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# Effects of Case Management on Risky Sexual Behaviors and Syphilis Among HIV-Infected Men Who Have Sex With Men in China: A Randomized Controlled Study

Nianhua Xie, MPH,\* Xuejiao Hu, MPH,\* Han Yan, MPH,\* Lianguo Ruan, PhD,† Cong Liu, MPH,\* Rong Hu, MPH,\* Hongfei Ma, MPH,\* Yanhe Luo, BD,† Li Liu, BD,† and Xia Wang, MPH\*

**Background:** The prevalence of syphilis is very high in human immunodeficiency virus (HIV)-positive men who have sex with men (MSM), and effective interventions are needed to educate HIV-positive individuals about behavioral and biological risk factors. Therefore, we developed a standard case management process and conducted a randomized controlled study to investigate the impact on risky sexual behaviors and syphilis in HIV-positive MSM. **Methods:** Men who have sex with men ( $n = 220$ ) were enrolled and randomized to the case management intervention group and the control group between May 2016 and January 2017. The control group received routine HIV-related care. In addition to routine HIV-related care, those in the intervention group regularly received extended services from a well-trained case manager. Epidemiological information was collected during the baseline face-to-face interviews by a trained investigator. Serological tests for syphilis and assessments of risky sexual behaviors were performed at baseline and 6 and 12 months after the initiation of treatment.

**Results:** The syphilis incidence rates in the intervention and control groups were 11.3 per 100 person-years and 20.6 per 100 person-years, respectively. The multivariable-adjusted hazard ratio (95% confidence interval) for syphilis in case management group was 0.34 (0.14–0.87). The percentages of participants who resumed risky sexual behaviors in both groups were significantly reduced ( $P < 0.05$ ) but did not significantly differ between the 2 groups.

**Conclusions:** A case management intervention reduced the incidence of syphilis in HIV-positive MSM. We should further increase the content of case management on the basis of providing routine HIV-related care to those people.

In the last few years, the prevalence of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) among men who have sex with men (MSM) in China has rapidly increased.<sup>1</sup> The reported prevalence of HIV in MSM ranges from an estimated 3.5% (northwest China) to 10.7% (southwest China).<sup>2</sup> Concurrent with the increasing prevalence of HIV/AIDS, the incidence of syphilis has also risen in MSM populations.<sup>3</sup> The positive association between syphilis and HIV infection among MSM can be explained on the same basis of biological mechanisms and risky behaviors.<sup>4</sup> Syphilis may increase the immune activation of host cells and the secretion of cytokines, thus enhancing HIV replication and decreasing CD4 cell counts.<sup>5</sup> Although antiretroviral therapy (ART) can restore immune function and reduce the HIV transmission rate, it cannot reduce the unsafe sexual behaviors or incidence and recurrence of syphilis in HIV-positive patients.<sup>6</sup> Therefore, interventions targeting psychology and behavior are needed to educate HIV-positive individuals about behavioral and biological risks factors for sexually transmitted diseases (STDs) and strategies for modifying those risk factors.<sup>7</sup>

HIV case management is a collaborative process of assessment, planning, facilitation, and advocacy for options and services to meet the social needs of patients of HIV/AIDS.<sup>8</sup> Previous studies showed that the percentage of HIV-positive patients reporting behaviors that put them at risk of transmitting the HIV declined from 41.3% to 29.4% after they received prevention case management services.<sup>9</sup> However, existing studies have mostly been conducted in countries other than China<sup>10,11</sup> and have focused on ART adherence,<sup>12</sup> clinical parameters,<sup>13</sup> and health-related quality of life.<sup>14</sup> Few studies have reported the impact of case management on the behavioral and biological risks factors for contacting syphilis among MSM in China.<sup>15,16</sup> Moreover, the interventional efficiency and effects of case management models differed according to a previous study.<sup>17</sup> Therefore, the influence of case management on high-risk sexual behaviors and the incidence of syphilis in patients with HIV/AIDS needs further investigation.

Wuhan introduced the case management model developed by Taiwan Chengkung University and was equipped with a trained full-time case manager to offer support to HIV-positive patients in 2014.<sup>12</sup> Therefore, we explored the impact of case management on unsafe sexual behaviors and the incidence of syphilis in HIV-positive individuals in Wuhan.

