

Supplementary

Further details on the methods

A. Search strategy & Selection criteria

Two authors (MYW and JL) independently performed the search on Pubmed, Embase and Cochrane Library. We searched for articles and abstracts using the terms (“syphilis”, “Treponema pallidum” OR “T. pallidum”) AND (“HIV”, “human immunodeficiency virus”, “human immuno deficiency virus”, “human immunodeficiency virus”, OR “human immune deficiency virus”) to screen all relevant studies of HIV acquisition after exposure to syphilis infection. Searches were not restricted by language or bibliographic database filters. 2861 clinical studies published to 21/09/2019 were identified. After removing 196 duplicate publications, 2691 relevant studies remained for examination with following criteria.

Supplementary table S1. Selection criteria.

Study subject	- Comparing the effect of preceding syphilis infection on HIV acquisition with syphilis negative group	✓
	- Limited to syphilis infected	✗
	- Limited to HIV-infected individuals only	✗
Study design	- Cohort study	✓
	- Case-control study (including nested case-control study)	✓
	- Cross-sectional study	✗
Study group	- Men who have sex with men*	✓
	- High-risk groups ^{&}	✓
Definition of unexposed group	- Syphilis remained negative throughout follow-up	✓
	- Syphilis negative at baseline (for studies in which syphilis retest was not done during follow-up)	✓
Timing sequences	- Syphilis happened definitely before HIV acquisition	✓
	- Syphilis happened in a previous or in the same interval as HIV acquisition (before and indeterminably close)	✓
	- syphilis might have happened after HIV infection (after and indeterminably close).	✓
	- Syphilis infection happened definitely after HIV infection	✗

Study quality	- Data reliability	
	- no primary data	×
	- relying on self-reported syphilis infection history	×
	- Newcastle-Ottawa Scale	

*Men who have sex with men are defined as individuals who at their baseline visit reported a biological sex and gender identity of male and identified either as gay or bisexual or reported having sex with another man in the past year. & Other high-risk groups including sex workers, serodiscordant couples, people who inject drugs and attendees of STI clinics.

Newcastle-Ottawa Quality Assessment Scale assessment (our criteria for awarding a star in each category of the Newcastle-Ottawa Quality Assessment Scale was as follows)

Supplementary table S2. Case-control studies (including nested case-control studies)

Criteria	Condition required to obtain a star	Bias assessed
Selection 1) Is the case definition adequate (HIV seroconversion)	Method for confirming HIV positive stated	Misclassification of outcome; selection of cases affected by exposure status
Selection 2) Representativeness of the Cases	Cases were representative of an epidemiological core group commonly of interest-MSM and other high-risk groups	Individuals in a serodiscordant partnership or with other higher-risk sexual behaviour excluded
Selection 3) Selection of Controls (HIV-negative)	Awarded for all studies	Selection of controls affected by exposure status
Selection 4) Definition of Controls	No	Misclassification of outcome
Comparability 1a) Comparability of Cases and Controls on the Basis of the Design or Analysis	Adjustment or matching for condom use was done	Confounding
Comparability 1b) Comparability of Cases and Controls on the Basis of the Design or Analysis	Adjustment or matching for number of sexual partners (any timeframe) was done	Confounding
Exposure 1) Ascertainment of Exposure (Syphilis infection status)	Unexposed group was defined as Syphilis seronegative throughout the study (rather than just at baseline)	Misclassification of outcome
Exposure 2) Same Method of Exposure Ascertainment for Cases and Controls	Awarded for all studies;	
Exposure 3) Non-Response Rate	Follow-up/response rate was at least 80%	Participants drop out for reasons related to the exposure or outcome