer can cure HIV					
Agree	143 (76.1)	427 (60.1)	570 (63.5)	2.10 (1.45-3.04)	0.000
Else	45 (23.9)	283 (39.1)	328 (36.5)	1.00	
Traditional healers/medicine can cure HIV					
Agree	9 (4.8)	35 (4.9)	44 (4.9)	0.97 (0.45-2.05)	1.000
Else	179 (95.2)	675 (95.1)	854 (95.1)	1.00	
ART works better when combined with prayers					
Agree	126 (67.0)	383 (53.9)	509 (56.7)	1.73 (1.23-2.43)	0.002
Else	62 (33.0)	327 (46.1)	389 (43.3)	1.00	
Perceptions about ART and food					
ART is not necessary without food					
Agree	37 (19.7)	154 (21.7)	191 (21.3)	0.88 (0.59-1.32)	0.618
Else	151 (80.3)	556 (78.3)	707 (78.7)	1.00	
ART is not effective without food					
Agree	20 (10.6)	77 (10.8)	97 (10.8)	0.97 (0.58-1.64)	1.000
Else	168 (89.4)	633 (89.2)	801 (89.2)	1.00	
ART can be harmful without food					
Agree	58 (30.9)	220 (31.0)	278 (31.0)	0.99 (0.79-1.40)	1.000
Else	130 (69.1)	490 (69.0)	620 (69.0)	1.00	
Perceptions about ART adherence					
Short treatment interruption is not harmful to a long-term ART user					
Agree	10 (5.3)	71 (10.0)	81 (9.0)	0.50 (0.25-1.00)	0.064
Else	178 (94.7)	639 (90.0)	817 (91.0)	1.00	
Skipping few ART doses is not harmful to a long-term ART user					
Agree	10 (5.3)	48 (6.8)	58 (6.5)	0.77 (0.38-1.56)	0.584
Else	178 (94.7)	662 (93.2)	840 (93.5)	1.00	
Skipping ART doses can worsen the disease					
Agree	135 (71.8)	434 (61.1)	569 (63.4)	0.69 (0.46-1.03)	0.087
Else	53 (28.2)	276 (38.9)	329 (36.6)	1.00	
ART should be taken life-long					
Agree	172 (91.5)	651 (91.7)	823 (91.6)	1.00 (0.45-2.23)	1.000
Else	16 (8.5)	59 (8.3)	75 (8.4)	1.00	
Perceptions about ART					
Perceived effectiveness of ART					
Yes	176 (93.6)	630 (88.7)	806 (89.8)	1.86 (0.99-3.49)	0.067
No	12 (6.4)	80 (11.3)	92 (10.2)	1.00	
Perceived ART harmfulness					
Yes	29 (15.4)	70 (9.9)	99 (11.0)	1.68 (1.10-2.55)	0.042
No	159 (84.6)	640 (90.1)	799 (89.0)	1.00	

ART, antiretroviral therapy; OR, odds ratio; Cl, confidence interval. doi:10.1371/journal.pone.0085327.t003

showing that alcohol use negatively affected patient adherence even for moderate levels of consumption [59,60]. Our findings also indicated that participants who were on ART for more than 4 years were more likely to be non-adherent compared to those who

were placed on ART since less than 4 years. Although this was only significant in bivariate analysis, it still supports previous studies showing that adherence decreases over time [61,62]. Contrary to previous studies [63-65], we found that participants

Table 4. Reasons for missing ART doses during the previous seven days.

Reason	Frequency (n=91)	%
Forgetfulness	36	39.5
Unable to pay for transport/ medical consultation	17	18.6
Ran out of pills	13	14.2
Lack of food	11	12
Travel	7	7.6
Pill fatigue	3	3.2
Alcohol	2	2.1
Away from home	2	2.1
Side effects	1	1.1
Felt tired	1	1.1
Felt depressed	1	1.1
Fell asleep	1	1.1

ART, antiretroviral therapy; Multiple responses are possible. doi:10.1371/journal.pone.0085327.t004

with psychological distress (depression, anxiety) had better adherence compared to those who did not have psychological distress. This uncommon association of psychological distress with better adherence merits further investigation: it is possible that efforts to sustaining ART adherence may over the long-term be source of psychological distress among some patients in the context of DRC, as a result of economic demands and/or sociocultural constraints around antiretroviral medication. Furthermore, a confounding personality trait associated with both psychological

distress and ART non-adherence may also explain the observed association. Lastly, it may also be due to the nature of the K-6 scale, which was only validated in a general population in developed settings [37,66,67] but never tested among poor individuals with HIV in developing countries.