## MATERIALS AND METHODS

### Study Setting and Population

Recruitment of this study was conducted between May 2016 and January 2017 in Wuhan. The participant inclusion criteria were

From the \*Department of HIV/AIDS Prevention and Control, Wuhan Center for Disease Control and Prevention; and †Department of Infectious Diseases, Wuhan Jin Yin-tan Hospital, Wuhan, Hubei, China

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**Ethics:** This study was approved by the ethics committee of Wuhan Center for Disease Control and Prevention.

N.X. and X.H. contributed equally to this work.

**Correspondence:** Xia Wang, MPH, Department of HIV/AIDS Prevention and Control, Wuhan Center for Disease Control and Prevention, No. 288 Machang Rd, Jiangnan District, Wuhan 430024, China. E-mail: wangxia1973@163.com.

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as follows: (1) male, (2) diagnosed with HIV, (3) ART-naive and planning to initiate ART, and (4) self-reported of having been infected with HIV by having had sex with a man. The excluded criteria were as follows: (1) severe neuropsychological impairment or psychosis, (2) current involvement in another behavioral intervention study related to HIV, and (3) refusal to participate in the investigation and follow-up. We calculated the appropriate and minimum sample size according to sample size calculation procedures in randomized trials. Considering 10% of lost to follow-up, the final sample size was 110 in each group (Supplement 1, <http://links.lww.com/OLQ/A710>).

This study was approved by the ethics committee of Wuhan Center for Disease Control and Prevention. Adult participants gave written informed consent before the survey, and minors younger than 18 years provided consent forms signed by their parents or guardians. The study flowchart is shown in Figure 1.

### Randomization and HIV Case Management Intervention

To account for the differences in regional economic conditions, all participants were stratified into urban and suburban groups based on their addresses. Then, the participants were randomized within their subgroups to participate in the intervention or control group. The control group received routine HIV-related care from a designated hospital, including ART guidance and laboratory follow-up tests. Those in the intervention group regularly received additional services from a well-trained case manager via face-to-face interviews. The medical worker who was selected to be the case manager attended 2- to 5-day trainings 3 or 4 times every year from April 2014 to November 2016 and practiced in the designated hospital before participating in our study. The training was conducted by the National Center for AIDS/STD Control and Prevention and included a comprehensive explanation of case management model, such as HIV-positive status notification, social support, and psychological and behavioral interventions. The case manager obtained second-level psychologist qualifications and was engaged in our study full-time.

The case management process was individually tailored to participants' specific life context, stressors, and goals. If a participant met the inclusion criteria and was randomized into the intervention group, the case manager met with the participant in a private environment and informed the participant of his status and offered support, giving them personalized advice with regard to ART and their lifestyle. The case manager performed face-to-face interviews with the patients every 2 weeks for the first month of the intervention and then every month for the next 2 months, followed by every 3 months for the next 9 months. The intervention provided

by the case manager consisted of 3 parts: (1) medical education to promote adherence to ART and address access to health services; (2) risky behavior interventions aimed at avoiding sexual-related and drug-related risky behaviors that increased the risk of HIV transmission or the acquisition of additional STDs, strategies for disclosing their HIV status to potential partners, and provision of a convenient way to offer testing to partners; and (3) mental health services, including social support and psychological counseling aimed at achieving a positive affect and cultivating supportive social relationships. The case manager evaluated the physical and psychological status of the patients during each interview and provided the appropriate services according to their needs. The different services for patients in the intervention and control groups are shown in Table 1.<sup>18</sup>

### Data Collection

Epidemiological data including sociodemographic factors (age, education, marital status, and employment status) and health status were collected during face-to-face interviews by a trained investigator at the baseline examination. Education was classified into junior high school or lower, senior high school, or college or higher. Marital status was classified as single, married, or divorced/widowed. The self-reported STDs, which were diagnosed in the last 1 year before enrollment, were categorized into yes, no, and unknown. The data extracted from the medical records included HIV-related symptoms, the HIV viral load, and the CD4 cell counts. Baseline and 6- and 12-month follow-up examinations were conducted at a designated hospital providing combined antiretroviral therapy (cART) for most people living with HIV (PLWH) in Wuhan.

Nontreponemal antibodies against *Treponema pallidum* were measured by the rapid plasma reagin (RPR) test (Rongsheng-biotech, Shanghai, China), and anti-treponemal-specific antibodies were measured by a chemiluminescent microparticle immunoassay (AR-CHITECT Syphilis TP; Abbott Laboratories, Chicago, IL). Positive RPR test (at any titer) and AR-CHITECT syphilis TP test results confirmed the diagnosis of syphilis (new infection). Patients who had a 4-fold increase in RPR test titers after the treatment of the prior infection were diagnosed as having a reinfection.

