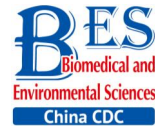# Letter to the Editor

Synthetic Characteristics Associated with HIV Diagnosis through Voluntary HIV Testing among HIV-positive People with Non-marital and Non-commercial Heterosexual Transmission in China[*]

YU Qiu Yan[1], YU Shi Cheng[2], XU Peng[1], YANG Juan[1], LI Xiao Yu[3,#], and LU Fan[1,#]

The Joint United Nations program on HIV/AIDS reported that 53% of new infections globally in 2017 were beyond key populations and their sexual partners[1]. In this report, although only 16% in Asia and the Pacific were people living with HIV (PLHIV) who did not report any HIV-risk behaviors (mainly including injective drug use, men who have sex with men, sexual workers, and their clients), increasing diagnosed cases who reported their own transmission as non-marital and non-commercial heterosexual contact (non-M&C sex, defined as those heterosexuals who have unpaid sex with any other sexual partners whom they have never married) in China have indicated that the HIV epidemic is spreading to the general population by the bridge of key populations[2]. Efforts in large-scale HIV testing among people having condomless non-M&C sex might work toward the goal of the 2016 United Nations Political Declaration.

Actively seeking HIV testing plays a crucial role in timely HIV diagnosis and treatments. A previous study revealed that provider-initiated HIV testing and counseling (PITC; health care providers that offer HIV testing to patients seeking care in public, private, and non-government organization-based health facilities) is significantly associated with delayed HIV diagnosis compared with voluntary HIV counseling and testing (VCT)[3]. Among young males, intention to marry, high economic income, high education, high-level HIV/AIDS knowledge, or fear of stigma are independently associated with willingness toward VCT among Chinese key populations and African residents, and few studies have attempted to learn the factors of VCT among non-key populations or heterosexuals engaged in non-M&C sex[4,5]. If biological, interpersonal, and structural factors associated with VCT can be collected comprehensively from one study population, then feasible and reasonable targeted interventions to promote the expansion of HIV testing can be developed and implemented into practices. However, in China, a substantial number of sexually active people still have never heard of HIV or condoms, and some were exposed to HIV during their premarital or extramarital sexual lives. Moreover, we might not have any opportunity to collect related HIV-risk information from sexually active populations except demographic characteristics. Thus, one of the challenges in the field is to fully use the limited information to guide the scale up of HIV testing so that more undetected PLHIV cases can be discovered.

Notably, abundant demographic data in the National Case Reporting System (NRS) must be explored and analyzed for interpretive and meaningful information to expand HIV testing, especially to identify those specific populations who have less access to related services of expanded HIV testing. For traditional cluster analysis, only continuous variables were allowed to perform cluster classification, not categorical variables. Latent class analysis (LCA), as one of many unsupervised machine learning methods, is used to help categorize the population into specific homogeneous subgroups from limited categorical variables to provide classified guidance to HIV control and prevention. Using the available data from NRS, factors associated with HIV diagnosis through the service of VCT among PLHIV who self-reported HIV during non-M&C sex can be learned, and the results might provide an understanding of the barriers and facilitators to seek

VCT for those undiscovered non-key populations who have suffered from HIV. The variables derived from NRS might be related to seeking HIV testing actively, including age, gender, education, marital status, vocation, ethnicity, migration status, number of non-marital sexual partners, sexually transmitted disease (STD) history, and history of HIV testing.

We assumed that socio-demographic characteristics represented their social positions, which might be associated with their action to seek HIV testing actively. For this analysis, we identified seven personal characteristics hypothesized to be related to VCT behavior before HIV diagnosis: age, gender, education, marital status, vocation, ethnicity, and migration status. This study aimed to use these seven variables available from the NRS to identify the common clusters of synthetic characteristics *via* LCA and analyze which specific subgroup was more linked to HIV diagnosis through VCT. Understanding of the specific synthetic features related to VCT may improve the development of targeted interventions to expand HIV testing for those individuals who might contract HIV during non-M&C sex but have yet to be discovered.

