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Global incidence of chlamydia infection and HIV pre-exposure prophylaxis

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Abstract

AIDS is associated with multiple kinds of sexually transmitted infections, including chlamydia. The global epidemiological status of chlamydia infection in individuals receiving AIDS pre-exposure prophylaxis can provide the crucial information. The researchers performed an updated systematic review and meta-analysis of the case-control studies or observational studies of chlamydia infection incidence in subjects receiving AIDS pre-exposure prophylaxis of the studies after 2018. A total of 24 studies, including 67810 subjects receiving AIDS pre-exposure prophylaxis, were included in the meta-analysis. The pooled incidence of chlamydia infection before receiving AIDS pre-exposure prophylaxis in the whole population of the 24 included studies was 46.9% ($p < 0.001$). After at least 6 months of pre-exposure prophylaxis, the pooled incidence of chlamydia infection was 51.8% ($p < 0.001$). For the men who have sex with men subgroup of subjects, the pooled incidence of pre-enrollment and post-pre-exposure prophylaxis was 47.9% and 53.1%, respectively ($p < 0.001$). Significant heterogeneity might influence the interpretations of the meta-analysis results. Chlamydia infection incidence seems to become higher after the implementation of pre-exposure prophylaxis. In addition, the men who have sex with men subgroup are associated with the higher incidence of chlamydia infection in the pre-enrollment and post-pre-exposure prophylaxis phases.

Keywords: *Chlamydia. Infection. Incidence. Pre-exposure prophylaxis.*

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Introduction

AIDS is a dangerous disease with multiple impacts on the worldwide health of people. It will lead to physical and mental impacts on the patients with AIDS[1]. Therefore, the World Health Organization recommended the implementation of pre-exposure prophylaxis (PrEP) to prevent the infection and spread of HIV, such as in the subgroup of men who have sex with men (MSM)[2-4]. Apart from MSM, the PrEP also showed the protection efficacy for the women at risk for HIV infection[5-7]. However, the HIV high-risk group will not only face the AIDS condition. This group of patients will have the risk of other concurrent sexually transmitted diseases, such as chlamydia, gonorrhea, syphilis[6,8-13]. It is important for clinicians to understand the characteristics of other sexually transmitted diseases in the subjects receiving PrEP for HIV infection, including the phase before PrEP and the phase after a duration of PrEP.

Among the other concurrent sexually transmitted diseases, chlamydia is a pathogen with high incidence and prevalence in the HIV high-risk group, even reaching almost 80% in the MSM group with PrEP for HIV infection[6,8-10]. In addition, the chlamydia infection might predispose to the risk of ovarian cancer[14], which might be crucial for women receiving the PrEP for HIV infection if considering the female fertility[15,16]. In the MSM group, the increased chlamydia infection might be associated with the frequent screening intensity, the resistance of antimicrobial treatment, and the potential misinterpretation of lower incidence[17,18]. The previous meta-analysis with most AIDS PrEP studies before 2018 indicated the incidence of chlamydia was around 21.5%[19]. Based on the above literature, the researchers designed the current systematic review and meta-analysis to understand the chlamydia incidence status of subjects receiving PrEP for HIV infection, including the phase before the PrEP and the phase after at least 6 months of PrEP. The AIDS PrEP studies after 2018 will be focused and collected in the present systematic review and meta-analysis. In addition, the chlamydia incidence status of MSM subjects with AIDS PrEP will be analyzed to understand the specific condition in this subgroup.

Methods

Selection of keywords and strategy

The keywords chosen for this research encompassed terms, such as "chlamydia," "infection," "disease," "sexually transmitted disease," "sexually transmissible disease," "sexually transmitted infection," "sexually transmissible disease infection," "chlamydia trachomatis," "genital infection," "genital disease," "genital disorder," " venereal infection," " venereal disease," " venereal disorder," "preexposure prophylaxis," "acquired immunodeficiency syndrome," "human immunodeficiency," "pre-exposure prophylaxis," "incidence," "anal," and "anogenital." A thorough literature search was performed across various databases, including ScienceDirect, PubMed, Web of Science, Embase, Scopus, the Cumulative Index for Nursing and Allied Health Literature, ProQuest, SciELO, and Google Scholar, concentrating on articles published before August 2025.

