



Research article

Prevalence of HIV and syphilis and their co-infection among men having sex with men in Asia: A systematic review and meta-analysis

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ABSTRACT

Background: Studies found that the group of men who have sex with men (MSM) is at a very high level of risk of HIV and sexually transmitted infections (STIs) in Asian regions due to multiple reasons. Although the prevalence of HIV among general people in Asia is considered low, the prevalence of HIV and Syphilis among MSM in this region was found very high and usually, it goes unnoticed. This study aimed to inspect the prevalence of and trends in HIV, Syphilis, and their co-infection among MSM in Asia.

Methods: A systematic search was performed on January 5, 2021, in PubMed, Web of Science, and Google Scholar databases. To evaluate the heterogeneity, Q-tests, and I^2 were used. To explore the publication bias, Eggers' test and funnel plot were used. The random-effect model and subgroup analysis were performed due to the significant heterogeneity.

Results: A total of 2872 articles were identified, and 66 articles were included in the final analysis. The overall prevalence of HIV and Syphilis among MSM was estimated considering 69 estimates from 66 studies whereas 19 estimates of co-infection were found in 17 studies. The pooled HIV prevalence was 8.48% (CI: 7.01–9.95) and the pooled Syphilis prevalence was 9.86% (CI: 8.30–11.41) with significant heterogeneity and publication bias. The pooled prevalence of HIV and Syphilis co-infection was 2.99% (CI: 1.70–4.27) with significant heterogeneity and no publication bias. The HIV, Syphilis, and HIV-Syphilis co-infection prevalence estimates exhibited an upward trend during 2002–2017.

Conclusions: HIV, Syphilis, and their co-infection are quite prevalent among MSM in the Asia-Pacific region. Integrated and intensified intervention strategies, HIV testing, and improved access to antiretroviral treatment as well as increased awareness are needed to reduce HIV, Syphilis, and their co-infection among the discussed vulnerable group.

Abbreviations: HIV, Human Immunodeficiency Virus; MSM, Men Having Sex with Men; STIs, sexually transmitted infections; AIDs, Anti Immune Deficiency Syndrome; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; MOOSE, Meta-analysis of Observational Studies in Epidemiology.

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1. Introduction

People who are sexual minorities and marginalized and disproportionately affected by HIV— particularly, homosexual men, bisexual men, and male-to-female transgender people, are known together as “men who have sex with men (MSM)” [1]. The MSM is the most vulnerable group of people who are being at a high level of risk of HIV and sexually transmitted infections (STIs) in Asia due to unprotected anal sex, heterosexuality, multiple sex partners, etc [2–5]. Globally in 2018, the chance of being infected with HIV in gay men was 22 times higher than in all-adult men [6]. The estimate of new infection rates among MSM or gay men globally is 17% and in Asia and the Pacific region, it is 30%, which is the second-highest after the Latin America region even though, most countries in Asia maintain very low (<0.1%) to low (<1%) HIV prevalence in the general population [1]. A high prevalence has been reported among MSM (between 10% and 30%) in India [7], Thailand [8,9], China [10–14], Cambodia [15], Indonesia, and Myanmar [16]. HIV infection among MSM is still increasing [17–19] and it has become a threat in those Asian countries [20]. The reasons behind this might be poor HIV prevention programs, HIV testing services, as well as sexual health services in this region [19]. It is assumed that the behavior of this specific group of people is strongly correlated to HIV infection and sexually transmitted infection (STI) risk. Therefore, “MSM” has been used as an epidemiologic term to recognize men based on behavior rather than identity [21,22]. In most of the countries in Asia where they are facing stigma, discrimination, and criminal sanctions, they are also known as “hidden” or “hard to find” populations for HIV prevention care and treatment and HIV surveillance [23–25]. Those stigmas, discrimination, criminal sanctions, and sociocultural heteronormative pressures influence them to have sex with women although they have diverse socio-cultural and behavioral contexts of sexuality [2,22]. Due to the hidden characteristics, low-risk perception, unwillingness to disclose attitudes, and scarcity of community communications of MSMW, they may not be sufficiently reached by sexual health and HIV prevention program [26].

Syphilis is a sexually transmitted disease that is also acquainted with syphilitic ulcers to shatter the mucosal barriers. Syphilis increases the likelihood of HIV infection. A certain epidemic of Syphilis occurred in the nearest past among MSM in different parts of the world [27]. An outbreak of Syphilis among MSM has been observed in the 2000s in many developed countries [28–30]. Among the HIV-positive MSMs, the Syphilis incidence rate has been observed at 2.9 to 6.2 per hundred people in the Western world [31–33]. Even, in some cities in Asian countries, the Syphilis prevalence has been reported from 0.9 to 30.9% from 2000 to 2019. Specifically, the prevalence has been found 2.2%–30% in China [34–37], 1.1%–9% in Indonesia, 2.6%–4.46% in Bangladesh, 2.5%–14.1% in Myanmar, 5.5% in Cambodia, 1.5%–4.8% in Nepal, 2.62%–17.5% in India, 1.65%–2.3% in the Philippines, 0.9%–1.3% in Vietnam, 2.5% in Taiwan. A resurrection in Syphilis infection among MSM was also observed in the recent past, which has a strong association with HIV prevalence [38–41]. In many countries, it is observed that among MSM, 50% of the Syphilis cases are HIV positive [42,43] which indicates a very high risk of re-infection among those MSM [44,45]. Nonetheless, researches and well-defined reports on Syphilis as well as HIV-Syphilis co-infection are limited and data are inconsistent to estimate the Syphilis infection rate among MSM in Asian countries [20].

Several countries with limited resources and evidence in Asia are facing a severe HIV epidemic. To control this epidemic, effective prevention programs are required [46]. Extended knowledge and evidence are essential for efficacious prevention programs. This study reveals the data gaps or paucity and provides new pieces of evidence. To our knowledge, this systematic review and meta-analysis is the first looking at the prevalence of HIV, Syphilis as well as HIV-Syphilis co-infection among MSM across Asia. Several systematic reviews and meta-analyses have been done, for example, in Asia [47] and central Asia [48] to observe the epidemic of HIV and sexual risk among men who have sex with men (MSM). Some meta-analyses have also been conducted in China to estimate HIV and Syphilis prevalence among MSM [49–52]. However, all of the studies conducted were country-specific, small-scale, and back-dated. Also, no study has been done yet to estimate the prevalence and inspect the trend of HIV, Syphilis, and HIV-Syphilis co-infection in Asia. For the first time, we are conducting a meta-analysis including all the countries of Asia (where a study was found) with the latest data to have a clear view of the prevalence and trend of HIV, Syphilis, and their co-infection among MSM in Asia.

2. Methods

The PRISMA statement and the MOOSE checklist [53–55] were followed in this systematic review and meta-analysis. The protocol of the review was not registered previously.

2.1. Search strategy and selection criteria

This is a comprehensive systematic review of the prevalence of HIV, Syphilis, and co-infection of HIV and Syphilis among men who have sex with men (MSM). The search took place on January 5, 2021, by searching the following databases: PubMed, Web of Science, and Google Scholar. The keywords “Prevalence”, “HIV”, “Syphilis”, “HIV and Syphilis co-infection”, “Men who have sex with men”, “MSM”, “Male sex workers”, “gay men” and all the countries in Asia (“India”, “Pakistan”, “Bangladesh”, “China”, and so on) and all possible combinations of them were used. For instance, one of the combinations is:

((Prevalence [Title]) AND ((HIV [Title]) OR (Syphilis [Title]) OR (co-infection [Title])) AND ((Men who have sex with men [Title]) OR (MSM [Title])) AND (China [Title]))).

We also searched websites for HIV surveillance and country-specific ministries of health. We considered the studies which were published between Jan 1, 2000, and December 30, 2020, and published only in English. All the identified research articles and reports were stored in EndNote software (Version X8.1).

2.2. Inclusion/exclusion criteria

The studies were included if and only if the study population or part of the study population of the corresponding study is MSM or male sex workers or gay men or other men who had sex with men. The studies were excluded if the full text were not available, unrelated to the topic, studies without sufficient data such as did not report the study design, study site, and sample size, or did not report at least one of the following information about MSM (1) prevalence of HIV, (2) Prevalence of Syphilis, and (3) prevalence of HIV-Syphilis co-infection. We also excluded qualitative articles, review papers, letters to the editor, brief reports, editorials, commentaries, correspondence, local reports, Ph.D. and Master thesis, conference abstracts, and presentations.

2.3. Screening and extraction

Initially, duplicate records and unrelated topics were removed by screening the titles and abstracts which was done by one author (SM). Two independent authors (AB, MI) randomly checked 10% of the initially screened records for accuracy and no inconsistencies were found. The screened records were considered for full-text review if titles and abstracts suggested that articles might have relevant information. Then two reviewers (AI, MM) independently did the full-text review. The confusion or inconsistency was resolved by consulting with reviewer HH. Data extracted from eligible studies in a standard data extraction form (Excel file). Then data were also cross-checked for accuracy by the reviewer (SM) against the source.

2.4. Statistical analysis

All statistical analyses were carried out using the syntax “meta” in the commercially available statistical software STATA (version 16). Firstly, the overall pooled prevalence along with 95% CI and heterogeneity statistics was estimated from the summary of the meta-analysis. The between-study heterogeneity for the selected studies was assessed using the Q-test and I^2 statistics with a 5% level of significance [55,56]. Then, we applied a random effect model to estimate the pooled prevalence of HIV, syphilis, and their co-infection with 95% confidence intervals and the relative weight for each study. All the results of the meta-analysis were presented in either forest plots or tables. Afterward, the sources of heterogeneity were identified by conducting a subgroup analysis. The univariate and multivariable meta-regressions were also applied to identify the potential source of heterogeneity. The study location/country, study duration, and sampling method were considered for conducting subgroup analysis to observe the prevalence of them from different stratifications. Finally, the funnel plot and Egger’s test were used to identify the potential publication bias [53,57]. The non-parametric trim-and-fill method was also employed to assess the publication bias. Trends in the pooled prevalence of HIV, syphilis, and their co-infection were inspected by assigning all selected studies to different groups based on the study duration.

3. Results

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig. 1) were followed for collecting and reviewing the articles in this systematic review and meta-analysis. In the initial search, we identified a total of 2704 articles including 168 surveillance reports. We removed 2407 duplicates and title mismatches from the list. Then, the screening was done for 465 records and we removed 194 studies. In the eligibility step, 205 studies were removed because at least one of the prevalence (HIV, Syphilis, Co-infection) was not reported, or study duration was not reported, or sampling method was not reported, the study location was not reported, or study period was before 2000. Finally, 66 eligible studies were included in the meta-analysis.

The information that has been extracted from the finally selected studies is as follows: Name of the first author, year of publication, study location, study duration, study design, sampling methods, sample size or number of MSM tested for HIV, and the number of positive cases, number of MSM tested for Syphilis and number of positive cases, and the number of co-infected individuals (HIV-Syphilis).

3.1. Study characteristics

Table 1 describes the characteristics of the selected studies [4,34,35,39,40,58–118]. Of the 40 studies that came from East Asia, 13 studies were from each region, South Asia, and South-East Asia. A total population of 128,510 for HIV and 129,090 for Syphilis has been covered under all eligible studies. Most of the eligible studies (52, including three consecutive sequential) are cross-sectional studies. Among the remaining studies, 13 are surveillance reports and one is a cohort study. A variety of sampling methods have been used among selected pieces of literature. Internet and venue-based sampling were used by 10.14% of selected studies, RDS (respondent-driven sampling) was considered in 27.54% of studies, Snowball sampling was considered in 15.94% of studies, Voluntary Counseling and Testing (VCT) was used by 5.80% of studies, Time location sampling was used by 5.80% of the studies, 11.59% of studies used Venue-day-time sampling (VDTS), whereas 5.80% studies used Convenience sampling methods, 10.14% of the studies used Multiple sampling methods and 7.25% of studies used other sampling methods (Community-based sampling, Long-chain referral sampling, Combination of RDS (respondent-driven sampling) and Snowball, Probability-based sampling, the combination of Cluster sampling and RDS. The average response rate is 92% (median = 99.3) with a minimum response rate is 43% and a maximum is 100%.