This study is part of the preliminary stage of the China HIV/AIDS survey project, a national cross-sectional research being performed in five city sites that were chosen by a two-stage cluster random sampling approach. Data were derived from case report forms of CRS between January 1, 2015 and December 31, 2017. At the first sampling stage, five provincial-level regions were selected from 15 regions (provinces, autonomous regions, or municipalities) where more than 1,000 newly heterosexual HIV infections were reported in central-southern China in 2017. Two provincial-level regions were randomly selected from six regions where more than 5,000 new HIV infections were reported; three were randomly selected from nine regions, which had newly reported cases less than 5,000. At the second stage, one city was selected randomly in each region. All five cities, namely, Fuyang in Anhui Province, Yueyang in Hunan Province, Yichun in Jiangxi Province, Qiandongnan Autonomous Prefecture in Guizhou Province, and Jiangmen in Guangdong Province, were selected as survey sites of this study. All HIV infections diagnosed with HIV in each site were reanalyzed by LCA. The inclusion criteria for the participants were as follows: 1) the HIV diagnosed cases, identified as HIV infection by Western blot confirmatory testing, were reported by local survey sites; 2) self-reported

sexual transmission through non-M&C sex; and 3) aged more than 15 years. The inclusion process is shown in Supplementary Figure S1 (available in www. besjournal.com). The Institutional Review Board at the National Center for STD/HIV Control and Prevention approved all study procedures (X180315508).

Participants voluntarily and actively sought HIV testing at VCT clinics, and they were diagnosed with HIV as PLHIV. For those who received HIV testing after PITC, we defined them as participants who were diagnosed with HIV through PITC rather than VCT. Gender, birth date, marital status, literary level, vocation, migration status, and ethnicity were recorded in disease report cards for each enrolled and diagnosed case. Age was calculated by diagnosed year minus birth year. Vocation was divided into two categories with one as farming and the other as non-farming vocation. The number of non-marital sexual partners, history of HIV testing, and STD history were recorded in the disease report cards. For enrolled cases with missing data for the numbers of non-marital sexual partners, local health care workers would contact and ask them to provide the answer. For cases with missing values for history of HIV testing and STD history, after discussing with local CDC, we assumed that they never received HIV testing and never contracted STD before the time of their HIV diagnosis.

LCA was performed using LatentGOLD Version 4.5 to create distinct subgroups based on available variables. After adjusting for research sites, the difference was assumed significant across participants in the five sites. Multi-sample LCA models with one to seven classes were considered and compared to produce the best-fitting model in accordance with the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), G^2 statistics, and entropy R^2. The best-fitting model was identified by minimizing the AIC, BIC, and G^2. When entropy R^2 exceeded 0.8, the minimal classification error of latent class assignment was based on posterior probability. To reach the full maximum likelihood estimate, each model ran with 1,000 random sets of starting values, with 1,000 as the maximum number of iterations for each run. After identifying the optimal LCA model, binary logistic regression was used to determine the factors associated with HIV diagnosis through the service of VCT, with latent classes as covariates. Adjusted odds ratios and confidence intervals were calculated to determine the relationship between HIV diagnosis

through the service of VCT and subgroups derived from latent classes, with stratified level, age, gender, vocation, marital status, education, ethnicity, migration status, STD history, history of HIV testing, and number of non-marital sexual partners as adjusted variables.

Table 1 lists the demographic characteristics among 2,096 selected participants in LCA. Of 2,096 participants, the average age was 50.0 ± 16.0 years; about 58.8% were male; 78.8% were married, widowed, or divorced; 42.0% received education less than six years; about 67.4% were Han; about 60.2% worked as farmers; and about 89.3% were permanent residents. Among 2,096 participants, 21.6% were diagnosed with HIV *via* VCT, and 78.4% were diagnosed with HIV *via* PITC. Of 453 participants who were diagnosed via VCT, the average age was 38.7 ± 14.4 years; about 63.1% were male; about 88.7% were Han; 74.8% were married, widowed, or divorced; 7.8% received education below primary school; about 46% worked as farmers; and about 89.6% were permanent residents.

Table 1. Demographic Characteristics among 2,096 PLHIV Whose Transmission Was Non-marital and Non-commercial Heterosexual Contact in Five Cities of China from 2015 to 2017

