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The prevalence of HSV-2 infection in HIV-1 discordant couples

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SUMMARY

We aimed to investigate the prevalence and associated factors of HSV-2 discordance and concordance in HIV-1-discordant couples. This study used the baseline data from a cohort study of HIV-1-discordant couples in Dehong prefecture of Yunnan province, China. Of 954 participating couples, 42·4% were affected by HSV-2, of which 20·4% were HSV-2-concordant positive, 7·6% were HSV-2-discordant where the male was HSV-2 positive, and 14·4% were HSV-2 discordant where the female was HSV-2 positive. Compared to HSV-2-negative concordance, HSV-2 discordance with an HSV-2-positive male spouse was significantly associated with characteristics of the male spouse, including Han ethnicity and being in a second marriage. HSV-2 discordance with an HSV-2-positive female spouse was significantly associated with characteristics of the female spouse, including Han ethnicity, having engaged in commercial sex, having a sexual relationship of <3 years and being HIV-1 infected. Compared to HSV-2 discordance, HSV-2-positive concordance was significantly associated with an education level of middle school or higher for both spouses, a sexual relationship of $\geqslant$3 years, more frequent sex and having an HIV-1-infected male spouse. The findings highlight the need for HSV-2 prevention and treatment efforts to reduce HSV-2 transmission in this population, and emphasize the importance of implementing prevention interventions early in couples' relationships.

Key words: China, couples, discordant, HIV-1, HSV-2, prevalence.

INTRODUCTION

Herpes simplex virus type 2 (HSV-2) is one of the most common sexually transmitted infections (STIs) worldwide and the leading cause of genital ulcer disease [1, 2]. HSV-2 is transmitted through symptomatic and asymptomatic viral shedding [3]. The synergistic relationship between HIV-1 and HSV-2 transmission has been well documented, with enhanced transmission and/or acquisition of HIV-1 or HSV-2 in the presence of the other virus [4–10].

Heterosexual contact has emerged recently as the primary mode of HIV transmission in China, accounting for 52·2% of estimated new infections in 2011 [11].

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It is noteworthy that an increased proportion of new infections occurred in couples engaged in stable, heterosexual HIV-1-discordant relationships (i.e. one partner is HIV-1 infected and the other is not) [12, 13]. High HSV-2 prevalence is observed in one or both members of HIV-1-discordant couples in many countries including China [14–16]. Prevention of HSV-2 infection, as part of HIV-1 prevention programmes, may be an important component in controlling the risk of HIV-1 transmission in these couples [9]. However, few data exist on the prevalence and risk factors of HSV-2 infection in this population in China.

In HIV-1-discordant couples, HSV-2 can be acquired either from within or outside the couple's relationship. To inform design of interventions it is important to separately identify risk factors that independently affect HSV-2 infection from outside the partnership or HSV-2 transmission within the couple. Most HSV-2 discordance arise due to HSV-2 infection of one partner from sexual activity outside the partnership, but HSV-2-positive concordance may reflect acquisition outside the partnership or HSV-2 transmission within the couple [14, 17]. Therefore, we separately assessed risk factors that were independently associated with HSV-2 discordance compared to HSV-2-negative concordance as well as risk factor that were independently associated with HSV-2-positive concordance compared to HSV-2 discordance in a sample of HIV-1-discordant couples.

METHODS

Study participants

This study used the baseline data from a prospective, longitudinal cohort study of HIV-1-discordant couples conducted from June 2009 to March 2011 in Dehong prefecture of Yunnan province, which is a region bordering Myanmar and is one of the areas most affected by HIV in China [18], as described previously [12]. All HIV-1-discordant couples in Dehong who were registered with the Chinese National Information System for AIDS Prevention and Control (CNISAPC) were invited to participate in this study [12]. Each study participant was administered a face-to-face confidential questionnaire interview by a trained public health worker in a private setting, usually the participant's home. The questionnaire captured data on sociodemographic characteristics and sexual behaviours.