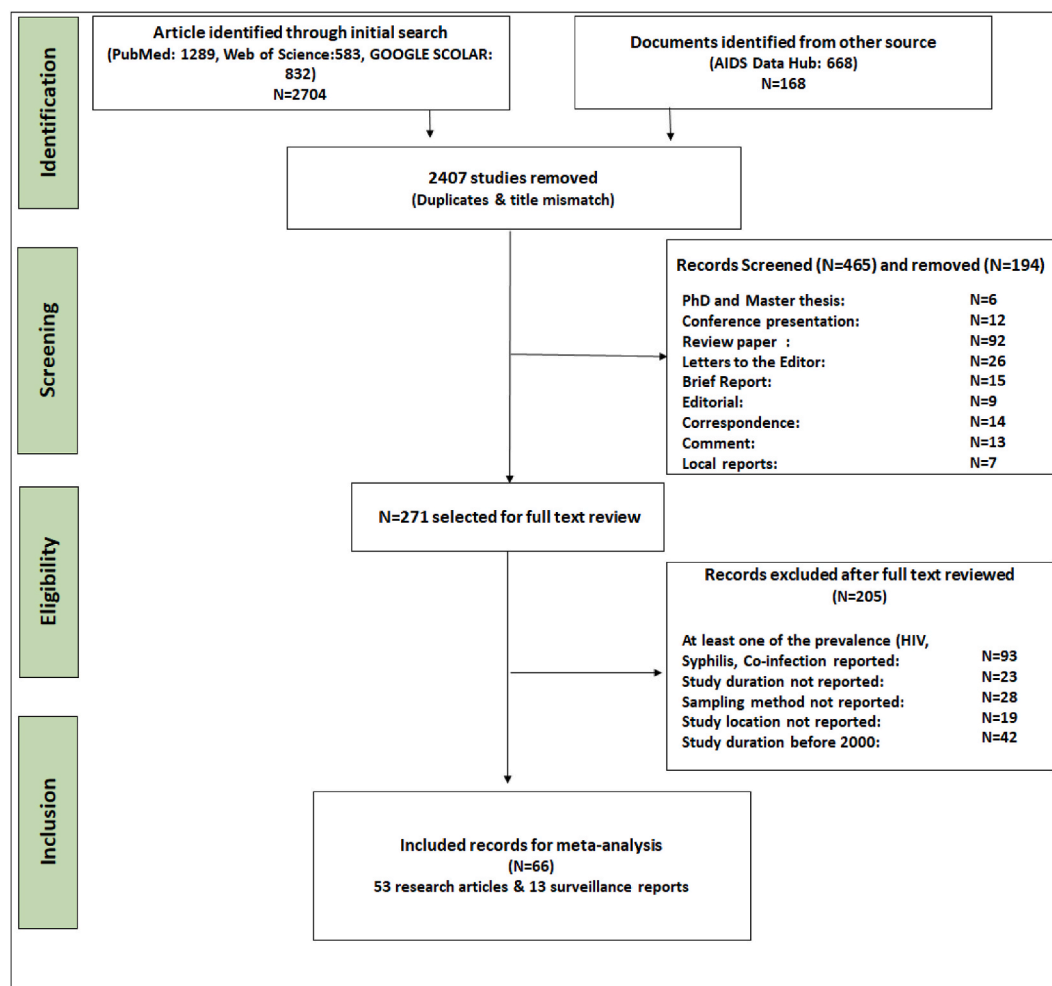


Fig. 1. Flowchart describing the study selection approaches by following the PRISMA 2009 guidelines.

3.2. Statistical heterogeneity and publication bias

The statistical tools Q-test and I^2 (%) with respective p -value were used to investigate the heterogeneity of the studies included in the analysis. We found statistically significant heterogeneity ($I^2 = 99.3$, $Q = \chi^2 (68) = 3414.66$, $P < 0.01$) for HIV, ($I^2 = 99.28\%$, $Q = \chi^2 (68) = 5684.81$, $P < 0.01$) for syphilis, and ($I^2 = 97.85\%$, $Q = \chi^2 (17) = 3273.71$, $P < 0.01$) for HIV and Syphilis co-infection. The Egger's test and funnel plot show that there was significant publication bias ($z = 5.7$, $P < 0.001$) for HIV (see Fig. 2a) and for syphilis ($z = 7.7$, $P < 0.001$) (see Fig. 2b). However, there was no significant publication bias ($z = -0.04$, $P > 0.05$) for HIV and Syphilis co-infection (see Fig. 2c). The nonparametric trim-and-fill analysis of publication bias shows that there was no missing study for estimating the prevalence of HIV, the prevalence of Syphilis, and the prevalence of their co-infection. Therefore, the overall estimated effect sizes were not affected by the publication bias.

3.3. Prevalence

The prevalence of HIV among MSM was assessed in 66 studies. The pooled prevalence of HIV was 8.48% (CI: 7.01–9.95, $I^2 = 99.35\%$) estimated from 69 estimates of 66 studies (presented in Fig. 3). Similarly, 69 estimates in 66 studies were considered to estimate the overall prevalence of Syphilis among MSM in this meta-analysis. The estimated pooled prevalence of Syphilis was 9.86% (CI: 8.30–11.41, $I^2 = 99.28\%$) (shown in Fig. 4). The prevalence of HIV and Syphilis co-infection was estimated in 17 studies out of 66 studies. The pooled prevalence of HIV- Syphilis co-infection was calculated as 2.99% (CI: 1.70–4.27, $I^2 = 97.85\%$) (Fig. 5).

3.4. Trends in HIV, syphilis, and HIV and syphilis co-infection prevalence

The pooled estimate of HIV prevalence among MSM in Asia has an increasing trend with some fluctuations during 2002–2017. The

Table 1

Features of the studies included in the Meta-analysis.

Study	Region	Design	Sampling Method	Study duration	Sample size for HIV	Sample size for Syphilis	Prevalence of HIV (95% CI)	Prev. of Syphilis (95% CI)	Prev. of Co-infection (95% CI)
Solomon et al., 2015	India	Cross-sectional	RDS (respondent-driven sampling)	2002	11997	279	2.50 (2.22–2.78)	1.10 (–0.12–2.32)	N.A.
Solomon et al., 2010	India	Cross-sectional	RDS (respondent-driven sampling)	Sep 2004–June 2005	721	477	1.47 (0.59–2.35)	13.47 (10.41–16.53)	0.42 (–0.16–1.00)
Pisani et al., 2004	Indonesia	Cross-sectional	Multiple methods	June–Nov 2005	279	526	3.20 (1.13–5.27)	11.20 (8.5–13.9)	N.A.
IBBS, 2011	Bangladesh	Cross-sectional	Venue-day-time sampling (VDTS)	January 2003–Dec 2004	1359	831	12.50 (10.74–14.26)	14.00 (11.64–16.36)	N.A.
Choi et al., 2007	China	Cross-sectional	Snowball sampling	2004	477	400	3.90 (2.16–5.64)	1.70 (0.43–2.97)	N.A.
Zhang et al., 2012	China	Cross-sectional	RDS (respondent-driven sampling)	October–November 2008	300	721	9.00 (5.76–12.24)	8.00 (6.02–9.98)	N.A.
Wu et al., 2013	China	Cross-sectional	RDS (respondent-driven sampling) & Snowball	Feb 2008–Sep 2009	47231	47231	4.90 (4.71–5.09)	11.80 (11.51–12.09)	12.50 (12.20–12.80)
Feng et al., 2009	China	Cross-sectional	Venue-day-time sampling (VDTS)	2006	1000	1000	10.40 (8.51–12.29)	9.30 (7.50–11.10)	1.70 (0.90–2.50)
Feng et al., 2009	China	Cross-sectional	Venue-day-time sampling (VDTS)	2007	1044	1044	12.50 (10.49–14.51)	8.50 (6.81–10.19)	2.70 (1.72–3.68)
Pham et al., 2012	Vietnam	Cross-sectional	Venue-day-time sampling (VDTS)	2009	389	389	6.30 (3.89–8.71)	1.30 (0.17–2.43)	N.A.
IBBS, 2007	Vietnam	surveillance	Cluster sampling and RDS	Aug–Nov 2007	790	749	5.20 (3.65–6.75)	4.30 (2.85–5.75)	N.A.
Huang et al., 2015	Taiwan	Cross-sectional	Venue-day-time sampling (VDTS)	2009	1208	307	5.90 (4.57–7.23)	20.20 (15.71–24.69)	N.A.
Morineau et al., 2011	Indonesia	Cross-sectional	Multiple methods	April 2008–Nov 2009	749	1651	5.70 (4.04–7.36)	16.50 (14.71–18.29)	N.A.
IBBS, 2015	Nepal	surveillance	RDS (respondent-driven sampling)	2007–2008	400	928	1.70 (0.43–2.97)	3.12 (2–4.24)	N.A.
IBBS, 2013	Philippines	surveillance	Time location sampling	2007	6281	294	4.80 (4.27–5.33)	11.40 (7.77–15.03)	1.70 (0.22–3.18)
IBBS, 2017	Nepal	surveillance	RDS (respondent-driven sampling)	Sep–Oct 2009	400	501	8.00 (5.34–10.66)	22.00 (18.37–25.63)	4.20 (2.44–5.96)
IBBS, 2012	Myanmar	surveillance	Convenience sampling methods	March–July 2007	400	513	9.10 (6.28–11.92)	28.10 (24.21–31.99)	N.A.
IBBS, 2011	Timor Leste	surveillance	RDS (respondent-driven sampling)	May–Aug 2006	159	423	1.30 (–0.46–3.06)	14.80 (11.42–18.18)	0.50 (–0.17–1.17)
Guo et al., 2012	China	Cross-sectional	Internet, and venue-based sampling	April–August 2008	307	1693	6.90 (4.06–9.74)	12.20 (10.64–13.76)	N.A.
Zhao et al., 2012	China	Cross-sectional	Venue-day-time sampling (VDTS)	July–Sep 2006	1651	4983	2.90 (2.09–3.71)	9.80 (8.97–10.63)	N.A.
Ruan et al., 2009	China	Cross-sectional	RDS (respondent-driven sampling)	June–Sep 2009	928	570	13.30 (11.12–15.48)	15.90 (12.9–18.9)	N.A.
Zhang et al., 2013	China	Cross-sectional	RDS (respondent-driven sampling)	Oct–Dec 2009	492	503	15.70 (12.49–18.91)	6.60 (4.43–8.77)	2.00 (0.78–3.22)
Zou et al., 2011	China	Cross-sectional	Internet, and venue-based sampling	May–July 2008	429	407	7.30 (4.84–9.76)	14.40 (10.99–17.81)	N.A.
Fan et al., 2012	China	Cross-sectional	RDS (respondent-driven sampling)	Feb–July 2008	501	617	16.20 (12.97–19.43)	11.70 (9.16–14.24)	4.20 (2.62–5.78)
Feng et al., 2010	China	Cross-sectional	Snowball sampling	2008	513	2936	7.70 (5.39–10.01)	14.30 (13.03–15.57)	2.60 (2.02–3.18)
He et al., 2009	China	Cross-sectional		April–August 2008	423	600	6.70 (4.32–9.08)	8.30 (6.09–10.51)	1.50 (0.53–2.47)

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Table 1 (continued)

