Supplementary Table S4. Information on participants characteristics and study characteristics & results of the Newcastle-Ottawa scale assessment.

Prevalent	Desai et al	Frits et al	Gabriele et al	Jin et al	Laia et al	Lee et al
Study year	2017	2013	2006	2010	2016	2008
Study design	CT	CT	CT	CT	CT	CC
Country	Europe (England)	Asia (Thailand)	Africa (Tanzania)	Australia (Australia)	Europe (Spain)	Asia (China)
Study population	MSM	MSM	FBW	MSM	MSM	STDA
No. of participants	9309	3750	360	5084	2876	392
Mean or Median age	34	26	25	35	33	NR
Syphilis prevalence (Baseline) (%)	1.9	4.7	17.5	2.9	0.6	3.4
Syphilis confirm test	NR	RPR&IC	RPR&TPPA	RPR&TTs	RPR&TPPA	VDRL& TPPA
Length of time between tests for HIV (1<=6 months or 2>6)	1	1	1	2	2	NR
Follow-up rate	NR	76.1%	74.5%	81.0%	63.4%	2.40%
HIV acquisition (%)	2.00	5.90	NR	0.78	2.40	NR
Timing of incident syphilis infection relative to HIV acquisition	DB	DB	B&C	DB	B&C	B&C
Definition of unexpoesed group	F-U	B	F-U	F-U	F-U	B
Adjusted for condom use?	N	Y	N	NR	N	Y
Adjusted for male circumcision status?	N	N	Y	NR	N	Y
Adjusted for genital ulcer disease?	Y	Y	N	NR	N	N
Adjusted for any sexual behavior (excluding condom use)?	N	Y	Y	NR	N	N
Adjusted for number of sexual partners?	N	Y	N	NR	N	N
Adjusted for age?	N	Y	N	NR	Y	N
Adjusted for drug use?	N	Y	N	NR	N	Y
Selection 1)	*	*	*	*	*	*
Selection 2)	*	*	*	*	*	*
Selection 3)	*		*		*	*
Selection 4)	*	*	*	*	*	*
Comparability 1a)		*				*

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Prevalent	Desai et al	Frits et al	Gabriele et al	Jin et al	Laia et al	Lee et al
Comparability 1b)		*				
Exposure 1)	*	*	*	*	*	
Exposure 2)	*	*	*	*	*	*
Exposure 3)				*		*

Prevalent	Matthew et al	Matthew et al	Mehta et al	Rebecca et al	Ruzagiza et al
Study year	2017	2016	2006	2011	2011
Study design	CC	CT	CT	CT	CT
Country	America (USA)	America (USA)	America (USA)	Australia (Australia)	Africa (Uganda)
Study population	MSM	MSM	STDA	MSM	HIV-DC
No. of participants	15107	2593	13693	4488	787
Mean or Median age	32	NR	25	32	36
Syphilis prevalence (Baseline) (%)	1.1	1.5	2.8	2.0	5.2
Syphilis confirm test	RPR	RPR	NTT&TT	NR	RPR&TPHA
Length of time between tests for HIV (1<=6 months or 2>6)	2	1	1	2	1
Follow-up rate	88.3%	88.1%	NR	NR	97.4%
HIV acquisition (%)	2.18	5.40	0.91	1.24	4.30
Timing of incident syphilis infection relative to HIV acquisition	DB	DB	B&C	DB	B&C
Definition of unexpoesed group	B	F-U	F-U	F-U	F-U
Adjusted for condom use?	NR	NR	N	Y	Y
Adjusted for male circumcision status?	NR	NR	N	N	Y
Adjusted for genital ulcer disease?	NR	NR	N	Y	Y
Adjusted for any sexual behavior (excluding condom use)?	NR	NR	Y	Y	N
Adjusted for number of sexual partners?	NR	NR	N	Y	N
Adjusted for age?	NR	NR	Y	Y	Y
Adjusted for drug use?	NR	NR	Y	N	N
Selection 1)	*	*	*	*	*
Selection 2)	*	*	*	*	*

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Prevalent	**Matthew et al**	**Matthew et al**	**Mehta et al**	**Rebecca et al**	**Ruzagiza et al**
Selection 3)	*		*	*	*
Selection 4)	*	*	*	*	*
Comparability 1a)					*
Comparability 1b)					*
Exposure 1)		*	*	*	*
Exposure 2)	*	*	*	*	*
Exposure 3)	*	*			*