Ethical standards

The study protocol, including study design, subject recruitment, consent procedure, etc., was reviewed and approved by the Institutional Review Board of the Chinese National Centre for AIDS/STD Control and Prevention, Chinese Centre for Disease Control and Prevention. Written informed consent was obtained from all participants, with one copy given to the study subject. Each participant was given compensation of CNY60 (~US$10) for their time. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

HIV-1, syphilis and HSV-2

HIV testing was performed using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Kehua Biotech, China). All samples screened positive for HIV-1 were confirmed by Western blot (Genelabs Diagnostics, Singapore). Participants with plasma positive for syphilis in both the rapid plasma regain test and *Treponema pallidum* haemagglutination assay were determined to be currently infected with syphilis. HSV-2 IgG antibody testing was performed using the Captia anti-HSV-2 IgG ELISA kit (Trinity Biotech, Ireland).

Statistical analysis

All statistical analyses were performed using SAS software v. 9·11 (SAS Institute Inc., USA). First, descriptive analyses were conducted to elucidate the sociodemographic characteristics and sexual behaviours of the study couples by gender and HIV-1 serostatus. Differences by gender and HIV-1 serostatus were examined using χ^2 test or Fisher's exact test as appropriate. Second, to identify the independent predictors of HSV-2 discordance compared to negative concordance and the independent predictors of HSV-2-positive concordance compared to discordance, we performed two separate backward stepwise logistic regression analyses, with an exit significance level of 0·15. Sociodemographic characteristics and sexual behaviours were considered as potential

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predictors. The interaction term of frequency of sex in the past year and length of sexual relationship was also assessed in the model for HSV-2-positive concordance compared to HSV-2 discordance. Here, we combined the individual demographic and sexual behaviuoral variables of male and female spouses of a couple into one couple-level variable to avoid correlation. Variables with a P value <0·10 in the univariate models were selected for entry into stepwise logistic regression models. If one category of a dummy variable was included in the final model, the other category was forced into the final model.

RESULTS

As of 31 June 2010, a total of 1618 HIV-1-discordant couples were eligible. Of these, 1167 HIV-1-infected spouses and 1052 HIV-1-uninfected spouses completed the baseline survey and HSV-2 testing, including both spouses of 954 couples, 213 HIV-1-infected spouses and 98 HIV-1-uninfected spouses alone. For the present analyses, only the 954 couples with both spouses participating in the baseline survey and receiving HSV-2 testing were included.

Participants' characteristics

Of the 954 participating couples, 78·3% had an HIV-1-infected male spouse and 21·7% had an HIV-1-infected female spouse. For the 954 male spouses, 19·6% were aged 16–29 years, 64·9% were of non-Han ethnicity, 64·7% were illiterate or had only primary school education and 86·6% were in their first marriage. For the 954 female spouses, 32·1% were aged 14–29 years, 72·4% were of non-Han ethnicity, 70·5% were illiterate or had only primary school education, and 82·1% were in their first marriage.

As shown in Table 1, 20·7% had been in the sexual relationship with the study partner for <3 years, whereas 79·3% had been in the relationship for ⩾3 years. In terms of sexual behaviours, slightly more than a half of the couples reported having had sex with the study partner ⩾4 times per month in the year prior to enrolment. Less than a quarter (22·9%) of the couples reported having had any unprotected sex with the study partner in the year prior to enrolment. Lifetime commercial sex, lifetime casual or anonymous sex, and syphilis infection, were all more common in HIV-1-infected male and female spouses than in HIV-1-uninfected male and female spouses ($P < 0·05$).

HSV-2 prevalence, discordance and concordance

HSV-2 prevalence was 35·2% in HIV-1-infected spouses and 27·7% in HIV-1-uninfected spouses, resulting in an overall prevalence of 31·4%. The highest HSV-2 prevalence (58·5%) was observed in HIV-1-infected females, compared to the lower prevalence in HIV-1-infected males (28·8%), HIV-1-uninfected females (28·3%), and HIV-1-uninfected males (25·6%) ($P < 0·05$) (Table 1).

Regarding HSV-2 status at the couple level, 405 (42·4%) couples were affected by HSV-2. These included 195 (20·4%) HSV-2-concordant-positive couples, 73 (7·6%) HSV-2-discordant couples where the male spouse was HSV-2 positive, and 137 (14·4%) HSV-2-discordant couples where the female spouse was HSV-2 positive.

Correlates of HSV-2 discordance compared to HSV-2-negative concordance

Table 2 shows results of univariate and multivariate analyses for variables associated with HSV-2 discordance compared to HSV-2-negative concordance. In the final multivariate model, compared to HSV-2-negative concordance, HSV-2 discordance with an HSV-2-positive male spouse was significantly associated with characteristics of the male spouse including Han ethnicity and being in a second marriage, but not with any sexual behavioural variables, syphilis or gender of the HIV-1-infected spouse.