Study	Region	Design	Sampling Method	Study duration	Sample size for HIV	Sample size for Syphilis	Prevalence of HIV (95% CI)	Prev. of Syphilis (95% CI)	Prev. of Co-infection (95% CI)
Ruan et al., 2007	China	Cross-sectional	Long-chain referral sampling	March 2008–Dec 2009	526	600	6.00 (3.97–8.03)	18.00 (14.93–21.07)	2.50 (1.25–3.75)
She et al., 2013	China	Cross-sectional	Community-based sampling	2008–2009	1693	483	30.50 (28.31–32.69)	6.60 (4.39–8.81)	N.A.
Xiao et al., 2010	China	Cross-sectional	Snowball sampling	April–July 2008	4983	394	5.30 (4.68–5.92)	14.30 (10.84–17.76)	N.A.
Zeng et al., 2014	China	Cross-sectional	Multiple methods	April 2008–Jan 2009	570	436	3.00 (1.60–4.40)	5.00 (2.95–7.05)	N.A.
Zhang et al., 2012	China	Cross-sectional	Snowball sampling	2008–2009	503	307	5.90 (3.84–7.96)	20.20 (15.71–24.69)	N.A.
Zhang et al., 2013	China	Cross-sectional	RDS (respondent-driven sampling)	2009	302	400	3.80 (1.64–5.96)	2.50 (0.97–4.03)	N.A.
Li et al., 2016	China	Cross-sectional	Snowball sampling	2008	1316	400	28.80 (26.35–31.25)	14.10 (10.69–17.51)	N.A.
Qu et al., 2016	China	Cross-sectional	RDS (respondent-driven sampling)	Aug–Nov 2007	1611	720	24.40 (22.30–26.50)	26.80 (23.56–30.04)	N.A.
Huan et al., 2015	China	Cross-sectional	Snowball sampling	June–Oct 2009	407	418	3.30 (1.56–5.04)	10.50 (7.56–13.44)	N.A.
Ma et al., 2016	China	Cross-sectional	RDS (respondent-driven sampling)	30 Sep 2012–24 June 2013	617	11997	7.00 (4.99–9.01)	2.62 (2.33–2.91)	N.A.
Das et al., 2015	China	Cross-sectional	RDS (respondent-driven sampling)	2011	2936	1359	1.00 (0.64–1.36)	4.46 (3.36–5.56)	N.A.
Luo et al., 2015	China	Cross-sectional	Snowball sampling	2011	259	300	7.00 (3.89–10.11)	12.00 (8.32–15.68)	2.90 (1.00–4.80)
Liu et al., 2016	China	Cross-sectional	Multiple methods	2012	3588	1208	4.38 (3.71–5.05)	2.15 (1.33–2.97)	N.A.
Wei et al., 2013	China	Cross-sectional	Internet, and venue-based sampling	2011	600	6281	3.41 (1.96–4.86)	1.65 (1.33–1.97)	N.A.
Zheng et al., 2016	China	Cross-sectional	Snowball sampling	2011	3717	400	7.80 (6.94–8.66)	2.50 (0.97–4.03)	N.A.
Gao et al., 2015	China	Cross-sectional	Multiple methods	2011	600	159	2.60 (1.33–3.87)	7.10 (3.11–11.09)	N.A.
Wu et al., 2016	China	Cross-sectional	Snowball sampling	2010	522	492	11.70 (8.94–14.46)	4.70 (2.83–6.57)	N.A.
Zhang et al., 2017	China	Cross-sectional	Venue-day-time sampling (VDTS)	May–July 2010	300	302	9.90 (6.52–13.28)	19.20 (14.76–23.64)	N.A.
Shen et al., 2017	China	Cross-sectional	Convenience sampling methods	April–July 2012	657	1611	6.83 (4.9–8.76)	23.65 (21.57–25.73)	3.17 (2.31–4.03)
Guanghua et al., 2018	China	Consecutive cross-sectional	The voluntary counseling and testing (VCT)	May–Dec 2011	1996	259	8.90 (7.65–10.15)	12.70 (8.64–16.76)	1.50 (0.02–2.98)
Guanghua et al., 2018	China	Consecutive cross-sectional	Internet, and venue-based sampling	June 2012–June 2013	1965	3717	11.10 (9.71–12.49)	8.80 (7.89–9.71)	N.A.
Guanghua et al., 2018	China	Consecutive cross-sectional	Internet, and venue-based sampling	March–August 2010	1697	522	3.40 (2.54–4.26)	4.40 (2.64–6.16)	N.A.
Liu et al., 2018	China	Cross-sectional	Internet, and venue-based sampling	2012–2013	3588	657	5.30 (4.57–6.03)	19.20 (16.19–22.21)	2.60 (1.38–3.82)
Liu et al., 2016	China	Cross-sectional	Snowball sampling	2013	587	1996	6.60 (4.59–8.61)	9.30 (8.03–10.57)	N.A.
Yang et al., 2014	China	Cohort study	Convenience sampling methods	2009–2011	839	277	11.90 (9.71–14.09)	11.10 (7.4–14.8)	N.A.
Storm et al., 2020	Nepal	Cross-sectional	RDS (respondent-driven sampling)	2011	340	768	24.79 (20.2–29.38)	2.62 (1.49–3.75)	N.A.
Narayanan et al., 2013	India	Cross-sectional	Voluntary counseling and testing (VCT)	2011	483	1250	8.00 (5.58–10.42)	9.00 (7.41–10.59)	N.A.

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Table 1 (continued)

Study	Region	Design	Sampling Method	Study duration	Sample size for HIV	Sample size for Syphilis	Prevalence of HIV (95% CI)	Prev. of Syphilis (95% CI)	Prev. of Co-infection (95% CI)
Hossain et al., 2018	India	Cross-sectional	Venue-day-time sampling (VDTS)	2015	277	400	2.40 (0.60–4.20)	4.80 (2.71–6.89)	N.A.
Kumta et al., 2010	India	Cross-sectional	Voluntary counseling and testing (VCT)	2015–2016	831	400	6.20 (4.56–7.84)	1.50 (0.31–2.69)	N.A.
Cai et al., 2010	China	Cross-sectional	Time location sampling	Sep 2014–January 2015	394	300	17.00 (13.29–20.71)	11.30 (7.72–14.88)	N.A.
Xu et al., 2011	China	Cross-sectional	Voluntary counseling and testing (VCT)	2014	436	1965	8.40 (5.80–11.00)	9.80 (8.49–11.11)	N.A.
Wang et al., 2013	China	Cross-sectional	Multiple methods	2015	307	1697	11.20 (7.67–14.73)	6.10 (4.96–7.24)	N.A.
IBBS, 2009	Nepal	surveillance	RDS (respondent-driven sampling)	2017	400	3588	12.70 (9.44–15.96)	7.50 (6.64–8.36)	2.10 (1.63–2.57)
IBBS, 2005	Nepal	surveillance	RDS (respondent-driven sampling)	42522	400	340	5.00 (2.86–7.14)	4.10 (1.92–6.08)	N.A.
IHBSS, 2009	Philippines	surveillance	Time location sampling	2014	3139	504	1.20 (0.82–1.58)	1.80 (0.64–2.96)	N.A.
IBBS, 2015	Sri Lanka	surveillance	RDS (respondent-driven sampling)	March–April 2015	504	205	18.00 (14.65–21.35)	17.6 (12.39–22.81)	5.40 (2.31–8.49)
IBBS, 2014	Thailand	Cross-sectional	RDS (respondent-driven sampling)	Oct 2005–June 2006	768	790	7.00 (5.20–8.80)	0.90 (0.24–1.56)	N.A.
IBBS, 2011	Indonesia	Cross-sectional	RDS (respondent-driven sampling)	Dec 2013–June 2014	1250	1316	14.00 (12.08–15.92)	11.40 (9.68–13.12)	N.A.
HSS, 2009	Myanmar	Cross-sectional	Convenience sampling methods	2013–2014	400	3588	12.70 (9.44–15.96)	7.50 (6.64–8.36)	N.A.
Colby et al., 2016	Vietnam	Cross-sectional	Snowball sampling	August 2013–May 2014	205	587	12.44 (7.92–16.96)	9.54 (7.16–11.92)	N.A.
Prabawanti et al., 2011	Indonesia	Cross-sectional	Multiple methods	July 2009–December 2010	748	839	15.00 (12.44–17.56)	21.20 (18.43–23.97)	N.A.
Subramanian et al., 2013	India	Cross-sectional	Probability-based sampling	2005–2009	403	3882	1.40 (0.25–2.55)	2.30 (1.83–2.77)	N.A.
Lui et al., 2012	China	Cross-sectional	Time location sampling	2009–2010	418	403	9.80 (6.95–12.65)	4.20 (2.24–6.16)	N.A.

N.A., Not available.

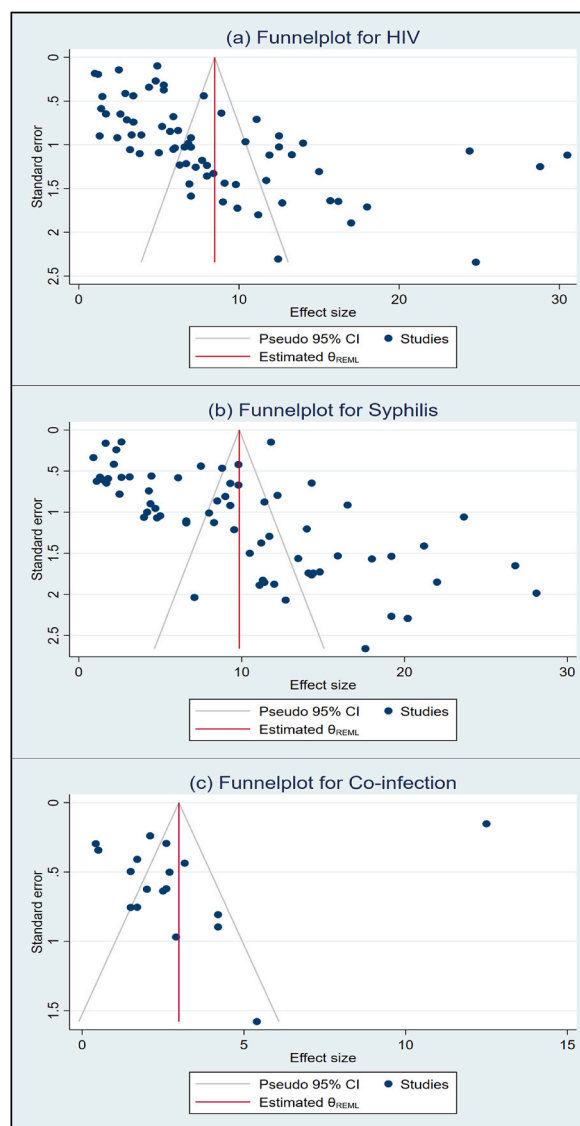


Fig. 2. Funnel plot of result of the prevalence of HIV (a), Syphilis (b), and HIV and Syphilis co-infection (c) among MSM.

prevalence of HIV was 2.50% (95% CI: 2.22–2.78) during 2002–2003 and then it gradually increased to 9.50% (95% CI: 6.25–12.74) during 2008–2009. Afterward, the prevalence fell to 7.83% (95% CI: 4.21–11.45) during 2010–2011 and stood at 6.82% (95% CI: 4.90–8.75) during 2012–2013. Then again the HIV prevalence increased and goes to its peak of 9.55% (95% CI: 3.84–15.25) during 2014–2015 and then reduced to 8.75% (95% CI: 1.20–16.29) during 2016–2017 (Fig. 6). The overall HIV prevalence estimate irrespective of the subgroups is 8.31 (95% CI: 6.64–9.98) which is considered to be a significantly high level of between-countries heterogeneity ($I^2 = 99.47\%$, $p < 0.001$) (Fig. 6).

According to the findings from the meta-analysis, the overall pooled estimate of Syphilis prevalence among MSM in Asia increased during the study period 2002–2007. The prevalence of Syphilis was 1.10% (95% CI: -0.12–2.32) in the 2002–2003 period and increased to 8.68% (95% CI: 1.53–15.83) during 2004–2005 and reached its peak at 14.01% (95% CI: 8.01–20.02) during 2006–2007. After that, the prevalence of Syphilis kept going down and it was 5.88% (95% CI: 2.46–9.30) during 2016–2017. The overall Syphilis prevalence estimate regardless of the subgroup analysis was 10.25% (95% CI: 8.55–11.96) which indicates a significantly high level of between-countries heterogeneity ($I^2 = 99.26\%$, $p < 0.001$) (Fig. 7).

The findings from the meta-analysis show ups and downs among pooled estimates of HIV-Syphilis co-infection among MSM in Asia across all the studies over several periods. The pooled prevalence estimates of HIV-Syphilis co-infection was 0.42% (95% CI: -0.16–1.00) during the 2004–2005 terms. With some fluctuations, the prevalence estimate was found to be 2.10% (95% CI: 1.63–2.57) during 2016–2017. The overall HIV-Syphilis co-infection prevalence estimate irrespective of subgroup analysis is 2.99% (95% CI: 1.70–4.27) indicating a considerably high level of between-studies heterogeneity ($I^2 = 97.85\%$, $p < 0.001$) (Fig. 8).