The meta-analysis utilized specific eligibility criteria to focus on the studies with the incidence data of chlamydia infection before PrEP and after at least 6 months of PrEP. Furthermore, only studies published in English and in international scientific journals were included, with a focus on the cohort or observational studies. Exclusion criteria were applied to exclude the studies that lacked chlamydia infection incidence data, or that the authors were inaccessible to the data, or review article, or studies without the chlamydia infection data before PrEP, or data after 6 months of PrEP.

The assessment and extraction of data from the included literature.

This systematic review and meta-analysis were performed in accordance with the Cochrane Handbook for Systematic Reviews and Interventions. The results are presented according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline[20]. The following data were extracted from the included articles. First, we collected the incidence data of chlamydia infection in individuals before AIDS PrEP from all included studies. Second, the incidence data of chlamydia infection in individuals after AIDS PrEP for at least 6 months from the included studies with such data were also collected. Third, the above two kinds of data in the subgroup of MSM were also collected.

Meta-analysis of pooled incidence

In light of the anticipated heterogeneity, a meta-analysis utilizing a Restricted Maximum Likelihood random-effects model was conducted to ascertain the pooled incidence of chlamydia infection in the subjects before receiving AIDS PrEP and after at least 6 months of AIDS PrEP. To assess the random variables in the included articles, Cochran's Q Chi-square statistics and

the I^2 statistical test were employed. Tau^2 was estimated by the Restricted Maximum-Likelihood method. Subgroup analyses were performed based on MSM subjects in instances of significant heterogeneity to identify potential moderators of the heterogeneity. The publication bias was assessed using the Rank Correlation Test for Funnel Plot Asymmetry and the Regression Test for Funnel Plot Asymmetry. The present meta-analysis was executed using Jamovi 2.3.28 software. Finally, a $p < 0.05$ was considered statistically significant for all analyses.

The collection and assessment of extracted data

X. Zhou, L. Huang, and D. Chen conducted a meticulous review of abstracts and articles to collect the relevant studies. We independently extracted clinical outcome data from the included articles, ensuring that the studies included either direct clinical outcome data or supplementary materials containing such information. To resolve any inconsistency in the findings, X. Zhou, L. Huang, and D. Chen participated in a collaborative review process. Ultimately, the results were assessed and validated by all authors involved in the present systematic review and meta-analysis.

Results

The PRISMA flow diagram

Our selection process is represented by the PRISMA flow diagram shown in figure 1. In total, the 24 included studies[2,3,7,12,21-40], encompassing 67810 subjects with AIDS PrEP, went through the qualitative and quantitative analyses. The assessment of bias risk in the included studies is illustrated in figure 2.

The pooled incidence of chlamydia infection before AIDS PrEP

In the random effects model, the pooled incidence of chlamydia infection before AIDS PrEP from the 24 studies is 46.9% (95% confidence interval [CI]: 40.4%-53.5%, $Z = 14.1$, $p < 0.001$), indicating that a substantial proportion of subjects had chlamydia infection before AIDS PrEP. However, considerable heterogeneity was noted (Fig. 3).

The pooled incidence of chlamydia infection after at least 6 months of AIDS PrEP

In the random effects model, the pooled incidence of chlamydia infection after at least 6 months of AIDS PrEP from the 22 studies is 51.8% (95% CI: 43.4%-60.2%, $Z = 12.1$, $p < 0.001$), indicating that a substantial proportion of subjects had chlamydia infection after at least 6 months of AIDS PrEP. However, considerable heterogeneity was noted (Fig. 4).