In the final multivariate model, compared to HSV-2-negative concordance, HSV-2 discordance with an HSV-2-positive female spouse was significantly associated with characteristics of the female spouse including Han ethnicity, having engaged in commercial sex, having a sexual relationship of <3 years and being HIV-1 infected.

Correlates of HSV-2-positive concordance compared to HSV-2 discordance

Table 3 shows results of univariate and multivariate analyses for variables associated with HSV-2-positive concordance compared to HSV-2 discordance. In the final multivariate model, compared to HSV-2 discordance, HSV-2-positive concordance was significantly and positively associated with an education level of middle school or higher for both spouses, a sexual

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Table 1. *Characteristics of study participants by gender and HIV status*

	Males		Females	
	HIV+ ($n = 747$)	HIV– ($n = 207$)	HIV+ ($n = 207$)	HIV– ($n = 747$)
HSV-2 serostatus				
Negative	532 (71·2)	154 (74·4)	86 (41·5)	536 (71·7)
Positive	215 (28·8)	53 (25·6)	121 (58·5)	211 (28·3)
Age (years)				
16–29	118 (15·8)	69 (33·3)	103 (49·8)	204 (27·3)
30–39	354 (47·4)	94 (45·4)	75 (36·2)	298 (39·9)
40–96	275 (36·8)	44 (21·3)	29 (14·0)	245 (32·8)
Ethnicity				
Non-Han	518 (69·3)	101 (48·8)	142 (68·6)	549 (73·5)
Han	229 (30·7)	106 (51·2)	65 (31·4)	198 (26·5)
Education				
Illiterate or primary	492 (65·9)	125 (60·4)	135 (65·2)	537 (71·9)
Middle school or higher	255 (34·1)	82 (39·6)	72 (34·8)	210 (28·1)
Current marital status				
First marriage	656 (87·8)	170 (82·1)	137 (66·2)	646 (86·5)
Second marriage	91 (12·2)	37 (17·9)	70 (33·8)	101 (13·5)
Length of sexual relationship (years)				
<3	119 (15·9)	79 (38·2)	79 (38·2)	119 (15·9)
⩾3	628 (84·1)	128 (61·8)	128 (61·8)	628 (84·1)
Frequency of sex with study partner in past year				
<4 times/month	387 (51·8)	71 (34·3)	71 (34·3)	387 (51·8)
⩾4 times/month	360 (48·2)	136 (65·7)	136 (65·7)	360 (48·2)
Any unprotected sex with study partner in past year				
No	576 (77·1)	154 (74·4)	154 (74·4)	576 (77·1)
Yes	171 (22·9)	53 (25·6)	53 (25·6)	171 (22·9)
Ever had commercial sex				
No	617 (82·6)	196 (94·7)	188 (90·8)	744 (99·6)
Yes	130 (17·4)	11 (5·3)	19 (9·2)	3 (0·4)
Ever had casual or anonymous sex				
No	688 (92·1)	202 (97·6)	185 (89·4)	739 (98·9)
Yes	59 (7·9)	5 (2·4)	22 (10·6)	8 (1·1)
Syphilis serostatus				
Negative	712 (97·5)	196 (99·0)	191 (96·0)	716 (98·6)
Positive	18 (2·5)	2 (1·0)	8 (4·0)	10 (1·4)

relationship of ⩾3 years, more frequent sex with study partner in the past year (⩾4 times/month) and having an HIV-1-infected male spouse. The interaction between frequency of sex and length of sexual relationship (⩾3 years) was marginally statistically significant (P = 0·056), with adjusted odds ratios (aORs) decreasing as the years in the sexual relationship increased.