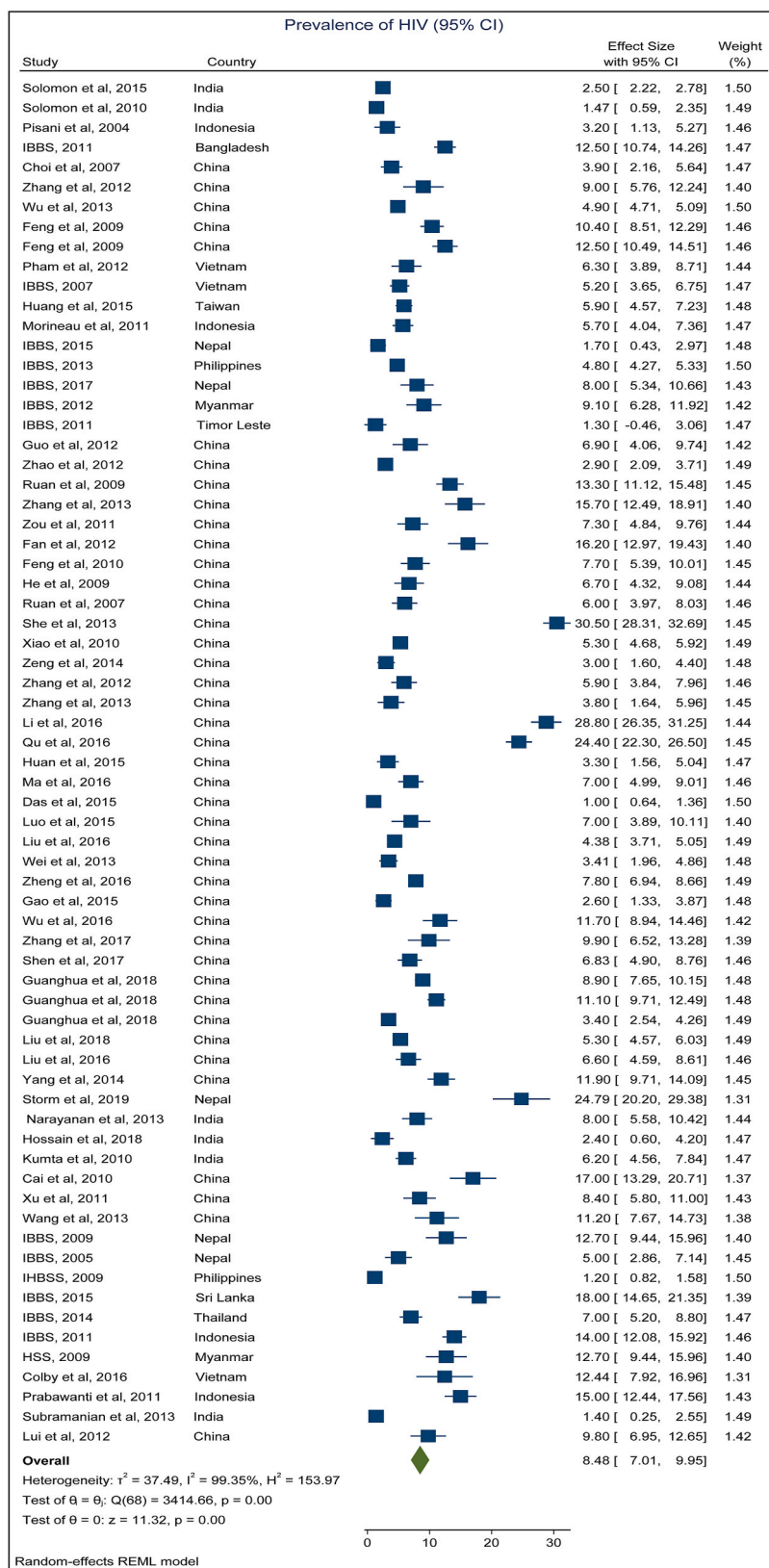


Fig. 3. Forest plot showing the results of the pooled prevalence of HIV among MSM.

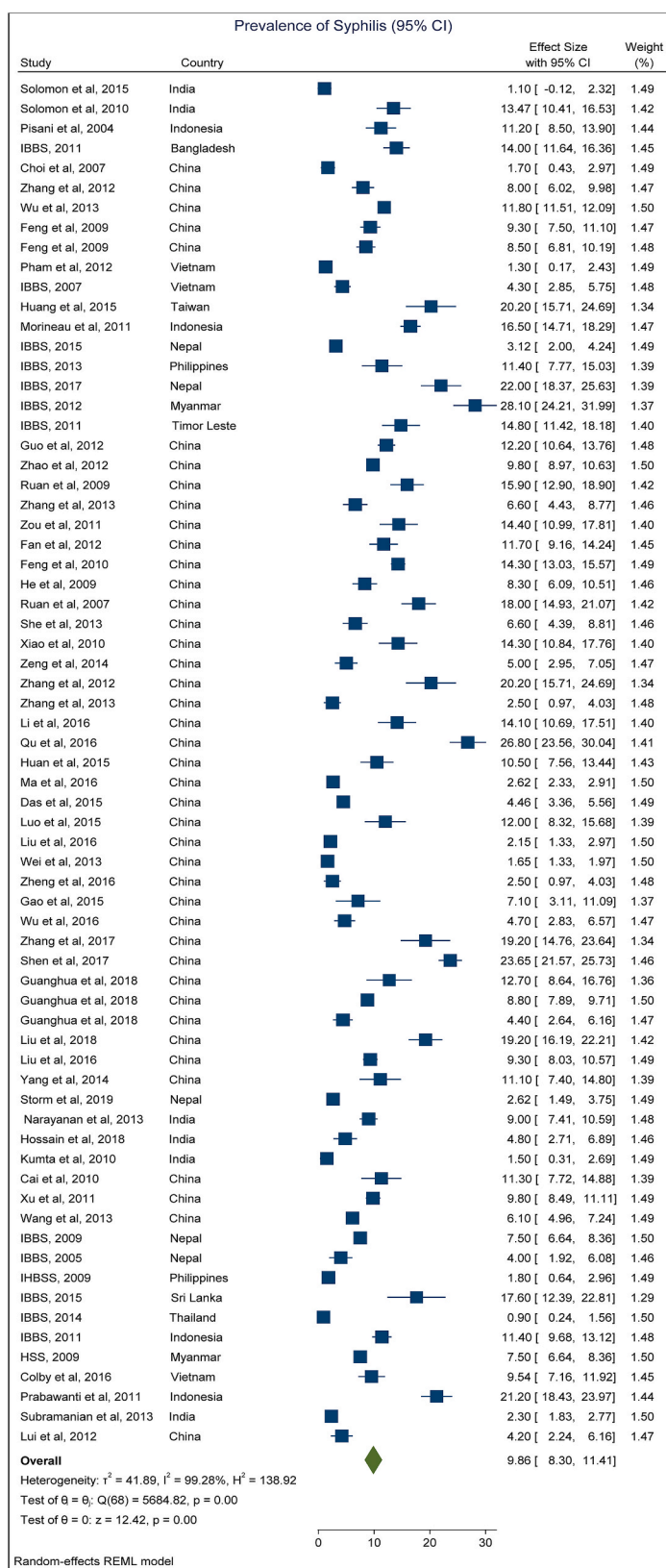


Fig. 4. Forest plot showing the results of the pooled prevalence of Syphilis among MSM.

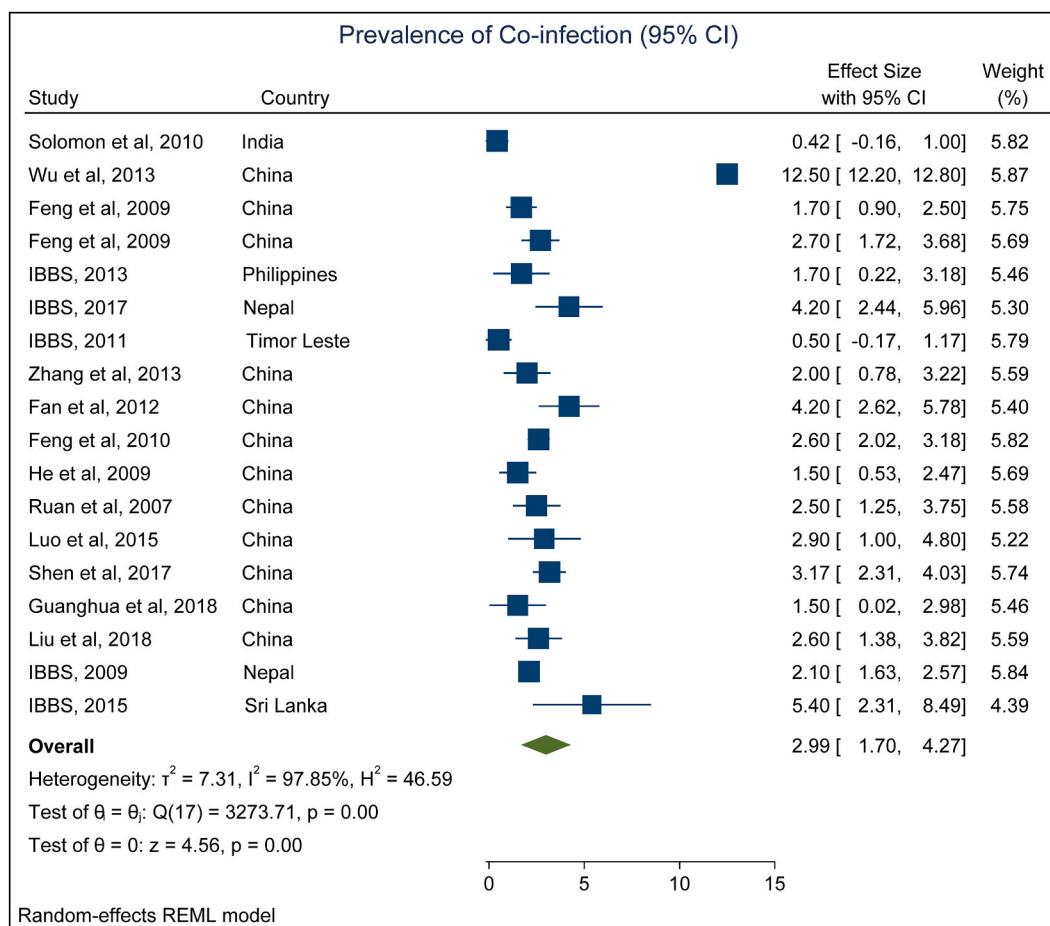


Fig. 5. Forest plot showing the results of the pooled prevalence of HIV-Syphilis co-infection among MSM.

The HIV, Syphilis, and HIV-Syphilis co-infection prevalence estimates exhibited an upward trend consistent with study periods and HIV prevalence exhibited the most increasing trend whereas Syphilis prevalence exhibited the least increasing trend among the studies during 2002–2017 (Fig. 9).

3.5. Subgroup analysis based on Asian regions and countries

The prevalence of HIV, Syphilis, and HIV and Syphilis co-infection were investigated in the different territories of Asia. A total of 43 studies for HIV and Syphilis prevalence were included from the East Asian region. An estimated overall HIV and Syphilis prevalence of 9% (95% CI: 7.06–10.93), presented in Fig. 10, and 10.26% (95% CI: 8.43–10.10), presented in Fig. 11, was found respectively. In addition, 13 studies were included in the analysis from the South Asian region, and the estimated overall HIV and Syphilis prevalence was 7.87% (95% CI: 4.08–11.66), presented in Figs. 10 and 7.72% (95% CI: 4.12–11.32), presented in Fig. 11 respectively. Totally 13 studies were included in this systematic review and meta-analysis from the Southeast Asian region and the estimated overall HIV prevalence was 7.38% (95% CI: 4.83–9.93), presented in Fig. 10, and Syphilis prevalence was 10.65% (95% CI: 6.30–15.00), presented in Fig. 11. A total of 12, 4, and 2 studies were included from the East Asian, South Asian, and Southeast Asian regions, and estimated overall HIV-Syphilis co-infection prevalence was 3.35% (95% CI: 1.60–5.09), 2.71% (95% CI: 0.64–4.78), and 0.91% (95% CI: 0.20–2.03) respectively presented in Fig. 12. The highest prevalence of HIV in the Asian region was found at 30.50% (95% CI: 28.31–32.69) in the East Asian region and the lowest prevalence was 1% (95% CI: 0.64–1.36) also in the East Asian region. The highest prevalence of Syphilis was found at 28.10% (95% CI: 24.21–31.99) in the Southeast Asian region and the lowest prevalence was 0.90% (95% CI: 0.24–1.56) also in the Southeast Asian region. The highest prevalence of HIV-Syphilis co-infection was found at 12.50% (95% CI: 12.20–12.80) in the East Asian region and the lowest prevalence was 0.42% (95% CI: 0.16–1.00) in the South Asian region.