The pooled incidence of chlamydia infection before AIDS PrEP and after at least 6 months of AIDS PrEP in MSM subgroup

In the random effects model, the pooled incidence of chlamydia infection before AIDS PrEP from the 19 studies of MSM subjects is 47.9% (95% CI: 40%-55.8%, $Z = 11.9$, $p < 0.001$), indicating that a substantial proportion of MSM subjects had chlamydia infection before AIDS PrEP. However, considerable heterogeneity was noted (Fig. 5). In the random effects model, the pooled incidence of chlamydia infection after at least 6 months of AIDS PrEP from the 19 studies of MSM subjects is 53.1% (95% CI: 43.9%-62.3%, $Z = 11.3$, $p < 0.001$), indicating that a substantial proportion of subjects had chlamydia infection after at least 6 months of AIDS PrEP. However, considerable heterogeneity was noted (Fig. 6).

The sensitivity analysis of chlamydia infection incidence in non-PrEP users

Only 5 included studies[25,30,32,38,39] had the follow-up data of chlamydia infection incidence in non-PrEP users, which are patients with HIV infection that not use PrEP. The sensitivity analysis results showed that the pooled incidence of chlamydia infection in the follow-up phase is 22.4% (95% CI: 8.6%-36.2%, $Z = 3.19$, $p = 0.001$).

Discussion

In the present systematic review and meta-analysis, the results indicated the relatively high incidence of chlamydia infection in the phase before AIDS PrEP. In addition, the incidence of chlamydia infection after at least 6 months of AIDS PrEP increased to 51.8%. It