DISCUSSION

This is the first study with a large sample size to examine the prevalence and risk factors of HSV-2 infection in HIV-1-discordant couples in China. We found that 42·5% of HIV-1-discordant couples were affected by HSV-2; lower than 75·3% of couples found in a previous study conducted in Kenya [14]. This discrepancy may be partially due to the different predominant transmission routes of HIV in the two study areas. As suggested by surveillance reports and previous studies, drug injection is the predominant mode of HIV-1 transmission in the study area [18], whereas heterosexual transmission remains the most prominent mode of HIV transmission in Kenya [19]. In addition, the overall prevalence of HSV-2 (31·4%) in our study

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Table 2. *Logistic regression analysis of factors associated with HSV-2 discordance compared to HSV-2-negative concordance*

	HSV-2 discordance: male HSV-2 positive*				HSV-2 discordance: female HSV-2 positive†			
	cOR (95% CI)	*P*	aOR (95% CI)	*P*	cOR (95% CI)	*P*	aOR (95% CI)	*P*
Individual characteristics								
Age (⩾30 years)	1·30 (0·64–2·63)	0·463			0·68 (0·39–0·85)	0·005		
Ethnicity (Han)	1·86 (1·12–3·07)	0·016	1·92 (115–3·20)	0·012	1·88 (1·26–2·82)	0·002	1·82 (1·16–2·87)	0·009
Education (middle school or higher)	1·17 (0·69–1·97)	0·555			1·59 (1·06–2·39)	0·024		
Marital status (second marriage)	3·23 (1·78–5·84)	<0·001	3·32 (1·82–6·05)	<0·001	1·80 (1·14–2·85)	0·011		
Couples' characteristics								
Length of sexual relationship (⩾3 years)	0·85 (0·85–1·58)	0·601			0·35 (0·23–0·53)	<0·001	0·49 (0·30–0·78)	0·003
Syphilis serostatus								
Both negative	1·00				1·00			
Male positive, female negative	2·17 (0·44–10·66)	0·340			0·56 (0·07–4·62)	0·593		
Female positive, male negative	<0·01 (<0·01–>99·99)	0·989			7·89 (1·43–43·56)	0·018		
Both positive	<0·01 (<0·01–>99·99)	0·992			3·95 (0·25–63·51)	0·333		
Ever had commercial sex								
Both no	1·00				1·00		1·00	
Male yes, female no	1·62 (0·84–3·12)	0·146			1·00 (0·55–1·83)	0·988	1·50 (0·79–2·84)	0·220
Female yes, male no	<0·01 (<0·01–>99·99)	0·993			19·26 (4·11–90·35)	<0·001	5·98 (1·21–29·48)	0·028
Both yes	<0·01 (<0·01–>99·99)	0·991			1·43 (0·15–13·86)	0·758	0·52 (0·05–5·35)	0·588
Ever had casual or anonymous sex								
Both no	1·00				1·00			
Male yes, female no	1·83 (0·77–4·33)	0·171			0·97 (0·42–2·27)	0·950		
Female yes, male no	0·78 (0·10–6·21)	0·817			2·92 (1·09–7·83)	0·033		
Both yes	–				>99·99 (<0·01–>99·99)	0·980		
Male HIV-1 infected	1·34 (0·62–2·91)	0·452			0·13 (0·09–0·20)	<0·001	0·17 (0·11–0·26)	<0·001

cOR, Crude odds ratio; aOR, adjusted odds ratio.

* Only male spouses were included in the regression analysis.

† Only female spouses were included in the regression analysis.

Table 3. *Logistic regression analysis of factors associated with HSV-2-positive concordance compared to HSV-2 discordance*