To further explore the reasons for the difference in the incidence of syphilis between the intervention group and the control group among HIV-positive MSM, we recorded the risky sexual behaviors, which included multiple anal sex partners or unprotected sexual intercourse engaged in by the members of both groups. The risky sexual behaviors of MSM were collected with the National Sentinel Monitoring Questionnaire.

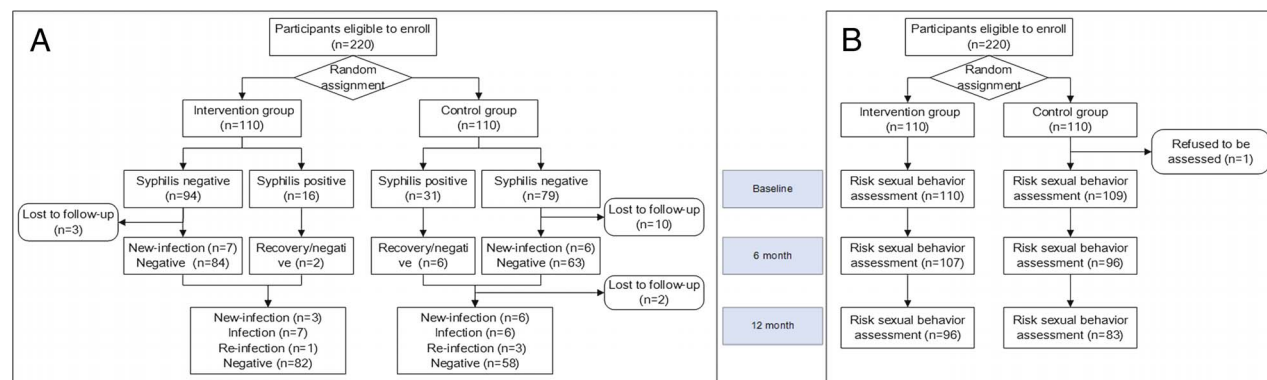


Figure 1. Study design and process. A, Flowchart of syphilis analysis. B, Flowchart of risky sexual behavior analysis.

**TABLE 1.** Case Management Intervention Group Versus Routine Care Control Group

Intervention	Control
Materials used	
1. Easy-to-remember graph explaining how to take the medicine 2. Pill box with electronic alarm clock to remind patients 3. Questionnaire to evaluate risky sexual behaviors. The risky sexual behaviors included sexual activities, the number of regular and casual sexual partners and the use of condoms 4. Real-world examples about risky sexual behaviors (e.g., crime for spreading HIV deliberately) 5. Information leaflet for safe sexual behaviors 6. Condom 7. HIV oral fluid self-test kits	1. Patient information leaflet 2. Questionnaire to evaluate risky sexual behaviors
Procedures (interventions and how they relate to the materials described)	
1. Patients are explained the risks (e.g., viral resistance) of nonadherence and benefits (e.g., healthy immune system) of adherence. Case manager use material 1 and material 2 to improve adherence 2. Patients are given a personal phone number to call in case of difficulties and reported medication spontaneously at any time 3. Collect risky sexual behaviors in the past 6 mo by questionnaire and why and how to reduce risky sexual behaviors by leaflets and cases (materials 3, 4 and 5) 4. Patients are provided condoms if they needed (material 6) 5. Promote partner testing by oral education and provided HIV oral fluid self-test kits (material 7) 6. Inform about the kinds and harm of new drugs, and consult patients with how to identify and avoid using them 7. If patients had anxiety, depression, or sleep disorders, the case manager carries out psychological consultation and referral to a psychiatrist when they need it 8. Inform patients of relevant social support, and provide consultation for patients' family and friends if they need to create a better supportive environment During follow-up: 9. Physician and case manager ask about any adverse effects and deal with them (if severe, change of regimen is considered) 10. Case manager evaluates whether risky sexual behaviors were reduced, if there were any new barriers, and how the patient dealt with them 11. Replicate step 4–8	When the physician and patient agreed that treatment should be initiated, typically the following activities were done: 1. Patients are explained the risks (e.g., viral resistance) of nonadherence and benefits (e.g., healthy immune system) of adherence (material 1) 2. Patients are given a working phone number to call in case of difficulties (e.g., side effects) 3. Collect risky sexual behaviors in the past 6 mo by questionnaire and explained why and how to reduce risky sexual behaviors (material 2) During follow-up visits: 4. Physician ask about any adverse effects and deal with them (if severe, change of regimen is considered) 5. Collect risky sexual behaviors by questionnaire every 6 mo

## Outcomes

Risky sex behaviors included sexual activities, the number of regular and casual sexual partners, and the use of condoms. Condom use was described as always or sometimes.