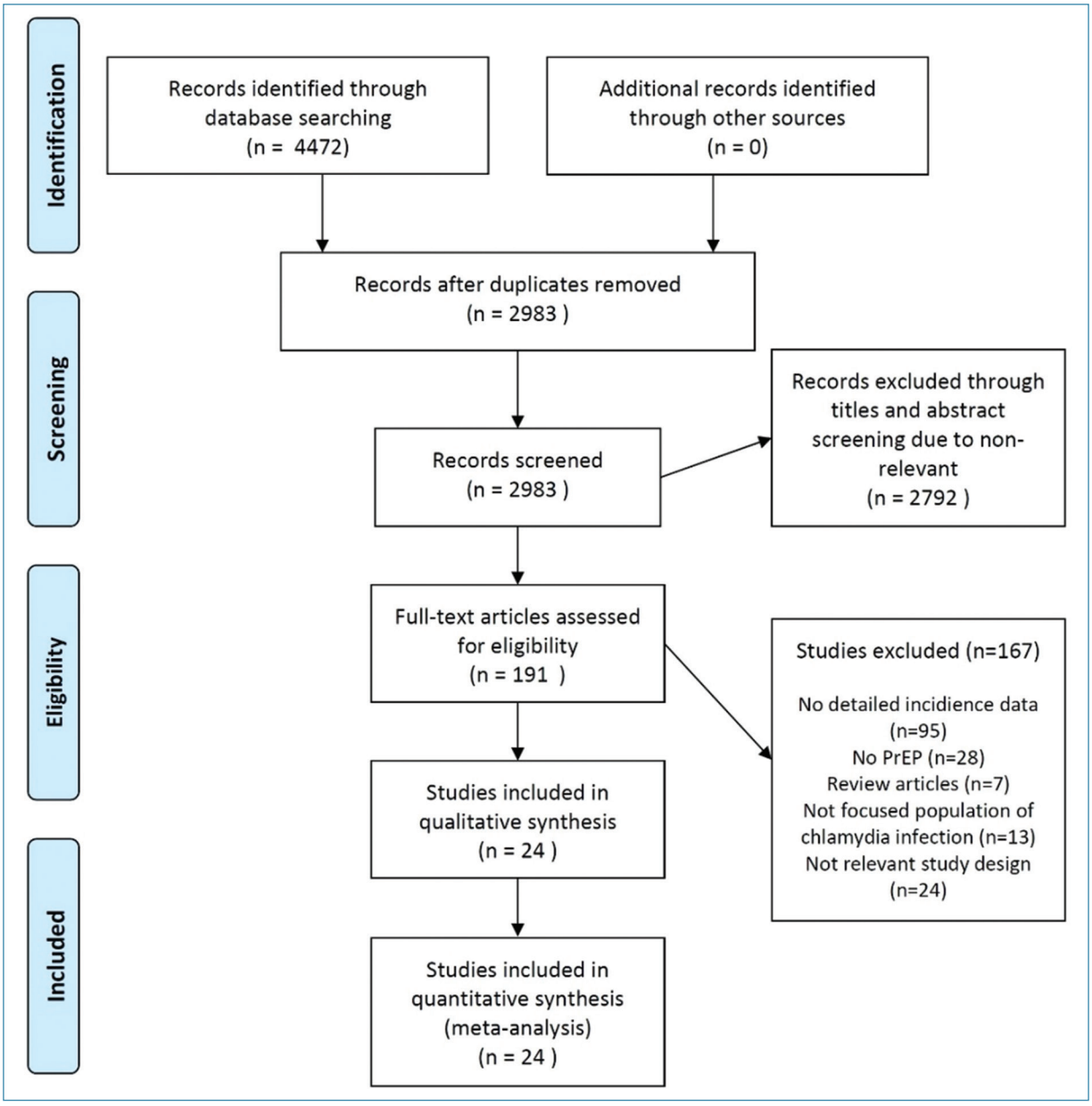

Figure 1. The selection process of enrolled studies.

suggested that the incidence of chlamydia infection still increased, which might be associated with the compensatory effect related to AIDS PrEP. The compensatory effect might be related to the increase of risky sexual behaviors or more frequent screening of sexually transmitted diseases during AIDS PrEP[39,41,42]. In the MSM subgroup analysis, the incidence of chlamydia infection before AIDS PrEP was higher than the chlamydia infection incidence in the whole population receiving AIDS PrEP. A similar increased incidence pattern after at least 6 months of AIDS PrEP was also observed in the MSM subgroup. The incidence results suggested that the relatively high incidence of chlamydia infection before AIDS PrEP and the incidence became higher after 6 months of AIDS PrEP, which suggested that the data after 2018 indicated a higher incidence of chlamydia infection in individuals with AIDS PrEP.

The Denmark study of MSM subjects with AIDS PrEP reported the increased incidence of chlamydia infection in the post-PrEP phase, which reached around 61%[23]. The Australian study of MSM subjects reported the similar pattern of the increased