This study has both limitations and strengths. First we cannot assume causality of the statistically significant associations with ART adherence in this study given its cross-sectional design. It is possible that unknown or unmeasured factors could have confounded the estimates of the observed associations in our results. Second, results could be biased by socially desirable answers especially in reporting of missed medication pills in the self-reported assessment of ART adherence since the interviews were conducted by health care workers. In order to minimize this potential bias, interviewers were provided extensive training to process the survey questionnaire in a non-judgmental manner and we used a composite measure coupling both subjective (selfreported adherence) and objective (pharmacy refill adherence) measures to assess the overall adherence. On the other hand the strengths of this study include that it is rooted in the results of our qualitative study on patients on ART treatment, retreatment and lost to follow up [23]. In addition, this study derives its data from a large sample of participants selected from geographically diversified recruitment sites, including both public and private health facilities in Kinshasa, DRC. The results of this study therefore may to large extent represent the situation of patients on ART treatment in Kinshasa. However, caution is warranted in generalizing the findings of this study to a broader population. Educational attainment of our sample was higher than the general population of the DRC. Although this could reflect the general trend of HIV prevalence being higher in wealthier socio-economic

Table 5. Multivariate analysis of factors associated with non-adherence to ART.

	Adjusted OR	95% CI	P value
Food insecurity yes (vs no)	1.99	1,36-2,90	0.000
Alcohol intake yes (vs no)	1.55	1.02-2.34	0.037
Internalized stigma score:3–6 (vs score:0–2)	1.11	0.76-1.61	0.571
Social support from family yes (vs no)	1.26	0.90-1.78	0.174
Psychological distress yes (vs no)	0.34	0.12-0.90	0.030
Duration of ART ≥48 months (vs <48 months)	1.27	0.90-1.80	0.170
Perceived ART harmfulness yes (vs no)	2.06	1.30-3.27	0.002
Perceived effectiveness of ART yes (vs no)	1.19	0.16-8.93	0.859
Short treatment interruption is not harmful to a long-term ART user Agree (vs else)	0.55	0.27-1.14	0.110
Skipping ART doses can worsen the disease Agree (vs else)	0.58	0.38-0.88	0.012
God/prayer can cure HIV/AIDS Agree (vs else)	1.48	0.92-2.37	0,098
ART works better when combined with prayer Agree (vs else)	1.01	0.64-1.59	0.952
HIV-infected person(s) in the household Yes (vs no)	0.72	0.45-1.15	0.173
Treatment sites			
HPGRK	1.00		
ACS/AMO CONGO	1.87	0.26-13.34	0.531
MONKOLE	0.98	0.13-7.07	0.988
ARMEE DU SALUT	0.77	0.10-5.47	0.798

ART, antiretroviral therapy; OR, odds ratio; CI, confidence interval; HPGRK, Hopital Provincial General de Référence de Kinshasa; ACS/AMO CONGO, Actions Communautaires Sida/Avenir Meilleur pour les Orphelins. doi:10.1371/journal.pone.0085327.t005 groups [68], it may also be due to the fact that Kinshasa is the country's capital and holds a more educated population.

In summary, we found that food insecurity is a significant risk factor for non-adherence to ART, and is highly prevalent among HIV-infected individuals in Kinshasa, DRC. There is urgent need of integrating effective food security strategies into HIV treatment and care programs to ensure patient adherence to ART and ultimately long-term success of HIV treatment in SSA.

#### Supporting Information

Table S1 Frequency of nonresponse: Perceptions about HIV/AIDS and ART. (DOC)

Table S2 Participants' food security status based on the HFIAS. (DOC)

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Table S3 Adherence status based on self-report, pharmacy refill, and combined assessment of adherence. (DOC)

Text S1 Supplemental information of variables. (DOC)

#### **Author Contributions**

Conceived and designed the experiments: PMM MK MOK EW PKK. Performed the experiments: PMM MKN SMM. Analyzed the data: PMM MK MOK EW PKK SPS TT BWL CE. Contributed reagents/materials/analysis tools: PMM MKN SMM. Wrote the paper: PMM MK MOK EW PKK PP SPS TT MKN SMM. Enrolled patients: PMM MKN SMM. Assisted in the interpretation of data: EW PKK SPS TT BWL CE PP MK MOK. Agreed with the manuscript results and conclusion: PMM EW PKK MKN SMM SPS TT BWL CE PP MOK MK.

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