Syphilis episodes included new infections and reinfections, which were both diagnosed by professional infectious disease specialists. A subject was defined as having a new episode of syphilis if he was syphilis negative at baseline and diagnosed with syphilis at 6 or 12 months of follow-up. Patients with syphilis reinfections were defined in a previous study as those who were diagnosed as having syphilis at baseline, diagnosed as having syphilis recovery at 6 months, and rediagnosed as having syphilis at 12 months.<sup>6</sup>

## Statistical Analysis

Baseline characteristics are presented as percentages for discrete variables, and the  $\chi^2$  test or Fishers exact test was used to evaluate the distribution of categorical data. Generalized estimating equation (GEE) modeling, which included those participants who attended at least 1 follow-up visit ( $n = 219$ ) across the 3 time points (baseline, 6 months, 12 months), was used to calculate odds ratios and 95% confidence intervals (CIs) for HIV transmission behaviors and the case management intervention.<sup>19</sup> Age group, education, marital status, employment status, and self-reported

STDs were entered into the GEE models as fixed variables, whereas time was entered as time-varying variables.

We evaluated the relations between the case management intervention and syphilis in HIV-positive MSM using Cox proportional hazard models. We calculated the unadjusted hazard ratio. The adjusted hazard ratio (aHR) was calculated after controlling for age group, education, marital status, employment status, HIV-related symptoms, HIV viral load, CD4 cell counts, and self-reported STDs.

Analyses were conducted with SAS (version 9.3; SAS Institute Inc.). A 2-sided  $P < 0.05$  was considered statistically significant.

## RESULTS

### Characteristics of Study Population

The baseline characteristics of the study participants are presented in Table 2. There were no statistically significant differences between the participants in the intervention and control groups with regard to sociodemographic factors, HIV-related symptoms, HIV viral load, CD4 cell counts, or self-reported STDs at baseline. A description of the 166 participants involved in the syphilis analysis is shown in Supplement 2, <http://links.lww.com/OLQ/A710>.

TABLE 2. Characteristics of Participants at Baseline

Characteristics	All Cases, n (%)	Intervention, n (%)	Control, n (%)	$\chi^2/t$	P
Age, mean $\pm$ SD, y	31.3 $\pm$ 11.2	31.8 $\pm$ 12.0	30.7 $\pm$ 10.4	0.76	0.449
Age group, y				2.00	0.369
$\leq 24$	71 (32.3)	34 (30.9)	37 (33.6)		
25–49	129 (58.6)	63 (57.3)	66 (60.0)		
$\geq 50$	20 (9.1)	13 (11.8)	7 (6.4)		
Marital status				1.95	0.377
Single	170 (77.3)	82 (74.5)	88 (80.0)		
Married	21 (9.5)	10 (9.1)	11 (10.0)		
Divorced/widowed	29 (13.2)	18 (16.4)	11 (10.0)		
Education				3.19	0.203
College or higher	141 (64.1)	72 (65.5)	69 (62.7)		
Senior high school	55 (25.0)	30 (27.3)	25 (22.7)		
Junior high school or lower	24 (10.9)	8 (7.3)	16 (14.5)		
Employment status				0.16	0.686
Permanent job	105 (47.7)	51 (46.4)	54 (49.1)		
Unemployed/temporary	115 (52.3)	59 (53.6)	56 (50.9)		
HIV-related symptoms* <sup>†</sup>				1.22	0.269
Yes	88 (40.4)	48 (44.0)	40 (36.7)		
No	130 (59.6)	61 (56.0)	69 (63.3)		
CD4 cell counts, cells/ $\mu$ L*				1.61	0.448
$< 200$	51 (23.4)	28 (25.7)	23 (21.1)		
200–350	78 (35.8)	41 (37.6)	37 (33.9)		
$\geq 350$	89 (40.8)	40 (36.7)	49 (45.0)		
HIV viral load (Log <sub>10</sub> ), copies/mL*				0.40	0.525
$< 5$	166 (76.1)	81 (74.3)	85 (78.0)		
$\geq 5$	52 (23.9)	28 (25.7)	24 (22.0)		
Self-reported STDs				5.19	0.075
Yes	16 (7.3)	10 (9.1)	6 (5.5)		
No	173 (78.6)	90 (81.8)	83 (75.5)		
Unknown	31 (14.1)	10 (9.1)	21 (19.1)		
Syphilis at baseline				6.09	0.014
Positive	47 (21.4)	16 (14.5)	31 (28.2)		
Negative	173 (78.6)	94 (85.5)	79 (71.8)		

\*Two participants were missing the information.