Table 2 displays the country-wise prevalence estimates of HIV, Syphilis, and HIV-Syphilis co-infection. From China, 42 studies were included in the analysis for the prevalence of HIV and Syphilis, and 12 studies for HIV-Syphilis co-infection. The estimated overall prevalence of HIV, Syphilis, and HIV-Syphilis co-infection were 9.07% (95% CI: 7.10–11.05), 10.04% (95% CI: 8.22–9.08) and 3.55% (95% CI: 1.60–5.09), respectively in the studies conducted in China. From India, five studies were included in the analysis for the

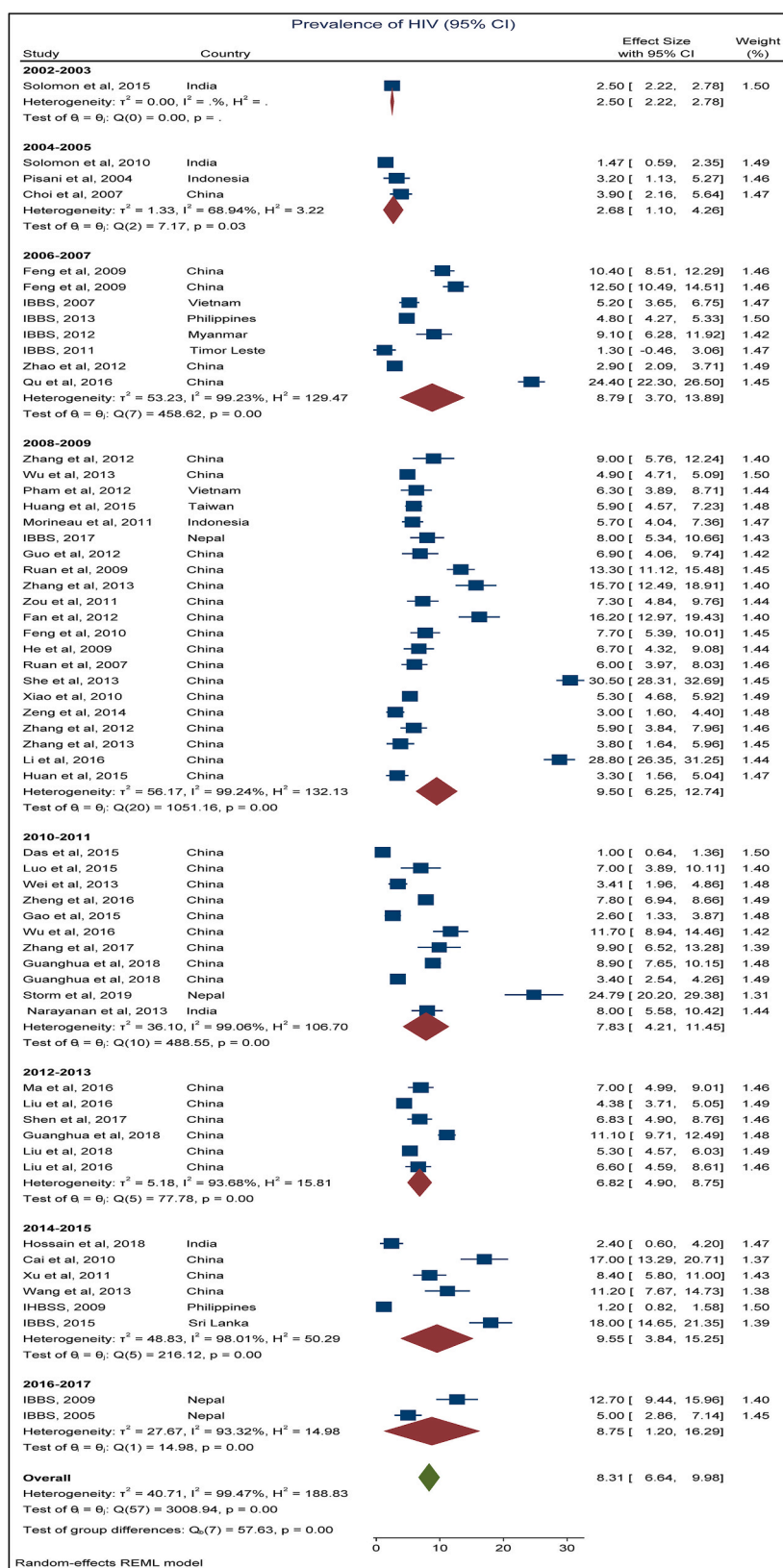


Fig. 6. Forest plot showing changes in the prevalence of HIV over time from 2002 to 2017.

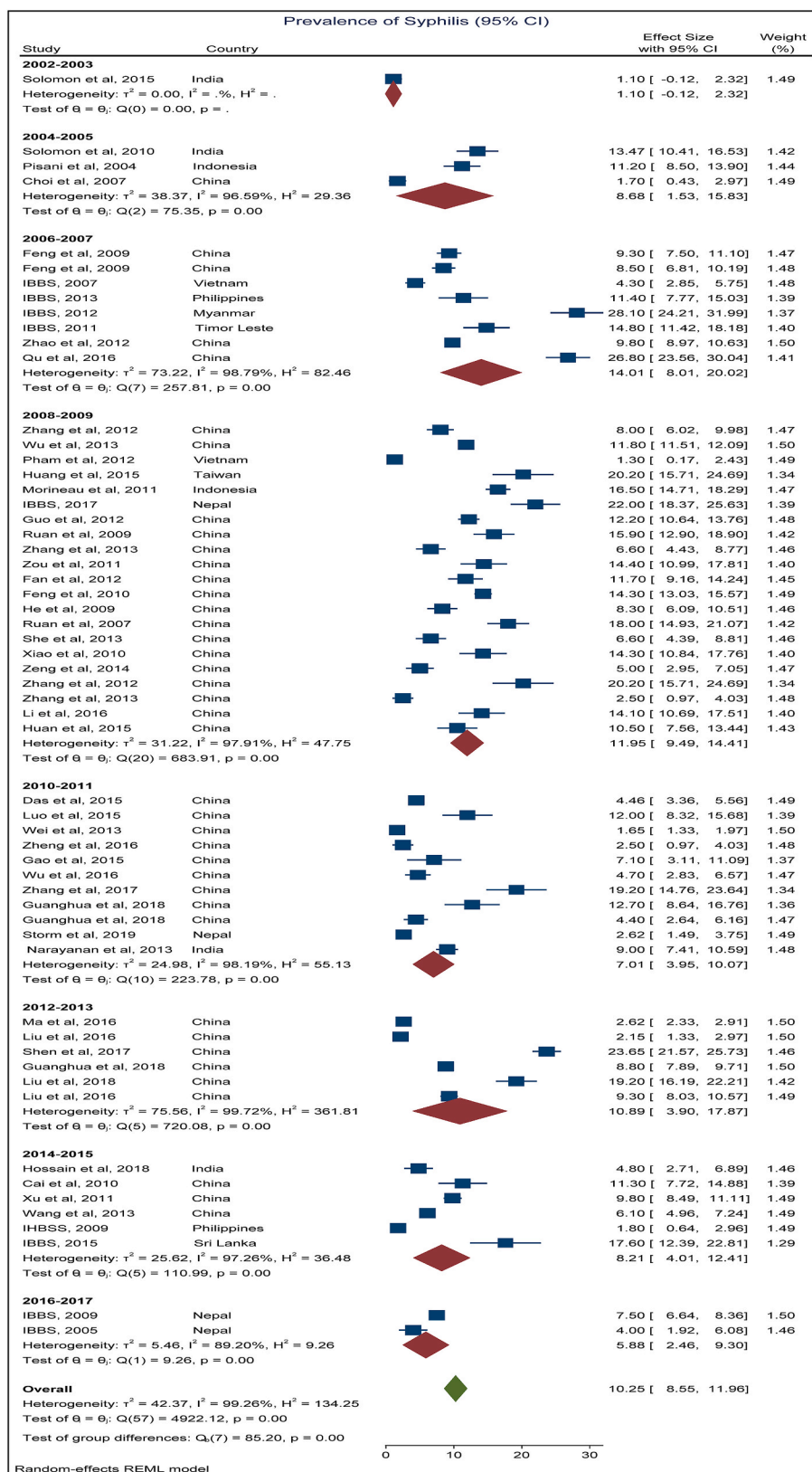


Fig. 7. Forest plot showing changes in the prevalence of Syphilis over time from 2002 to 2017.

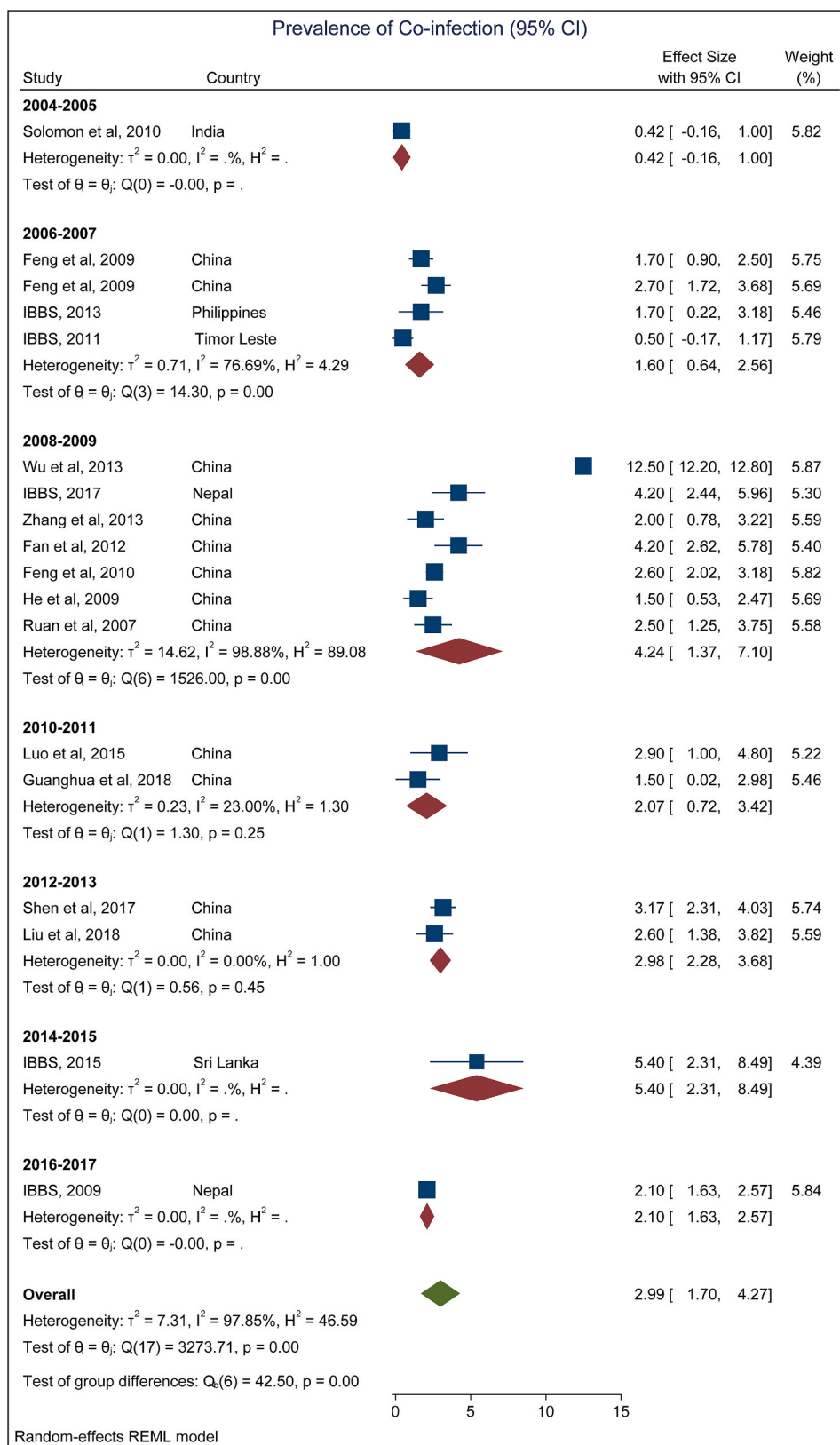


Fig. 8. Forest plot showing changes in the prevalence of HIV and Syphilis co-infection over time from 2002 to 2017.