Variable	cOR (95% CI)	*P*	aOR (95% CI)	*P*
Age (years)				
Both <30	1·00			
Male <30, female ⩾30	0·66 (0·18–2·36)	0·520		
Female <30, male ⩾30	1·44 (0·75–2·78)	0·236		
Both ⩾30	1·28 (0·77–2·13)	0·240		
Ethnicity				
Both non-Han	1·00			
Male Han, female non-Han	0·70 (0·28–1·77)	0·452		
Female Han, male non-Han	1·14 (0·66–1·98)	0·642		
Both Han	1·20 (0·76–1·90)	0·435		
Education				
Both illiterate or primary	1·00		1·00	
Male illiterate or primary, female middle or higher	1·04 (0·56–1·94)	0·903	1·20 (0·63–2·32)	0·578
Female illiterate or primary, male middle or higher	1·00 (0·58–1·71)	0·997	1·03 (0·59–1·81)	0·840
Both middle or higher	1·91 (1·16–3·16)	0·011	2·03 (1·21–3·43)	0·008
Current marital status				
Both first marriage	1·00			
Male first marriage, female second marriage	0·72 (0·38–1·38)	0·321		
Female first marriage, male second marriage	1·33 (0·61–2·92)	0·472		
Both second marriage	0·59 (0·31–1·11)	0·103		
Male HIV-1 infected	2·22 (1·44–3·43)	<·001	2·35 (1·49–3·71)	0·003
Length of sexual relationship (⩾3 years)	1·60 (1·02–2·51)	0·042	3·39 (1·35–8·51)	0·009
Frequency of sex with study partner in past year (⩾4 times/month)	1·32 (0·89–1·96)	0·171	3·71 (1·39–9·87)	0·009
Frequency of sex in past year × length of sexual relationship	–	–	0·33 (0·11–0·98)	0·047
Any unprotected sex with study partner in the past year	0·69 (0·44–1·10)	0·119		
Ever had commercial sex				
Both no	1·00			
Male yes, female no	1·82 (1·08–3·08)	0·025		
Female yes, male no	0·66 (0·22–2·01)	0·464		
Both yes	2·37 (0·21–26·43)	0·433		
Ever had casual or anonymous sex				
Both no	1·00			
Male yes, female no	1·19 (0·56–2·53)	0·660		
Female yes, male no	0·97 (0·34–2·73)	0·951		
Both yes	4·43 (0·49–39·99)	0·185		
Syphilis serostatus				
Both negative	1·00			
Male positive, female negative	1·82 (0·43–7·70)	0·419		
Female positive, male negative	1·91 (0·55–6·62)	0·310		
Both positive	3·27 (0·34–31·69)	0·307		

cOR, Crude odds ratio; aOR, adjusted odds ratio.

is lower than prevalences reported in female commercial sex workers (33·2–68%) in other areas in Yunnan province [20, 21], but higher than in rural residents (13·4%) in Taizhou, Zhejiang province [22] and male general migrants (5·5%) in Shanghai [23]. These results, combined with the synergistic effect between HSV-2 and HIV-1 infections, demonstrate the importance of screening and treatment of HSV-2 infection in HIV-1-discordant couples.

Consistent with previous reports [14], we observed that female spouses had a higher prevalence of HSV-2 than males, even though males had a higher HIV-1 prevalence than females. Women are at greater risk of HSV-2 infection because of higher efficiency of HSV-2 transmission from men to women compared to transmission from women to men [24]. This suggests that HSV-2 prevention programmes should target women in particular. With regards to ethnicity, our

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results indicate that Han ethnic participants were more likely to be infected with HSV-2 than non-Han ethnic minorities regardless of their gender. Our previous study indicated that compared to Han ethnicity, these minorities had a higher percentage of HIV infection through injection drug use but had a lower percentage of HIV infection through sexual contact [25]. HSV-2 is primarily transmitted through sexual activity [14], and there is a repeatedly observed strong association between HSV-2 infection and sexual risk behaviours [26]. This reinforces the need of sexual risk reduction interventions in the Han ethnic population. Furthermore, the association of second marriage with HSV-2 infection is not surprising because a higher number of sex partners increases the risk of HSV-2 infection [26, 27].

We observed that lifetime commercial sex by the female spouse was significantly associated with HSV-2 discordance where the female spouse was HSV-2 positive, compared to HSV-2-negative concordance. This suggests that commercial sex (i.e. selling sex) was one of the main routes for females to become infected with HSV-2 from a partner outside the marital partnership, as our data indicated that 9·2% of HIV-1-infected female spouses have ever had commercial sex. This is consistent with the route of sexual transmission of HIV-1 in females in the study area [18], highlighting the urgent need for HSV-2 and HIV-1 control and prevention in female sex workers in this area. Nevertheless, we did not find this association in male spouses. It may be attributed to the relatively small sample size of HSV-2-discordant couples where the male spouse was HSV-2 positive in our study, or/and the underreporting of outside sexual engagements by male spouses.