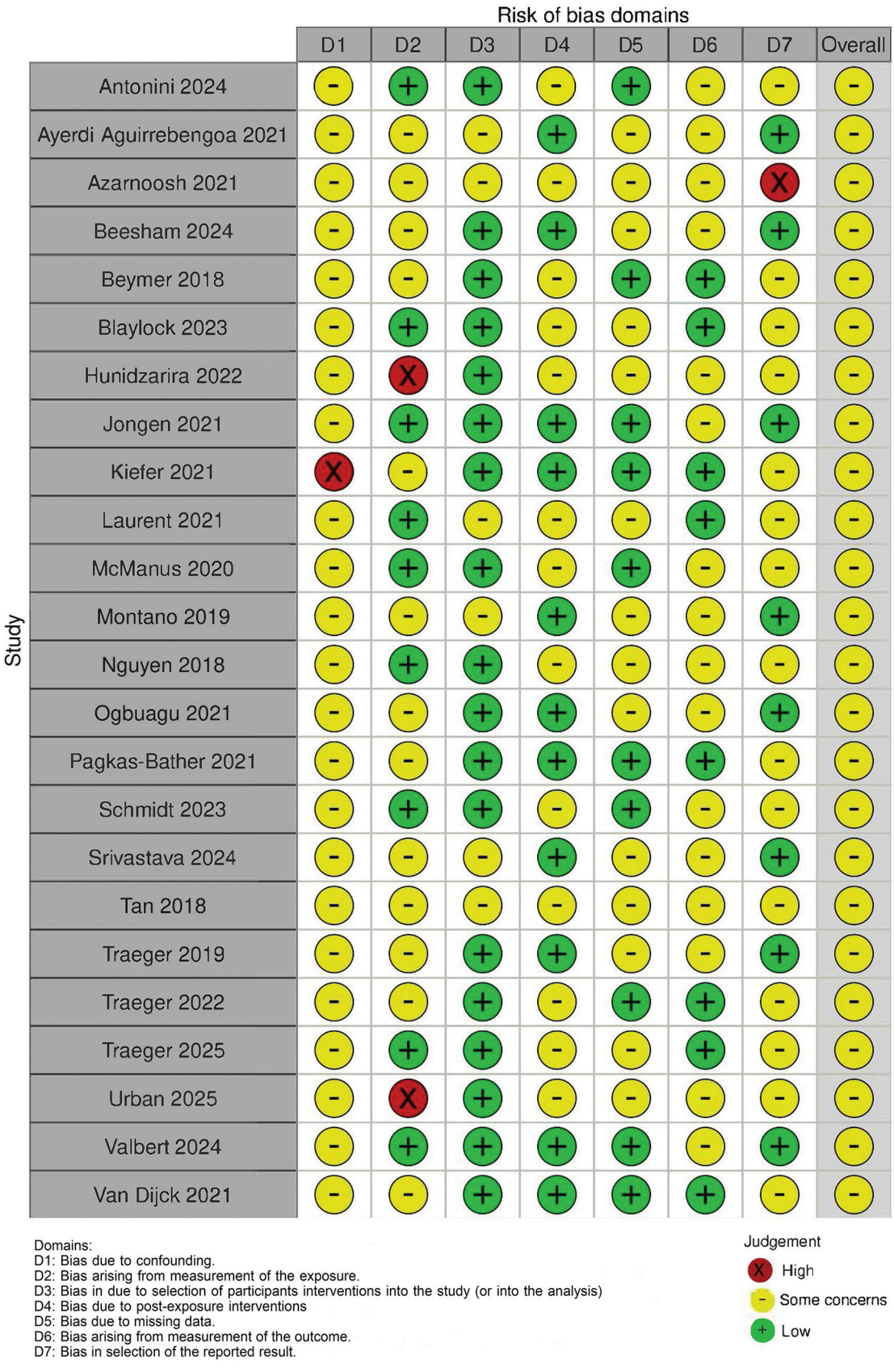

Figure 2. The risk of bias of included studies.