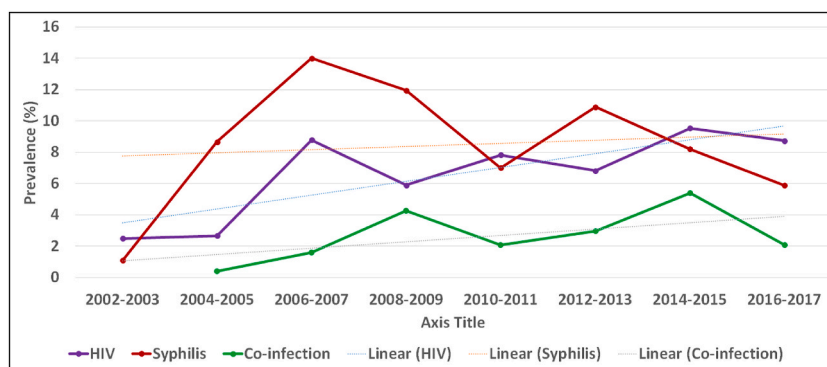


Fig. 9. Trend in HIV, Syphilis, and HIV and Syphilis co-infection prevalence.

prevalence of HIV and Syphilis, and one study for HIV-Syphilis co-infection. Overall prevalence estimates of HIV, Syphilis, and HIV-Syphilis co-infection in the Indian studies were 3.52% (95% CI: 1.43–5.62), 5.23% (95% CI: 1.39–9.08) and 0.42% (95% CI: -0.16–1.00), respectively. From Indonesia, four studies were included and the estimated overall HIV and Syphilis prevalence were 9.45% (95% CI: 3.67–15.22) and 15.04% (95% CI: 10.44–19.64), respectively. Four studies were included in the analysis for the prevalence of HIV and Syphilis, two studies for HIV-Syphilis co-infection from Nepal, and estimated overall HIV, Syphilis, and HIV-Syphilis co-infection prevalence were 10.26% (95% CI: 2.53–17.99), 7.22% (95% CI: 0.77–14.67) and 2.97% (95% CI: 0.94–5.00), respectively. For a complete view of all countries, see [Table 2](#).

3.6. Subgroup analysis based on sampling methods

[Table 3](#) exhibits the prevalence estimates of HIV, Syphilis, and HIV-Syphilis co-infection by different sampling methods used. Internet and venue-based sampling methods were used to estimate the prevalence of HIV and Syphilis in 7 studies, for HIV-Syphilis co-infection in 2 studies among MSM. Here, estimated overall HIV, Syphilis, and HIV-Syphilis co-infection prevalence were 5.25% (95% CI: 2.34–8.17), 8.67% (95% CI: 4.65–12.69) and 6.46% (95% CI: -5.38–18.30) respectively. The estimated overall HIV, Syphilis, and HIV-Syphilis co-infection prevalence based on the community-based sampling method were 7.08% (95% CI: 4.46–9.71), 10.00% (95% CI: 3.07–16.94) and 2.70% (95% CI: 1.72–3.68) respectively. See [Table 3](#) for other methods.

3.7. Meta-regression analysis

The univariate meta-regression revealed that there were no significant predictors of the prevalence of HIV at a 5% level of significance among all the considered variables ([Table 4](#)). However, the multivariable meta-regression shows that the sampling method is a source of significant heterogeneity for HIV prevalence. The prevalence of HIV was increased by 5.94 units (95% CI: 0.16, 11.71) for applying snowball sampling compared to internet and venue-based sampling. Two predictors, age and study time, were identified as the sources of significant heterogeneities for Syphilis prevalence from both univariate and multivariable meta-regressions. The prevalence of Syphilis was increased by 3.34 units (95% CI: -0.24, 6.93) for the median age older than 26 years compared to the median age of 26 years or less. On the contrary, the prevalence of Syphilis was decreased by 5.65 units (95% CI: -9.49, -1.81) in the studies conducted between 2010 and 2020 compared to those studies conducted between 2001 and 2010. All the predictors considered in the multivariable meta-regression were identified as the sources of significant heterogeneity for co-infection. The co-infection prevalence of HIV and Syphilis was increased by 2.38 units (95% CI: 0.62, 4.15) for using the snowball sampling method compared to the internet and venue-based sampling method. The co-infection was also increased by 2.07 units (95% CI: 0.6, 3.54) among MSM with a median age of more than 26 years compared to MSM with a median age of less than or equal to 26 years. In the East-Asia region, the co-infection prevalence was increased by 4.03 units (95% CI: 2.5, 5.56) compared to the South-East Asia region. Moreover, the prevalence of co-infection was increased by 3.65 units (95% CI: 2.05, 5.26) among the studies conducted during 2010–2020 compared to those conducted during 2001–2010.

4. Discussion

To our knowledge, this meta-analysis provides the first comprehensive quantitative analysis of the prevalence of HIV, Syphilis, and their co-infection and also inspected the trends (2002–2017, with a 5-year interval) in HIV, Syphilis, and their co-infection among MSM across Asia. This review paper also illustrates the heterogeneity of the epidemiology of HIV, and Syphilis and their co-infection over different geographical regions and countries.

The Burden of HIV, Syphilis, and co-infection of HIV and Syphilis is disproportionately high among high-risk populations, especially among men who have sex with men (MSM). Globally, this is inspected that the Syphilis epidemic has a strong association with the increase in HIV incidence among MSM [38,40,41]. Despite the early victories at abridging the spread of HIV in some regions like

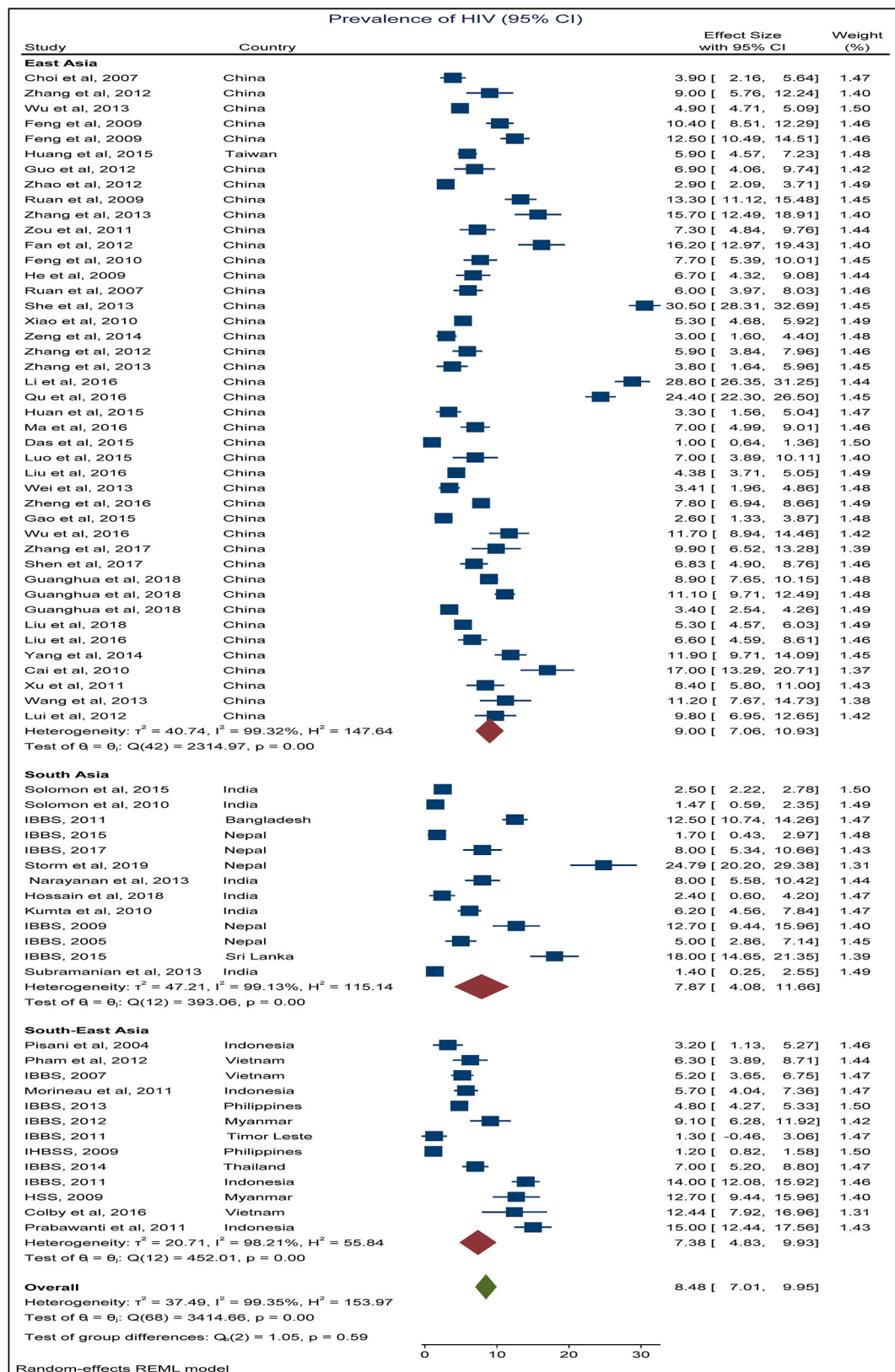


Fig. 10. Forest plot showing regional disparities in the prevalence of HIV from 2002 to 2017 in Asia.