<sup>†</sup>HIV-related symptoms refer to continuous or intermittent fever ( $>38^\circ\text{C}$ ), skin damage, thrush, persistent diarrhea, and others.

### Risky Sexual Behaviors of Participants During the 12-Month Follow-Up

As shown in Table 3, the proportion of participants who always used condoms with regular sexual partners (25.6%–87.5%,  $P < 0.001$ ) or casual sexual partners (31.8%–94.4%,  $P < 0.001$ ) significantly increased over the 12 months in the intervention group. The same trend was observed in the percentage of participants who did not have casual sexual partners (23.9%–50.0%,  $P < 0.001$ ). A total of 56.6% and 40.6% of the control group and intervention groups, respectively, had sexual activities in the past 6 months, although the proportions significantly decreased in both groups at follow-up. However, GEE model analyses showed that there were no significant differences in sexual behaviors over time between the intervention and control groups.

### Associations Between Case Management and Syphilis Among PLWH

After an average of 12.3 months (total person-years, 166) of follow-up, we documented 26 incident infection syphilis cases (22 new infections and 4 reinfections). The incidence rates in the intervention and control groups were 11.3 per 100 person-years and 20.6 per 100 person-years, respectively, and Kaplan-Meier survival analysis showed no significant difference between the 2 groups ( $P = 0.098$ , Supplement 4, <http://links.lww.com/OLQ/A710>). The number needed to treat in our study was 11. The unadjusted HR (95% CI) for the intervention group was 0.52

(0.24–1.14), and multivariable-adjusted HR (95% CI) was 0.34 (0.13–0.90). The significant predictors of a new case of syphilis during follow-up among HIV-positive MSM were being divorced or widowed (aHR = 5.86, 95% CI = 1.46–23.62), being unemployed (aHR = 2.99, 95% CI = 1.05–8.47), and having self-reported STDs at baseline (aHR = 6.14, 95% CI = 1.80–20.93; Table 4).

### DISCUSSION

In this study, we found that supporting patients by case management reduced the risk of syphilis in HIV-positive MSM China. We also observed a significant reduction in multiple anal sex partners or unprotected sexual intercourse in both the intervention and control groups over the 1-year follow-up but did not differ by group.

The risk of syphilis in the intervention group in our study was significantly reduced, which indicated the effectiveness of this strategy. Studies on behavioral interventions aimed at preventing concurrent syphilis have rarely been conducted among HIV-positive MSM. Previous studies have shown that interventions educating individuals could enhance their understanding of risky sexual behaviors and increase self-reported condom use, thereby preventing them from contacting syphilis.<sup>20</sup> In addition, case management services could address the need for emotional counseling and other supportive services and improve adherence to highly active antiretroviral therapy.<sup>21</sup> Treatment of HIV infections with highly active antiretroviral therapy



**TABLE 3.** Sexual Behaviors Changes Among Participants in Different Groups During the 12-Month Follow-Up

Behaviors in the Past 6 mo	Intervention			Control			χ <sup>2</sup>	P	OR (95% CI)*	aOR (95% CI)†
	Baseline, n (%)	6 mo, n (%)	12 mo, n (%)	Baseline, n (%)	6 mo, n (%)	12 mo, n (%)				
Sexual activities‡							19.79	<0.001	0.26 (-0.16 to 0.68)	0.21 (-0.28 to 0.69)
No	22 (20.0)	57 (53.3)	57 (59.4)	24 (22.0)	49 (51.0)	36 (43.4)				
Yes	88 (80.0)	50 (46.7)	39 (40.6)	85 (78.0)	47 (49.0)	47 (56.6)				
Regular sexual partners							3.22	0.200	0.97 (0.58 to 1.63)	0.97 (0.39 to 2.43)
No	45 (51.1)	17 (34.0)	14 (35.9)	41 (48.2)	17 (36.2)	16 (34.0)				
Yes§	43 (48.9)	33 (66.0)	25 (64.1)	44 (51.8)	30 (63.8)	31 (66.0)				
Condom use with regular sexual partner¶							30.41	<0.001	1.21 (0.64 to 2.26)	1.05 (0.21 to 5.24)
Always	11 (25.6)	24 (72.7)	21 (87.5)	9 (20.5)	21 (72.4)	24 (77.4)				
Sometimes	32 (74.4)	9 (27.3)	3 (12.5)	35 (79.5)	8 (27.6)	7 (22.6)				
No, casual sexual partner							2.56	<0.281	0.76 (0.46 to 1.23)	0.47 (0.18 to 1.21)
0	21 (23.9)	29 (58.0)	19 (50.0)	33 (38.8)	23 (48.9)	24 (52.2)				
≥1	67 (76.1)	21 (42.0)	19 (50.0)	52 (61.2)	24 (51.1)	22 (47.8)				
Condom use with casual sexual partner							9.01	0.011	1.20 (0.66 to 2.17)	0.23 (0.03 to 1.67)
Always	21 (31.8)	17 (85.0)	17 (94.4)	17 (32.7)	15 (62.5)	14 (63.6)				
Sometimes	45 (68.2)	3 (15.0)	1 (5.6)	35 (67.3)	9 (37.5)	8 (36.4)				