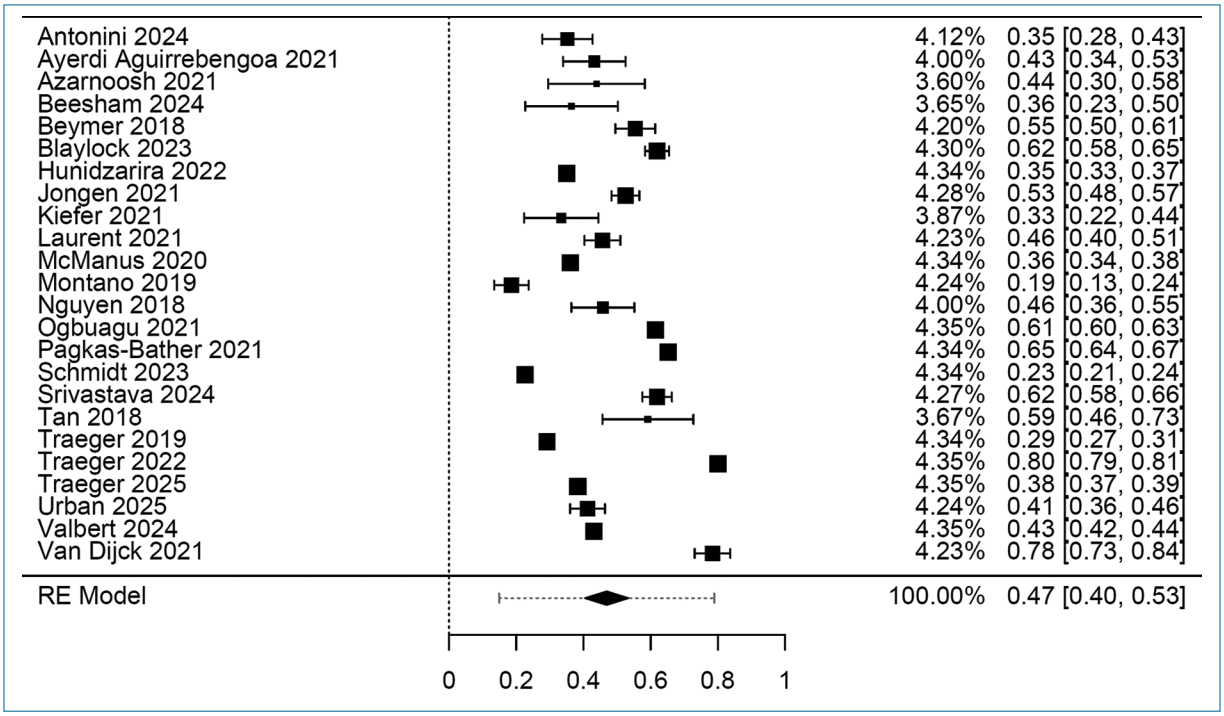

Figure 3. The pooled incidence of chlamydia infection before AIDS pre-exposure prophylaxis.