Variables	Total (%)	HIV Diagnosis through the Service of VCT (%)
Age (years)		
Mean ± SD	50.0 ± 16.0	38.7 ± 14.4
15-29	370 (17.6)	95 (21.0)
30-44	631 (30.1)	148 (32.7)
45-59	616 (29.4)	132 (29.1)
60-74	396 (18.9)	71 (15.7)
> 74	83 (4.0)	7 (1.5)
Gender[#]		
Female	864 (41.2)	167 (36.9)
Male	1,232 (58.8)	286 (63.1)
Marriage		
Not married	441 (21.0)	114 (25.2)
Married	926 (44.2)	180 (39.7)
Widowed or divorced	725 (34.6)	159 (35.1)
Education		
≤ Primary school	880 (42.0)	164 (7.8)
Junior or high school	1,093 (52.1)	255 (56.3)
> high school	123 (5.9)	34 (7.5)
Ethnicity		
Han	1,413 (67.4)	402 (88.7)
Others	683 (32.6)	51 (11.3)
Vocation		
Farming	1,261 (60.2)	207 (45.7)
Others	825 (39.8)	246 (44.3)
Migration status		
Permanent residents[&]	1,871 (89.3)	406 (89.6)
Migrants	225 (10.7)	47 (10.4)
Number of non-marital sexual partners		
1-2	1,762 (84.1)	387 (85.4)
3 and more	334 (15.9)	66 (14.6)
STD history		
With history	88 (4.2)	7 (1.5)
No history	2,008 (95.8)	446 (98.5)
History of HIV testing		
With history	7 (0.3)	7 (1.5)
No history	2,089 (97.6)	446 (98.5)

Note. [#]Four participants did not report marital status. [&]Permanent residents in five sites.

LCA model estimations suggested that the four-class model best illustrated the data when age was converted as a two-level categorical variable (Table 2). Although values of the AIC and G^2 both declined through one to seven classes with different definitions of age, the BIC was lowest for the four-class model when age was converted as the dichotomous variable. Among models with one class to seven classes when age was converted into the dichotomous variable, the four- and five-class models had relatively better latent class separation with the entropy R^2 value of more than 0.80. Considering the entropy R^2 and BIC among all models, the four-class model with age as the dichotomous variable was the optimal model.

On the basis of item response probability, latent class labels were (1) the educated, non-farming, and Han youth (39.2%); (2) young male farmers (20.9%); (3) young female farmers (20.7%), and (4) old farmers (19.2%) (Table 3). In class one, about three-fifths of participants were diagnosed *via* VCT (30.56%), more than 90% were aged 59 years or less (92.8%), more than 90% received education above primary school (90.9%), over four-fifths of participants were non-farmers (84.1%), 84.5% of participants were the Han, and about one-fifth of participants were migrants (20.6%). In class two,

about 15% of participants were diagnosed *via* VCT (14.7%); most of the total were males (97.7%), farmers (99.4%), and permanent residents (99.3%); over 90% were aged 59 years or less (90.7%); 57.7% received education above primary school; 73.7% experienced marriage; and nearly half were the minorities (50.0%). In class three, about one-fifth of participants were diagnosed *via* VCT (19.2%); most of the total were female (98.1%) and experienced marriage (97.0%); nearly half were the minorities (43.3%); about four-fifths of participants were farmers (21.3%); and about 10% of participants were migrants. In class four, one-sixth of participants were diagnosed *via* VCT (15.9%); most of the total were more than 60 years old (94.3%), permanent residents (98.2%), and experienced marriage (97.9%); about three-fifths of participants were male; nearly 10% received education above primary school (10.2%); five-eighths of participants were of Han ethnicity (62.5%); and 87.7% of participants were farmers.

The first group comprised participants from the four cities of Yueyang, Jiangmen, Qiandongnan, and Yichun. The second and fourth groups were from Yueyang, Fuyang, Qiandongnan, and Yichun. Social context is an important recognized influence to increase universal prevention awareness of HIV[6].

Table 2. Test of Model Fit for One Through Seven Classes of 2,096 Participants Across Five Cities of China

Number of Latent Classes	Degree of Freedom	AIC	BIC	G^2	Entropy R^2
Models with age assigned as two-level categorical variable (1 = 15-59; 2 > 59)					
1	947	19283.757	19328.940	4231.402	1.000
2	938	19052.470	19148.480	3073.804	0.721
3	929	18138.768	18285.612	3050.412	0.812
4	920	18001.464	18172.136	2895.108	0.854
5	911	17938.071	18186.573	2784.313	0.725
6	902	17926.669	18226.009	2753.963	0.681
7	893	17914.318	18264.482	2731.664	0.675
Models with age assigned as three-level categorical variable (1 = 15-29; 2 = 30-59; 3 > 59)					
1	2,086	21820.927	21877.405	5343.979	1.000
2	2,075	20656.865	20775.468	4157.917	0.745
3	2,064	20314.268	20494.997	3793.321	0.783
4	2,053	20138.040	20380.895	3595.093	0.757
5	2,042	19988.670	20293.650	3423.722	0.744
6	2,031	19946.583	20313.690	3359.637	0.774
7	2,020	19913.673	20342.905	3304.726	0.828

Note. AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion. Included variables: Gender (1 = male, 2 = female); education (1 = primary school and less, 2 = junior school and more); Marital status (1 = unmarried, 2 = married, 3 = divorced or widowed); Ethnicity (1 = Han, 2 = others); Vocation (1 = farmers, 2 = others); Residency (1 = permanent residents, 2 = migrants).