It is not surprising that HSV-2-discordant couples with an HSV-2-positive female spouse were more likely to have an HIV-1-infected female spouse than HSV-2-concordant negative couples. This is consistent with our data that HIV-1-infected female spouses had a higher prevalence of HSV-2 than HIV-1-uninfected female spouses. Higher prevalence of HSV-2 was also observed in HIV-1-infected male spouses than in HIV-1-uninfected male spouses. This indicates a tendency of HIV-1 and HSV-2 co-infection in HIV-1-discordant couples, particularly in female spouses. A similar pattern has also been observed in a previous study [14]. HSV-2-concordant positive couples were more likely to have an HIV-1-infected male spouse compared to HSV-2-discordant couples. The possible explanation was that there were two types of HSV-2-discordant couples, and HSV-2-discordant couples with an HSV-2-positive female spouse had the lowest percentage of HIV-1-infected male spouses (i.e. highest percentage of HIV-1-infected female spouses) compared to other types of couples (data not shown) .

Consistent with a previous study [28], we observed that frequency of sex was associated with an increased likelihood of HSV-2-positive concordance. It is important to note that the interaction between the length of sexual relationship and frequency of sex was statistically significant, with aORs decreasing as the length of the sexual relationship increased. The frequency of sex in the previous year was not as strongly associated with HSV-2 in couples with a sexual relationship of $\geqslant 3$ years as those with a sexual relationship of <3 years. This suggests that HSV-2 transmission within the couple is more likely to occur in the first year of the sexual relationship. Therefore, prevention efforts should begin as early as possible in the relationship in order to reduce the likelihood of HSV-2 transmission within couples.

Several limitations of this study should be noted. First, all participating couples were recruited from a rural area in China; our findings may not be generalizable to other areas of China. Second, because this was a cross-sectional study design, the causal relationship between associated factors and outcomes could not be confirmed. Third, like most studies of sexual behaviours, this study was also potentially subject to social desirability bias, and frequency of unprotected sex and outside sexual partners may be underestimated. However, this was not a problem for judging the magnitude of HSV-2 infection in the study population. Fourth, HSV-2-positive concordance may reflect acquisition from outside the partnership or HSV-2 transmission within the couple, which limits the ability to identify the factors that affect HSV-2 transmission within the couple. In addition, because multiple testing bias remains a concern in multivariate models when interpreting individual covariates, our results should be interpreted with caution.

In conclusion, our observation of high HSV-2 prevalence in HIV-1-discordant couples highlights the need for HSV-2 prevention and treatment efforts in this population in order to reduce HSV-2 acquisition and transmission. Specifically, routine HSV-2 screening, risk reduction counselling and suppressive therapy for HSV-2 infection should be given to this population, particularly females. The implementation of HIV-1

pre-exposure prophylaxis in HIV-1-discordant heterosexual couples is also recommended, which has been recently shown to significantly reduce the risk for HSV-2 acquisition [29], besides offering protection against HIV acquisition. Our findings also emphasize the importance of implementing prevention interventions early in couples' relationships.

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DECLARATION OF INTEREST

None.