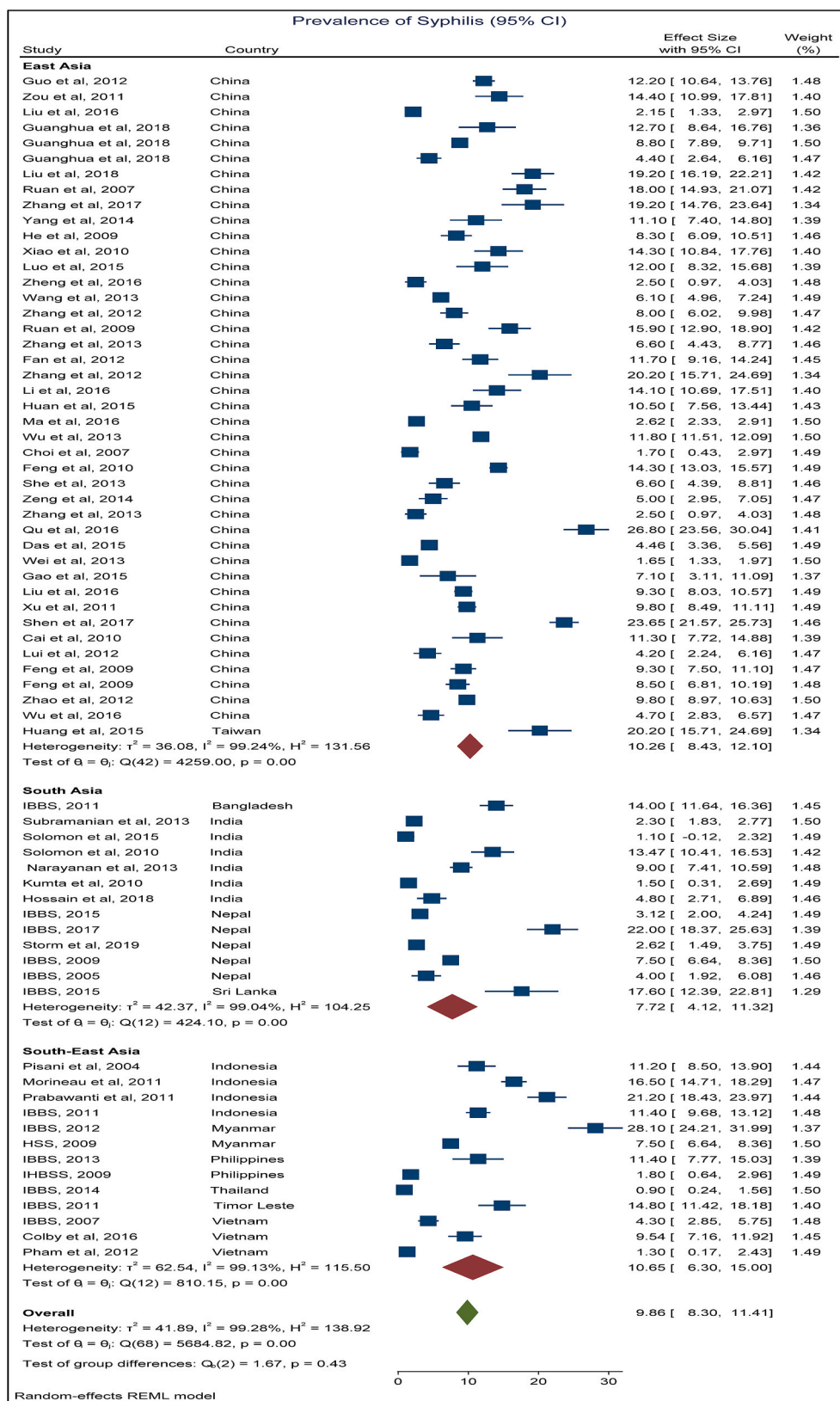


Fig. 11. Forest plot showing regional disparities in Syphilis of HIV from 2002 to 2017 in Asia.

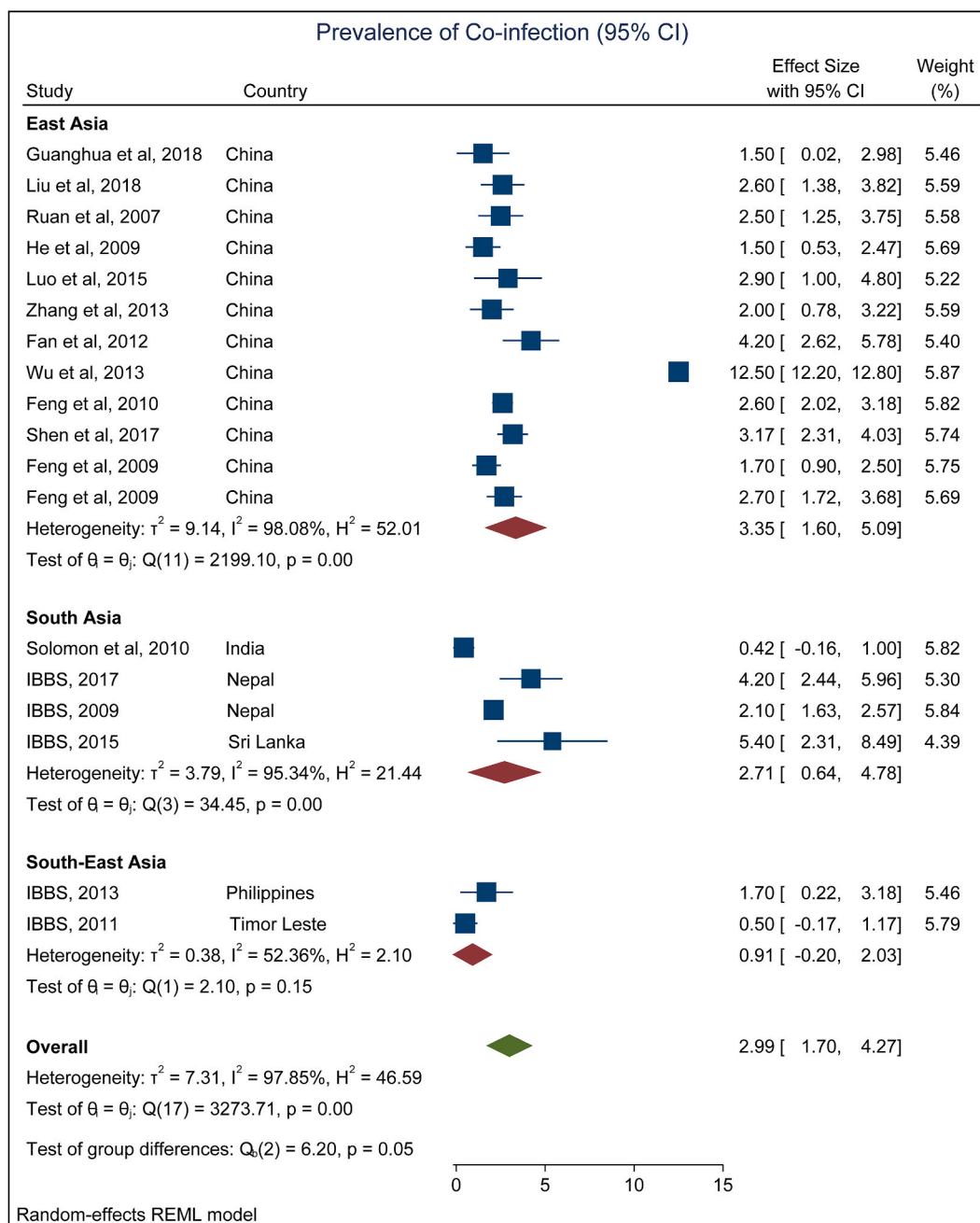


Fig. 12. Forest plot showing regional disparities in the prevalence of HIV and Syphilis co-infection from 2002 to 2017 in Asia.

Thailand and Cambodia, the HIV/AIDS epidemic proceeds to develop in pockets across Asia. Studies in the near past demonstrated that the incidence of sexually transmitted infections (STI) rapidly increases among risk groups and the general population. The scenario of the HIV/AIDS epidemic varies from nation to nation, with countries in East Asia carrying a heavy burden of the illness. HIV/AIDS also differs considerably from the political, cultural, and economical diversity of the nations in Asia [46].

A total of 66 studies including 13 surveillance reports were found eligible from different countries for this systematic review and meta-analysis. A total of 69 prevalence estimates from those 66 studies provide the pooled prevalence of HIV of 8.48% with a combined total of 128,510 participants, Syphilis of 9.86% with a combined total of 129,090 respondents. In addition, 17 studies with a combined total of 61,802 participants showed the prevalence of HIV-Syphilis co-infection at 2.99% across Asia. A higher prevalence of HIV was observed in 2018 in Eastern and Southern Africa (13.2%), western and central Africa (13.7%), and Latin America (12.6%). Comparatively lower prevalence was found in 2018 in Eastern Europe and Central Asia (6.2%), Western and Central Europe and North

Table 2
Subgroup analysis of the prevalence of HIV, Syphilis, and co-infection by country.

Region	HIV % (95% CI) (I^2 , Q (df.) P-value)	Syphilis % (95% CI) (I^2 , Q (df.) P-value)	Co-infection % (95% CI) (I^2 , Q (df.) P-value)
Bangladesh	12.50 (10.74–14.26) ^a	14.00 (11.64–16.36) ^a	–
China	9.07 (7.10–11.05) (I^2 = 99.34, Q (41) = 2312.93, p-value <0.001)	10.04 (8.22–9.08) (I^2 = 99.23, Q (41) = 4221.71, p-value <0.001)	3.55 (1.60–5.09) (I^2 = 98.08, Q (11) = 2199.10, p-value <0.001)
India	3.52 (1.43–5.62) (I^2 = 96.11, Q (5) = 48.21, p-value <0.001)	5.23 (1.39–9.08) (I^2 = 98.29, Q (5) = 125.03, p-value <0.001)	0.42 (–0.16–1.00) ^a
Indonesia	9.45 (3.67–15.22) (I^2 = 96.97, Q (3) = 92.22, p-value <0.001)	15.04 (10.44–19.64) (I^2 = 94.51, Q (3) = 45.62, p-value <0.001)	–
Myanmar	10.80 (7.28–14.33) (I^2 = 62.67, Q (1) = 2.68, p-value = 0.10)	17.7 (–2.48–37.90) (I^2 = 99.03, Q (1) = 102.70, p-value <0.001)	–
Nepal	10.26 (2.53–17.99) (I^2 = 98.09, Q (4) = 123.71, p-value <0.001)	7.22 (0.77–14.67) (I^2 = 99.26, Q (4) = 144.15, p-value <0.001)	2.97 (0.94–5.00) (I^2 = 80.49, Q (1) = 5.13, p-value = 0.02)
Philippines	3.00 (–0.53–6.52) (I^2 = 99.15, Q (1) = 117.16, p-value <0.001)	6.44 (–2.96–15.84) (I^2 = 95.89, Q (1) = 24.34, p-value <0.001)	1.70 (0.22–3.18) ^a
Sri Lanka	18.00 (14.65–21.35) ^a	17.60 (12.39–22.81) ^a	5.40 (2.31–8.49) ^a
Taiwan	5.90 (4.57–7.23) ^a	20.20 (15.71–24.69) ^a	–
Thailand	7.00 (5.20–8.80) ^a	0.90 (0.24–1.56) ^a	–
Timor-Leste	1.30 (–0.46–3.06) ^a	14.80 (11.42–18.18) ^a	0.50 (–0.17–1.17) ^a
Vietnam	7.51 (3.56–11.45) (I^2 = 85.76, Q (2) = 8.88, p-value = 0.01)	4.95 (0.29–9.61) (I^2 = 96.27, Q (2) = 40.43, p-value <0.001)	–

- refers there is no studies were considered in this subgroup.

CI, Confidence Interval.

^a Refers to only one study was included in this subgroup.

America (6.7%), and Asia and the Pacific (4.9%) [119]. A global systematic review estimated a higher prevalence of Syphilis in Latin America and the Caribbean (10.6%) and lower in Australia and New Zealand (1.9%) during 2000–2020 compared to our estimates [120].

Despite a relatively lower prevalence of HIV, Syphilis, and their co-infection in 2002–2003, the overall pooled estimate of HIV prevalence among MSM in Asia substantially fluctuated throughout the study period during 2000–2017. However, the overall prevalence of HIV, Syphilis, and their co-infection among MSM had a slightly upward trend across Asia (Figs. 8 and 9). This finding is consistent with previous research [49,51,121]. The highest prevalence of HIV (9.55%), and co-infection (5.40%) was found during 2014–15, and the lowest prevalence estimates of HIV (2.50%) and co-infection (0.42%) were observed during 2002–03, and 2004–2005, respectively. Besides, the highest prevalence of Syphilis was 14.01% during 2006–07 and the lowest prevalence was 1.10% during 2002–03. The spread might be linked to MSM's unique position in the world. The mainstream public still has a hard time accepting homosexuality. As a result, MSM and women marry often, and MSM may function as a conduit for HIV transmission to other MSM and the general population.