Prevalent	**Su et al**	**Ulrich et al**	**Xu et al**	**Xu et al**	**Yang et al**	**Yang et al**
Study year	2016	2006	2013	2010	2010	2016
Study design	CT	CC	CT	CT	CT	CC
Country	Asia (China)	Europe (Germany)	Asia (China)	Asia (China)	Asia (China)	Asia (China)
Study population	FSW	MSM	MSM	MSM	MSM	MSM
No. of participants	3106	356	313	122	286	303
Mean or Median age	27	36	28	27	NR	28
Syphilis prevalence (Baseline) (%)	7.4	41.0	5.8	25.4	12.6	12.2
Syphilis confirm test	RPR&TPPA	RPR&TPHA	RPR&TPPA	RPR&TPPA	RPR&TPPA	TRUST
Length of time between tests for HIV (1<=6 months or 2>6)	1	NR	1	1	1	NR
Follow-up rate	NR	47.5%	70.0%	56.0%	72.0%	NR
HIV acquisition (%)	1.06	5.60	3.50	5.40	5.12	NR
Timing of incident syphilis infection relative to HIV acquisition	DB	DB	DB	DB	DB	B&C
Definition of unexpoesed group	B	F-U	F-U	B	B	B
Adjusted for condom use?	Y	NR	Y	Y	NR	Y
Adjusted for male circumcision status?	Y	NR	Y	N	NR	N
Adjusted for genital ulcer disease?	N	NR	N	N	NR	N
Adjusted for any sexual behavior (excluding condom use)?	N	NR	Y	Y	NR	Y

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Prevalent	Su et al	Ulrich et al	Xu et al	Xu et al	Yang et al	Yang et al
Adjusted for number of sexual partners?	Y	NR	Y	Y	NR	Y
Adjusted for age?	N	NR	Y	N	NR	N
Adjusted for drug use?	Y	NR	Y	N	NR	N
Selection 1)	*	*	*	*	*	*
Selection 2)	*	*	*	*	*	*
Selection 3)	*	*				*
Selection 4)	*	*	*	*	*	*
Comparability 1a)	*		*	*		*
Comparability 1b)	*		*	*		*
Exposure 1)	*	*	*	*	*	
Exposure 2)	*	*	*	*	*	*
Exposure 3)						*

Incident	Li et al	Li et al	Sarah et al	Tang et al	Wang et al
Study year	2010	2012	2011	2014	2014
Study design	CT	CC	CT	CT	CT
Country	Asia (China)	Asia (China)	Africa (Rwanda)	Asia (China)	Asia (China)
Study population	MSM	MSM	FSW	MSM	MSM
No. of participants	425	593	373	359	557
Mean or Median age	26	28	24	NR	36
Syphilis prevalence (Baseline) (%)	16.9	16.4	7.3	12.6	30.9
Syphilis confirm test	RPR&TPPA	RPR&TPPA	RPR&TPPA	RPR&TPPA	TRUST&TPPA
Length of time between tests for HIV (1<=6 months or 2>6)	1	1	1	1	1
Follow-up rate	86,2%	86.8%	85.0%	51.2%	60.3%
HIV acquisition (%)	2.60	8.09	5.60	3.60	6.78
Timing of incident syphilis infection relative to HIV acquisition	B&C	DB	B&C	DB	B&C
Definition of unexpoesed group	F-U	F-U	F-U	F-U	F-U
Adjusted for condom use?	N	Y	Y	Y	Y

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Incident	**Li et al**	**Li et al**	**Sarah et al**	**Tang et al**	**Wang et al**
Adjusted for male circumcision status?	N	N	N	N	N
Adjusted for genital ulcer disease?	Y	Y	N	N	N
Adjusted for any sexual behavior (excluding condom use)?	N	Y	N	N	N
Adjusted for number of sexual partners?	N	Y	N	N	N
Adjusted for age?	N	Y	Y	Y	Y
Adjusted for drug use?	N	N	N	N	N
Selection 1)	*	*	*	*	*
Selection 2)	*	*	*	*	*
Selection 3)	*		*		*
Selection 4)	*	*	*	*	*
Comparability 1a)		*	*	*	*
Comparability 1b)		*			
Exposure 1)	*	*	*	*	*
Exposure 2)	*	*	*	*	*
Exposure 3)	*	*	*		

CT=Cohort study; CC=Case-control study; MSM=Men who have sex with men; FBW=Female bar workers; STDA=STD clinic attendees; HIV-DC=HIV discordant couples; FSW=Female sex workers; NR=Not reported; DB=Definitely before; B&C=Before and indeterminably close; F-U=Follow-up (Syphilis negative throughout follow-up/retrospective); B=Baseline (Syphilis negative at baseline); N=No; Y=Yes; NTT=nontreponemal test; TT=treponemal test; VDRL=Venereal Disease Research Laboratory; RPR=rapid plasma regain; TRUST=toluidine red unheated serum test; FTA-ABS=fluorescent treponemal antibody absorbed test; TPPA=T. pallidum passive particle agglutination; TPHA=T. pallidum haemagglutination assay; IA=immunoassay.

C. Analytic Methods

Principal meta-analysis

We did data analyses using the meta packages of STATA (version 15.0). Considering that most of our studies (18 of 22 studies) are cohort study, we chose the relative risk (RR) as effect size to measure the association between syphilis and HIV. For those case-control studies, we used the following formulae to convert OR to RR.

Relative risk=odds ratio/(1-p_0+(p_0×odds ratio)) （Where p_0 is the baseline risk）

To estimate the overall effect size, we used the random-effect method of DerSimonian and Laird to pool weighted RR of HIV risk estimates. An RR >1 indicated an increased likelihood of an outcome of interest among syphilis positive population compared with syphilis negative population, while an RR <1 indicated a reverse outcome.