REFERENCES

1. **Fanfair RN, *et al.*** Trends in seroprevalence of herpes simplex virus type 2 among non-Hispanic blacks and non-Hispanic whites aged 14 to 49 years – United States, 1988 to 2010. *Sexually Transmitted Diseases* 2006; **40**: 860–864.
2. **Looker KJ, Garnett GP, Schmid GP.** An estimate of the global prevalence and incidence of herpes simplex virus type 2 infection. *Bulletin of the World Health Organization* 2008; **86**: 805–812.
3. **Gupta R, Warren T, Wald A.** Genital herpes. *Lancet* 2007; **370**: 2127–2137.
4. **Corey L, *et al.*** The effects of herpes simplex virus-2 on HIV-1 acquisition and transmission: a review of two overlapping epidemics. *Journal of Acquired Immune Deficiency Syndromes* 2004; **35**: 435–445
5. **Corey L.** Synergistic copathogens – HIV-1 and HSV-2. *New England Journal of Medicine* 2007; **356**: 854–856.
6. **Mayer KH, Venkatesh KK.** Interactions of HIV, other sexually transmitted diseases, and genital tract inflammation facilitating local pathogen transmission and acquisition. *American Journal of Reproductive Immunology* 2011; **65**: 308–316.
7. **Barnabas RV, *et al.*** NIAID HIV Vaccine Trials Network. Impact of herpes simplex virus type 2 on HIV-1 acquisition and progression in an HIV vaccine trial (the Step study). *Journal of Acquired Immune Deficiency Syndromes* 2011; **57**: 238–244.
8. **Augenbraun M, *et al.*** Increased genital shedding of herpes simplex virus type 2 in HIV-seropositive women. *Annals of Internal Medicine* 1995; **123**: 845–847.
9. **Mbopi-Kéou FX, *et al.*** Interactions between herpes simplex virus type 2 and human immunodeficiency virus type 1 infection in African women: opportunities for intervention. *Journal of Infectious Diseases* 2000; **182**: 1090–1096.
10. **Mahiane SG, *et al.*** Transmission probabilities of HIV and herpes simplex virus type 2, effect of male circumcision and interaction: a longitudinal study in a township of South Africa. *AIDS* 2009; **23**: 377–383.
11. **China Ministry of Health.** 2012 China AIDS response progress report. Beijing: China Ministry of Health, 2012.
12. **He N, *et al.***; China National HIV Prevention Study Group. Antiretroviral therapy reduces HIV transmission in discordant couples in rural Yunnan, China. *PLoS ONE* 2013; **8**: e77981.
13. **Jia Z, *et al.*** Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003–11): a national observational cohort study. *Lancet* 2013; **382**: 1195–1203.
14. **Muiru AN, *et al.*** Incident HSV-2 infections are common among HIV-1-discordant couples. *Journal of Infectious Diseases* 2013; **208**: 1093–1101.
15. **Camara M, *et al.*** Association between herpes simplex virus type 2 and HIV-1 in a population of married couples from Dakar, Senegal. *International Journal of STD & AIDS* 2012; **23**: 810–814.
16. **Zhu Q, *et al.*** A retrospective study on HIV transmission among HIV-positive male drug users and their spouses in Guangxi. *Modern Preventive Medicine* (*Chinese*) 2013; **40**: 2843–2847.
17. **Mujugira A, *et al.*** Risk factors for HSV-2 infection among sexual partners of HSV-2/HIV-1 co-Infected persons. *BMC Research Notes* 2011; **4**: 64.
18. **Jia Y, *et al.*** Estimates of HIV prevalence in a highly endemic area of China: Dehong Prefecture, Yunnan Province. *International Journal of Epidemiology* 2008; **37**: 1287–1296.
19. **Gouws E, *et al.*** Short term estimates of adult HIV incidence by mode of transmission: Kenya and Thailand as examples. *Sexually Transmitted Infections* 2006; **82**: iii51–iii55.
20. **Wang H, *et al.*** Prevalence and predictors of herpes simplex virus type 2 infection among female sex workers in Yunnan Province, China. *International Journal of STD & AIDS* 2008; **19**: 635–639.
21. **Ngo TD, *et al.*** Herpes simplex virus type 2 infection among commercial sex workers in Kunming, Yunnan Province, China. *International Journal of STD & AIDS* 2008; **19**: 694–697.
22. **Lin H, *et al.*** Herpes simplex virus infections among rural residents in eastern China. *BMC Infectious Diseases* 2011; **11**: 69.
23. **He N, *et al.*** Herpes simplex virus-2 infection in male rural migrants in Shanghai, China. *International Journal of STD & AIDS* 2009; **20**: 112–114.
24. **Gottlieb *et al.*** Seroprevalence and correlates of herpes simplex virus type 2 infection in five sexually transmitted disease clinics. *Journal of Infectious Diseases* 2002; **186**: 1381–1389.
25. **He N, *et al.*** Multiple viral coinfections among HIV/AIDS patients in China. *Bioscience Trends* 2011; **5**: 1–9.

26. **Patnaik P, *et al.*** Type-specific seroprevalence of herpes simplex virus type 2 and associated risk factors in middle-aged women from 6 countries: the IARC multicentric study. *Sexually Transmitted Diseases* 2007; **34**: 1019–1024.
27. **Weiss H.** Epidemiology of herpes simplex virus type 2 infection in the developing world. *Herpes* 2004; **11**: 24–35.
28. **Wald A, *et al.*** The relationship between condom use and herpes simplex virus acquisition. *Annals of Internal Medicine* 2005; **143**: 707–713.
29. **Celum C, *et al.*** Daily oral tenofovir and emtricitabine-tenofovir preexposure prophylaxis reduces herpes simplex virus type2 acquisition among heterosexual HIV-1-uninfected men and women: a subgroup analysis of a randomized trial. *Annals of Internal Medicine* 2014; **161**: 11–19.