The stratified analyses among geographical regions (East Asia, South Asia, and South-East Asia) showed that the prevalence of HIV, Syphilis, and their co-infection varied by region. In East Asia, the overall prevalence of HIV and Syphilis were 9% and 10.26%, respectively. China exhibits the highest and lowest prevalence in all three cases. Most of the studies included in this research were conducted in the East Asian country China where HIV, Syphilis, and co-infection prevalence is comparatively higher. Also, there is significant variation in the prevalence of HIV, Syphilis, and co-infection in China by region [121]. This might be the reason for finding both the highest prevalence and the lowest prevalence in China. A study was conducted in China to find the frequency of bisexual activity among MSM and was found to be as high as 31.2% [122] which is consistent with our findings. Another systematic review in China observed an increased risk of HIV acquisition after Syphilis exposure [123]. In South Asia, the overall prevalence estimates of HIV and Syphilis were 7.87%, and 7.72%, respectively. Among all South Asian countries, the highest prevalence of HIV and Syphilis was found in Nepal. On the other hand, the lowest prevalence was found in India. Besides, the highest prevalence of co-infection was found in Sri Lanka. Although HIV and Syphilis cases are declining as compared to previous decades, according to UNAIDS, Nepal has still 30,000 HIV-positive adults estimated in 2020 [124]. High-risk groups in Nepal include MSM which is consistent with our study [125]. Sex worker trafficking across borders is a serious issue in Nepal, leading to rising HIV rates. With a greater focus on a two-way flow paradigm, the old idea of HIV, and Syphilis entering Nepal from India is being questioned [126]. Although Sri Lanka is thought to have an extremely low HIV prevalence rate [125], in our study, we found a higher risk of co-infection among MSM in Sri Lanka. The prevalence of Syphilis and co-infection among MSM was 5% in Sri Lanka estimated in 2020 [127] which is consistent with our findings of overall co-infection of 5.40% in Sri Lanka.

In Southeast Asia, the pooled prevalence of HIV and Syphilis are 7.38%, and 10.65%, respectively. The highest (and lowest) prevalence of HIV and Syphilis in this region are in Indonesia (Philippines), and in Myanmar (Thailand), respectively which is consistent with previous studies where MSM showed to have a high and growing HIV prevalence rate, particularly in India, Indonesia, Myanmar, and Thailand [127]. In these regions, a sizable proportion of the MSM population engages in high-risk HIV behaviors. Multiple male sexual partners of all sorts – regular, casual, and paid – combined with irregular condom usage with male and female partners are linked to a high risk of HIV transmission and infection. Despite this, a large proportion of MSM throughout Asia and the

Table 3

Subgroup analysis of HIV prevalence, Syphilis prevalence, and Co-infection of HIV and Syphilis prevalence by sampling method.

Sampling Methods	HIV % (95% CI) (I^2 , Q (df.) P-value)	Syphilis % (95% CI) (I^2 , Q (df.) P-value)	Co-infection % (95% CI) (I^2 , Q (df.) P-value)
Internet and venue-based sampling	5.25 (2.34–8.17) (I^2 = 99.49, Q (6) = 323.65, p-value <0.001)	8.67 (4.65–12.69) (I^2 = 98.49, Q (6) = 502.63, p-value <0.001)	6.46 (–5.38–18.30) (I^2 = 99.92, Q (1) = 1316.53, p-value <0.001)
Community-based sampling	7.08 (4.46–9.71) (I^2 = 91.38, Q (4) = 38.53, p-value <0.001)	10.00 (3.07–16.94) (I^2 = 98.82, Q (4) = 250.91, p-value <0.001)	2.70 (1.72–3.68) ^a
Long-chain referral sampling	1.70 (0.43–2.97) ^a	3.12 (2.00–4.24) ^a	–
Multiple methods	6.51 (3.49–9.54) (I^2 = 97.20, Q (6) = 110.59, p-value <0.001)	16.18 (11.39–20.96) (I^2 = 96.97, Q (6) = 130.78, p-value <0.001)	2.02 (–0.09–4.12) (I^2 = 87.85, Q (2) = 15.66, p-value <0.001)
RDS (respondent-driven sampling)	9.17 (5.15–13.18) (I^2 = 99.57, Q (18) = 1773.44, p-value <0.001)	9.59 (6.45–12.72) (I^2 = 99.46, Q (18) = 965.66, p-value <0.001)	2.59 (1.81–3.38) (I^2 = 58.34, Q (4) = 8.78, p-value = 0.07)
Snowball sampling	9.62 (6.55–12.69) (I^2 = 97.74, Q (10) = 219.38, p-value <0.001)	11.22 (7.19–15.25) (I^2 = 98.34, Q (10) = 424.59, p-value <0.001)	2.58 (1.67–3.49) (I^2 = 45.75, Q (2) = 3.71, p-value = 0.16)
Voluntary counseling and testing (VCT)	8.34 (2.42–14.27) (I^2 = 96.46, Q (3) = 52.39, p-value <0.001)	6.71 (2.29–11.14) (I^2 = 96.18, Q (3) = 94.91, p-value <0.001)	–
Time location sampling	7.33 (2.00–12.65) (I^2 = 96.42, Q (3) = 86.86, p-value <0.001)	4.89 (2.39–7.40) (I^2 = 94.25, Q (3) = 62.77, p-value <0.001)	2.10 (1.63–2.57) ^a
Venue-day time sampling (VDTS)	11.17 (7.46–14.87) (I^2 = 99.03, Q (1) = 102.70, p-value <0.001)	9.15 (4.21–14.09) (I^2 = 99.03, Q (1) = 102.70, p-value <0.001)	5.40 (2.31–8.49) ^a
Other	11.03 (6.36–15.70) (I^2 = 95.35, Q (7) = 240.12, p-value <0.001)	9.92 (5.62–14.22) (I^2 = 99.39, Q (7) = 459.31, p-value <0.001)	1.79 (1.12–2.46) (I^2 = 0.00, Q (1) = 0.16, p-value = 0.69)

- refers to no studies were considered in this subgroup.

CI, Confidence Interval.

^a Refers to only one study was included in this subgroup.

Pacific lack access to HIV prevention and care programs [128,129].

Identifying protective factors for HIV, Syphilis, and co-infection is crucial in the fight against these diseases. In this study, meta-regressions were run to identify the possible predictors of heterogeneity for HIV, Syphilis, and co-infection with a number of explanatory variables, and the results are displayed in Table 4. The prevalence of HIV and co-infection significantly varied by the sampling methods used. A cross-sectional study among MSM conducted across China did not find significant differences in the prevalence estimates of HIV and Syphilis by sampling methods used [63]. However, in this study, we included 66 articles with a range of sampling methods used. Hence, this finding is stronger than a finding derived from a single study. Therefore, we recommend being careful in selecting sampling methods while studying HIV, Syphilis, and co-infection among MSM. Contrary to other studies [63], we did not find a statistically significant association between HIV prevalence and age. However, the prevalence of Syphilis was 3.34 units (95% CI: -0.24, 6.93) higher for the median age older than 26 years compared to the median age of 26 years or less. For co-infection, sampling methods used, participants' ages, study time, and study locations were all significant sources of heterogeneity. In comparison to research conducted between 2001 and 2010, the prevalence of co-infection was 3.65 units (95% CI: 2.05, 5.26) higher in studies conducted between 2010 and 2020. It clearly shows that the co-infection is on the rise. This finding is consistent with other studies [121] conducted in Asia among MSM. The co-infection rate illustrates how the two epidemics interact among MSM in Asia. The rising trend of co-infections may indicate a larger MSM sub-population with a stronger HIV infectivity and/or susceptibility because syphilis increases the probability of HIV transmission [121]. It's also probable that some of the rise in the HIV epidemic among MSM in Asia is being caused by syphilis infections.

In the subgroup analyses, inconsistency between studies was alleviated. The highest prevalence of HIV (11.17%) was found in the studies sampling through Venue-day time sampling (VDTS), the highest Syphilis (16.18%) was found in the studies through multiple methods, and the highest co-infection (6.46%) was found in the studies used the Internet and venue-based sampling (Table 3). An almost opposite finding was observed in a previous study in China [50]. In England [130] individuals with high risk were willing to be tested with the VCT clinic or MSM network method. Therefore, a more appropriate and scientific sampling method needs to be applied in Asian regions as well for a more appropriate estimate of HIV, Syphilis, and their co-infection.

A few limitations of this study should be mentioned. Most of the selected studies were cross-sectional. Non-English literature has been excluded. For some regions or countries, no study was found and most of the studies the findings are based on were conducted in China. Therefore, findings from this meta-analysis and systematic review would not represent all regions of Asia. A large number of included studies used RDS, probability sampling, and snowball sampling rather than population-based sampling which may lead the selection bias [50]. Another drawback is that the publication bias could not be avoided completely. In addition, in the meta-regression

Table 4
Meta-regression for HIV, Syphilis, and their co-infection prevalence.

Variable	Label	Univariate meta-regressions		Multivariable meta-regressions	
		Coeff. (95% CI)	P-values	Coeff. (95% CI)	P-values
HIV prevalence					
Sampling method	Internet, and venue-based sampling	Ref		Ref	
	Snowball sampling	2.25 (−1.6, 6.10)	0.25	5.94 (0.16, 11.71)	0.04
	Others	0.20 (−3.8, 4.21)	0.92	2.86 (−3.33, 9.05)	0.37
Age	≤26	Ref		Ref	
	>26	3.78 (0.3, 7.8)	0.07	3.46 (−1.00, 7.92)	0.13
Study's location	South-East Asia	Ref		Ref	
	East Asia	1.15 (−1.51, 4.51)	0.32	1.11 (−3.46, 5.69)	0.63
Study's conducted time	2001–2010	Ref		Ref	
	2010–2020	−0.18 (−2.82, 3.21)	0.90	−0.14 (−4.91, 4.64)	0.96
Sample size	≤1000	Ref		Ref	
	>1000	−4.91 (−13.53, 3.67)	0.26	−6.55 (−21.42, 8.33)	0.39
Syphilis prevalence					
Sampling method	Internet, and venue-based sampling	Ref		Ref	
	Snowball sampling	−0.56 (−4.67, 3.54)	0.79	2.39 (−2.26, 7.05)	0.31
	Others	1.36 (−2.92, 5.64)	0.53	4.01 (−0.98, 9)	0.12
Age	≤26	Ref		Ref	
	>26	4.90 (1.31, 8.49)	0.01	3.34 (−0.24, 6.93)	0.07
Study's location	South-East Asia	Ref		Ref	
	East Asia	0.53 (−2.68, 3.74)	0.75	−0.64 (−4.32, 3.05)	0.73
Study's conducted time	2001–2010	Ref		Ref	
	2010–2020	−3.42 (−6.5, −0.34)	0.03	−5.65 (−9.49, −1.81)	0.00
Sample size	≤1000	Ref		Ref	
	>1000	−3.49 (−12.65, 5.68)	0.46	−9.54 (−21.46, 2.39)	0.12
Co-infection prevalence of HIV and Syphilis					
Sampling method	Internet, and venue-based sampling	Ref		Ref	
	Snowball sampling	0.43 (−2.92, 3.79)	0.8	2.38 (0.62, 4.15)	0.01
	Others	–		–	
Age	≤26	Ref		Ref	
	>26	0.25 (−1.72, 2.23)	0.8	2.07 (0.6, 3.54)	0.01
Study's location	South-East Asia	Ref		Ref	
	East Asia	1.12 (−1.64, 3.87)	0.43	4.03 (2.5, 5.56)	0.00
Study's conducted time	2001–2010	Ref		Ref	
	2010–2020	−0.19 (−3.02, 2.63)	0.89	3.65 (2.05, 5.26)	0.00
Sample size	≤1000	Not retained		Not retained	
	>1000				

analyses, we used only a few predictor variables because we did not find many variables that are common in the included studies.

5. Conclusion

The findings of this systematic review will have several important implications. First, it will suggest a reappraisal of priorities and systems for HIV/STI surveillance in Asia to enable more robust, valid, and reliable prevalence estimates. Second, information from routine and periodic surveillance could be further validated and strengthened by highly focused, policy-relevant research to address key knowledge gaps in the epidemiological and socio-behavioral profile of specific subpopulations. The findings indicate that HIV, Syphilis, and their co-infection among MSM in Asia pacific region have not slowed down yet. To limit the spread of HIV and Syphilis infection, MSM should be targeted for increased HIV and Syphilis screening, and the development of efficient public health intervention programs is an important recommendation.

6. Declarations

Ethics approval and consent to participate

This study is a systematic review and meta-analysis that used extracted data from different published studies. Therefore, ethical approval and consent to participate are not relevant.

Consent for publication

Not relevant to this study.

Author contribution statement

Sultan Mahmud, Md Mohsin: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Abdul Muyeed: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Md Mynul Islam, Sorif Hossain, Ariful Islam: Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no competing interests.

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