The results of this study revealed different distributions in five cities for each identified subgroup. The numbers of educated non-farming youth after LCA estimations were few from Fuyang City, whereas the participants in Jiangmen City hardly included two subgroups of old farmers and young male farmers. To control the HIV epidemic among the population experiencing non-M&C sex, resource assignment of HIV-related health services should consider the classified principle to discover more people who have contracted HIV but have not been detected.

In the binary logistic regression model, class memberships were linked to HIV diagnosis *via* VCT among PLHIV whose transmission was non-M&C sex. Controlling for gender, education, vocation, marriage, residency (permanent residents versus migrants), ethnicity, and history of HIV testing, compared with class four, participants in class one were 2.37 times more likely to be diagnosed with HIV through the service of VCT (*OR*: 2.37, 95% *CI*: 1.29-4.36). However, one routine HIV testing program discovered that young and unmarried PLHIV have a high rate of no prior HIV testing[7]. Previous research also demonstrated that young sexually active individuals perceive more prevention awareness against HIV but are less likely to seek for VCT[8]. For educated non-farming youth, the risk

Table 3. Item Response Probability of Latent Class Analysis for the Four-class Model of Included Participants in Five Cities of China (*N* = 2,096)

Variables	Latent Classes				χ^2 Value
	Class one	Class two	Class three	Class four	
Sample size	0.392	0.209	0.207	0.192	
Age (years)					1446.869[*]
15-59	0.928	0.907	0.999	0.057	
> 59	0.072	0.093	0.001	0.943	
Gender					887.255[*]
Male	0.685	0.977	0.019	0.580	
Female	0.315	0.023	0.981	0.420	
Education					796.621[*]
≤ Primary school	0.091	0.423	0.597	0.898	
> Primary school	0.909	0.577	0.403	0.102	
Marriage					418.951[*]
Unmarried	0.374	0.263	0.030	0.021	
Married	0.307	0.504	0.672	0.403	
Widowed or divorced	0.319	0.233	0.298	0.576	
Ethnicity					211.360[*]
Han	0.849	0.500	0.567	0.625	
Others	0.151	0.500	0.433	0.375	
Vocation					1139.047[*]
Farming	0.159	0.994	0.787	0.877	
Others	0.841	0.006	0.213	0.123	
Migration status					164.040[*]
Permanent residents	0.794	0.993	0.897	0.982	
Migrants	0.206	0.007	0.103	0.018	
Site					494.252[*]
Yueyang	0.366	0.126	0.108	0.086	
Fuyang	0.047	0.128	0.168	0.166	
Jiangmen	0.248	0.021	0.128	0.047	
Qiandongnan	0.226	0.605	0.494	0.509	
Yichun	0.113	0.120	0.102	0.192	

Note. [*]*P* < 0.05.

of non-M&C sex linked to HIV exposure should be emphasized. For old farmers, being a life-time farmer and low levels of education might impede the opportunity to learn, receive, and seek HIV prevention knowledge, which are associated with a low probability of seeking VCT. Given the low levels of education and being a permanent resident in remote areas, HIV/AIDS stigma and refusal of HIV testing have become a critical barrier among rural populations to promote active actions to voluntary HIV testing. Previous studies also demonstrated that residents in rural China have significantly lower access to sexual health service compared with those in urban areas[9,10].

The included participants were all HIV-positive who were not representative of heterosexuals engaged in non-M&C sex across central-southern China. The heterosexual participants in this study were not those who self-reported experiencing transactional paid sex with sexual workers, those who had HIV-positive partners, or those who ever self-reported exposed to HIV risk.

The findings from the present study illustrated that the educated, non-farming, and Han youth accounted for more than two-fifths of non-M&C sex adults with HIV. The demographic profiles among non-M&C sex PLHIV support the targeted interventions to deliver different acceptable and accessible messages for different subgroups. A specific program is needed to mobilize rural residents to respond to HIV-risk sexual behaviors and inspire them to seek voluntary HIV testing when facing HIV exposure.