\*Odds ratios (ORs) and 95% confidence intervals (CIs) for HIV transmission behaviors and case management intervention with bivariable GEE model.

†Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) HIV transmission behaviors and case management intervention adjusted by age, marital status, education, employment status, self-reported STDs, time, and group × time.

‡Sexual activities was defined as participants having sex with men during the last 6 months.

§ Participants who had at least one regular sexual partner.

¶ There are one participant in the intervention group who refused to answer this question at 12 months and one participant in the control group who refused to answer this question at 6 months.

|| There is one participant in the intervention group who refused to answer this question at 12 and 6 months, respectively.

TABLE 4. Hazard Ratio (95% CIs) for Case Management Intervention and Syphilis Among PLWH

Characteristics	Unadjusted Hazard Ratio (95% CI)	P	Adjusted Hazards Ratio (95% CI) <sup>†</sup>	P
Group				
Control	Ref		Ref	
Intervention	0.52 (0.24–1.14)	0.104	0.34 (0.14–0.87)	0.023*
Age group, y				
≤24	Ref		Ref	
25–49	1.29 (0.52–3.21)	0.578	0.55 (0.17–1.74)	0.306
≥50	2.80 (0.89–8.82)	0.079	0.75 (0.14–3.93)	0.736
Marital status				
Single	Ref		Ref	
Married	1.38 (0.40–4.71)	0.609	2.46 (0.55–10.95)	0.237
Divorced/Widowed	3.11 (1.22–7.92)	0.017*	5.86 (1.46–23.62)	0.013*
Education				
Junior high school or lower	Ref		Ref	
Senior high school	1.15 (0.47–2.79)	0.763	0.33 (0.09–1.20)	0.092
College or higher	0.126 (0.37–4.31)	0.717	0.32 (0.08–1.31)	0.113
Employment status				
Permanent job	Ref		Ref	
Unemployed/Temporary	2.79 (1.19–6.29)	0.018*	2.99 (1.05–8.47)	0.040*
HIV-related symptoms <sup>‡</sup>				
No	Ref		Ref	
Yes	0.84 (0.38–1.86)	0.668	1.08 (0.46–2.58)	0.855
CD4 cell counts, cells/μL				
<200	Ref		Ref	
200–350	1.17 (0.39–3.51)	0.774	1.41 (0.45–4.48)	0.558
≥350	1.27 (0.45–3.60)	0.658	1.68 (0.54–5.30)	0.373
HIV viral load (Log10), copies/mL				
<5	Ref		Ref	
≥5	1.19 (0.52–2.74)	0.682	1.63 (0.65–4.10)	0.298
Self-reported STDs				
No	Ref		Ref	
Yes	4.69 (1.82–12.06)	0.001*	6.14 (1.80–20.93)	0.004*
Unknown	1.25 (0.42–3.74)	0.695	1.04 (0.32–3.46)	0.944

\* $P < 0.05$ <sup>†</sup>Adjusted age, marital status, education, employment status, BMI, HIV-related symptoms, CD4 cell counts, HIV viral load, and self-reported STDs.<sup>‡</sup>HIV-related symptoms refer to continuous or intermittent fever ( $>38^{\circ}\text{C}$ ), skin damage, thrush, persistent diarrhea, and others.

improves syphilis serological responses in coinfecting patients,<sup>22</sup> which could promote recovery from syphilis and reduce reinfections.

However, participants who received the case management intervention did not differ significantly from those receiving routine care with regard to the reduction in multiple anal sex partners or unprotected sexual intercourse. This finding was similar to the effects on risky sexual behaviors observed in other studies on interventions among HIV-infected MSM.<sup>23</sup> Previous studies have shown that HIV-positive patients decrease the frequency of engaging in risky sexual behaviors by 30% to 55% under regular medical care, especially in the initial years, followed by a 61% increase in unprotected anal sex 4 years after seroconversion.<sup>24</sup> Subjects recruited for our study were newly diagnosed HIV-positive patients and were followed up for 1 year, which was too short a duration to reveal the long-term effect. It is necessary to extend the follow-up period to determine the long-term impact of case management. In addition, studies have shown that syphilis is a more objective biological outcome than self-reported sexual behaviors.<sup>25</sup>

Our study revealed that the observed incidence of syphilis was approximately 11.8%, with 11.3 incident cases per 100 person-years of follow-up, in the case management group and 20.5%, with 20.6 incident cases per 100 person-years of follow-up, in the control group. This prevalence was higher than that previously reported among heterosexual males in Jiangsu, China,<sup>26</sup> males in Singapore,<sup>27</sup> and MSM in Taiwan, China.<sup>16</sup> The high

incidence of asymptomatic syphilis supports the need for routine annual syphilis testing for HIV-positive persons.<sup>28</sup> We also found that being divorced or widowed may be a risk factor for syphilis, as were being unemployed and self-reported STDs at baseline. Participation in syphilis screening is important for these high-risk groups.

To our knowledge, this is the first study to demonstrate that supporting PLWH beyond supplying the ART regimen with standard case management could reduce the incidence of syphilis in MSM in China. Nevertheless, our study has several limitations. First, 19% of the participants did not complete the 3 follow-up visits, which could have affected the analysis of risky behaviors. We calculated the proportion of patients with missing data (Supplement 3, <http://links.lww.com/OLQ/A710>), and the GEE model is capable of addressing random missing repeated-measures data.<sup>29</sup> Meanwhile, the unbalanced loss to follow-up in syphilis analysis between the 2 groups could underestimate the treatment effect. In addition, relying on self-reports of sexual behavior could have led to reporting bias, which may have led to the underestimation of risky sexual behaviors.<sup>30</sup> Hence, we used syphilis as the main outcome to evaluate the effect of case management.

In conclusion, there is a substantial risk to contacting syphilis for HIV-positive MSM who receive regular ART in Wuhan. Case management is an effective and feasible strategy to reduce the risk of syphilis.