#Correspondence should be addressed to LU Fan, PhD, Tel: 86-10-58900958, Fax: 86-10-58900957, E-mail: fanlv@chinaaids.cn; LI Xiao Yu, Tel/Fax: 86-10-58516688, E-mail: lxyjst@163.com

REFERENCES

1. The Joint United Nations programme on HIV/AIDS. UNAIDS data 2018. 2018. http://www.unaids.org/en/resources/documents/2018/unaids-data-2018. [2018-01-9]

2. Wang LY, Ding ZW, Qin QQ, et al. Characteristics of HIV transmission through heterosexual contact in China, 2008-2014. Chin J Epidemiol, 2015; 36, 1332-6. (In Chinese)

3. Jin L, Cheng XL, Qin YZ, et al. Analysis of the influential factors of late diagnosis among newly identified HIV/AIDS cases in Anhui Province, 2011 -2015. Chin J Prevent Med, 2018; 52, 415-8. (In Chinese)

4. Jiang J, Pan XH, Yang JZ, et al. Willingness for HIV test and associated factors among 535 college students who had sex in Zhejiang province. Chin J Epidemiol, 2016; 37, 1356. (In Chinese)

5. Shalinee B, Anuradha J, Koroma MA, et al. Facilitators and barriers related to voluntary counseling and testing for HIV among young adults in Bo, Sierra Leone. J Community Health, 2014; 39, 514-20.

6. Hargreaves JR, Delany-Moretlwe S, Hallett TB, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. Lancet HIV, 2016; 3, e318-e22.

7. Sisay S, Erku W, Medhin G, et al. Perception of High School Students on risk for acquiring HIV and utilization of Voluntary Counseling and Testing (VCT) service for HIV in Debre-berhan Town, Ethiopia: a quantitative cross-sectional study. BMC Research Notes, 2014; 7, 518.

8. Conserve D, Sevilla L, Mbwambo J, et al. Determinants of previous HIV testing and knowledge of partner's HIV status among men attending a voluntary counseling and testing clinic in Dar es Salaam, Tanzania. Am J Mens Health, 2013; 7, 450-60.

9. Lin C, Li L, Ji G, et al. Emotional social support and access to care among older people living with HIV in rural China. Int J Geriatr Psychiatry, 2015; 38, 1041-7.

10. Zhang X, Miège P, Zhang Y. Decentralization of the provision of health services to people living with HIV/AIDS in rural China: the case of three counties. Health Res Policy Syst, 2011; 9, 9.
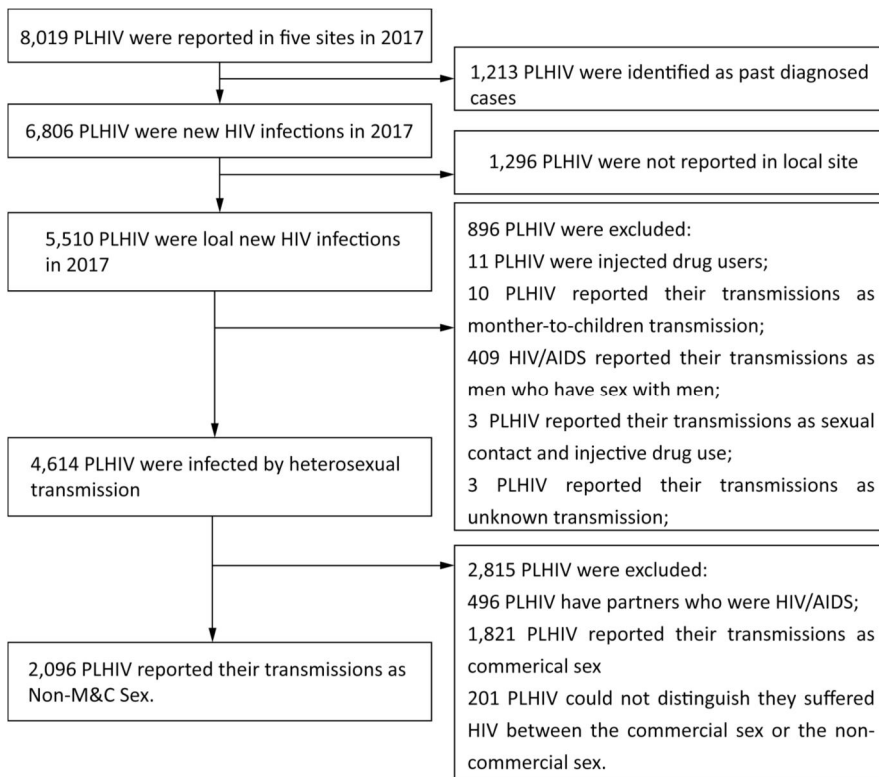
Supplementary Figure S1. Participants' inclusion.