## REFERENCES

1. Li Y, Xu J, Reilly KH, et al. Prevalence of HIV and syphilis infection among high school and college student MSM in China: A systematic review and meta-analysis. *PLoS One* 2013; 8:e69137.
2. Dong MJ, Peng B, Liu ZF, et al. The prevalence of HIV among MSM in China: A large-scale systematic analysis. *BMC Infect Dis* 2019; 19:1000.
3. Marcus U, Kollan C, Bremer V, et al. Relation between the HIV and the re-emerging syphilis epidemic among MSM in Germany: An analysis based on anonymous surveillance data. *Sex Transm Infect* 2005; 81:456–467.
4. Sarigul F, Sayan M, Inan D, et al. Current status of HIV/AIDS–syphilis co-infections: A retrospective multicentre study. *Cent Eur J Public Health* 2019; 27:223–228.
5. Rosario P, Francisco JO, Manuela A, et al. Impact of syphilis infection on HIV viral load and CD4 cell counts in HIV-infected patients. *J Acquir Immune Defic Syndr* 2007; 44:356–359.
6. Courjon J, Hubiche T, Dupin N, et al. Clinical aspects of syphilis reinfection in HIV-infected patients. *Dermatology* 2015; 230:302–307.
7. He H, Wang M, Zaller N, et al. Prevalence of syphilis infection and associations with sexual risk behaviours among HIV-positive men who have sex with men in Shanghai, China. *Int J STD AIDS* 2014; 25:410–419.
8. Wilson MG, Husbands W, Makoroka L, et al. Counselling, case management and health promotion for people living with HIV/AIDS: An overview of systematic reviews. *AIDS Behav* 2013; 17:1612–1625.
9. Mari G, Michelle RL, Wayne DF, et al. Reductions in transmission risk behaviors in HIV-positive clients receiving prevention case management services: Findings from a community demonstration project. *AIDS Educ Prev* 2005; 17:40–52.
10. Sorensen JL, Dilley J, London J, et al. Case management for substance abusers with HIV/AIDS: A randomized clinical trial. *Am J Drug Alcohol Abuse* 2003; 29:133–150.
11. Avery A, Ciomica R, Gierlach M, et al. Jail-based case management improves retention in HIV care 12 months post release. *AIDS Behav* 2019; 23:966–972.
12. Ko NY, Lai YY, Liu HY, et al. Impact of the nurse-led case management program with retention in care on mortality among people with HIV-1 infection: A prospective cohort study. *Int J Nurs Stud* 2012; 49:656–663.
13. Lopez JD, Shacham E, Brown T. The impact of clinic policy attendance and the Ryan White HIV/AIDS medical case management program on HIV clinical outcomes: A retrospective longitudinal study. *AIDS Behav* 2020; 24:1161–1169.
14. William EC, Mitch W, Ron DH. Case management and health-related quality of life outcomes in a national sample of persons with HIV/AIDS. *J Natl Med Assoc* 2008; 100:840–847.
15. Dai L, Yu X, Shao Y, et al. Effect of a multi-dimensional case management model on anti-retroviral therapy-related outcomes among people living with human immunodeficiency virus in Beijing, China. *BMC Infect Dis* 2020; 20:489.
16. Ko NY, Liu HY, Lee HC, et al. One-year follow-up of relapse to risky behaviors and incidence of syphilis among patients enrolled in the HIV case management program. *AIDS Behav* 2011; 15:1067–1074.
17. Byun J, Post RH, Frost CJ, et al. Assessing the approach to HIV case management. *Soc Work Public Health* 2019; 34:307–317.
18. National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention. Technical Manual of HIV Case Management. Beijing, China: People's Medical Publishing House, 2018.
19. Magee C, Norena M, Hubley AM, et al. Longitudinal associations between perceived quality of living spaces and health-related quality of life among homeless and vulnerably housed individuals living in three Canadian cities. *Int J Environ Res Public Health* 2019; 16:4808.
20. Eaton LA, Kalichman SC, Kalichman MO, et al. Randomised controlled trial of a sexual risk reduction intervention for STI prevention among men who have sex with men in the USA. *Sex Transm Infect* 2018; 94:40–45.
21. Ogburn DF, Schoenbach VJ, Edmonds A, et al. Depression, ART adherence, and receipt of case management services by adults with HIV in North Carolina, medical monitoring project, 2009–2013. *AIDS Behav* 2019; 23:1004–1015.
22. Ghanem KG, Moore RD, Rompalo AM, et al. Antiretroviral therapy is associated with reduced serologic failure rates for syphilis among HIV-infected patients. *Clin Infect Dis* 2008; 47:258–265.
23. Brown JL, Vanable PA, Bostwick RA, et al. A pilot intervention trial to promote sexual health and stress management among HIV-infected men who have sex with men. *AIDS Behav* 2019; 23:48–59.
24. Heijman T, Geskus RB, Davidovich U, et al. Less decrease in risk behaviour from pre-HIV to post-HIV seroconversion among MSM in the combination antiretroviral therapy era compared with the pre-combination antiretroviral therapy era. *AIDS* 2012; 26:489–495.
25. Cheng SH, Yang CH, Hsueh YM. Highly active antiretroviral therapy is associated with decreased incidence of sexually transmitted diseases in a Taiwanese HIV-positive population. *AIDS Patient Care STDS* 2013; 27:155–162.
26. Liu XY, Hao C, Jiang H, et al. Syphilis and its correlates among heterosexual males attending sexually transmitted infection clinics—observation from a multicity cohort in Jiangsu Province, China. *PLoS One* 2014; 9:e95289.
27. Ang LW, Wong CS, Ng OT, et al. Incidence of syphilis among HIV-infected men in Singapore, 2006–2017: Temporal trends and associated risk factors. *Sex Transm Infect* 2020; 96:293–299.
28. Novak RM, Ghanem A, Hart R, et al. Risk factors and incidence of syphilis in human immunodeficiency virus (HIV)-infected persons: The HIV Outpatient Study, 1999–2015. *Clin Infect Dis* 2018; 67:1750–1759.
29. Chen XGYB, Wang PG. *Applied Longitudinal Data Analysis for Epidemiology*. Beijing, China: People's Medical Publishing House, 2016.
30. Phillips AE, Gomez GB, Boily MC, et al. A systematic review and meta-analysis of quantitative interviewing tools to investigate self-reported HIV and STI associated behaviours in low- and middle-income countries. *Int J Epidemiol* 2010; 39:1541–1555.