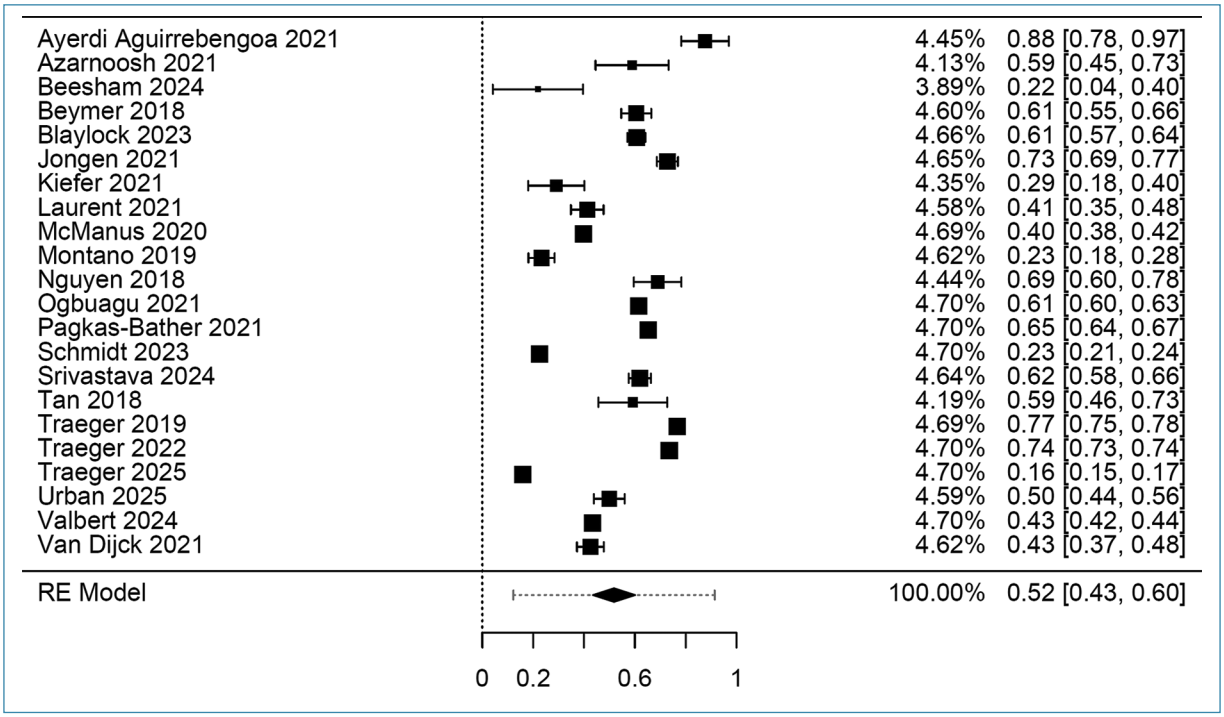

Figure 4. The pooled incidence of chlamydia infection after at least of 6 months of AIDS pre-exposure prophylaxis.

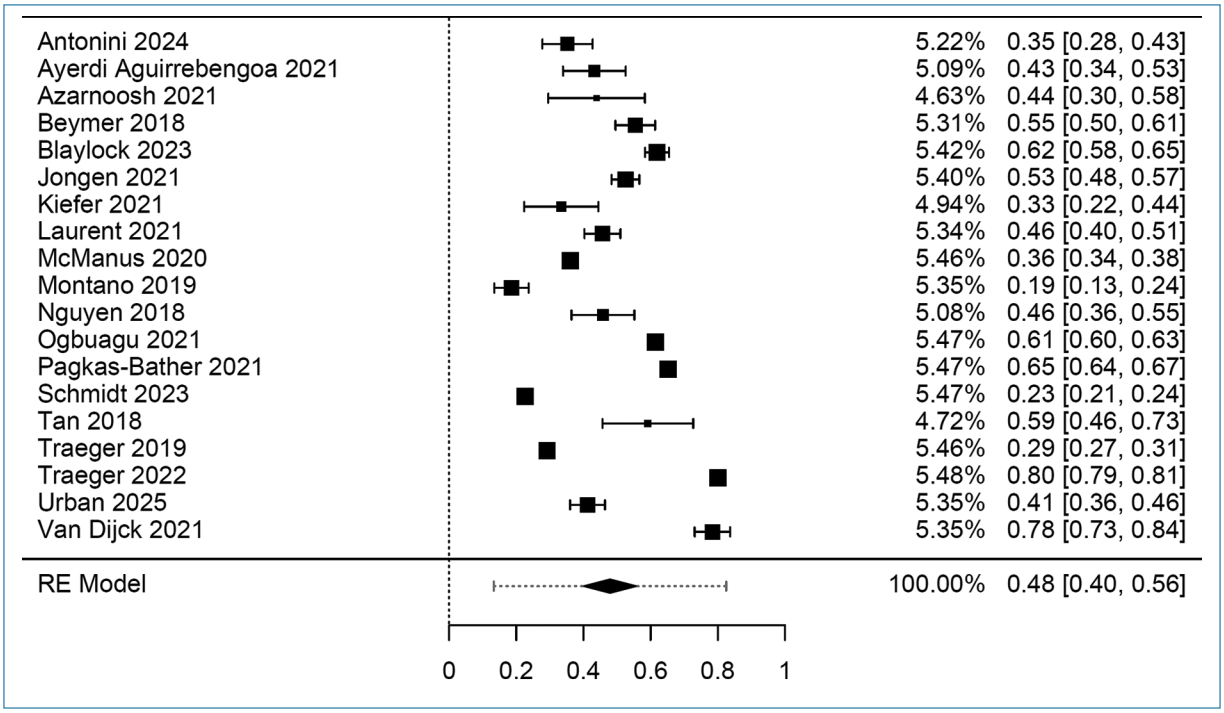

Figure 5. The pooled incidence of chlamydia infection before AIDS pre-exposure prophylaxis in men who have sex with men subgroup.

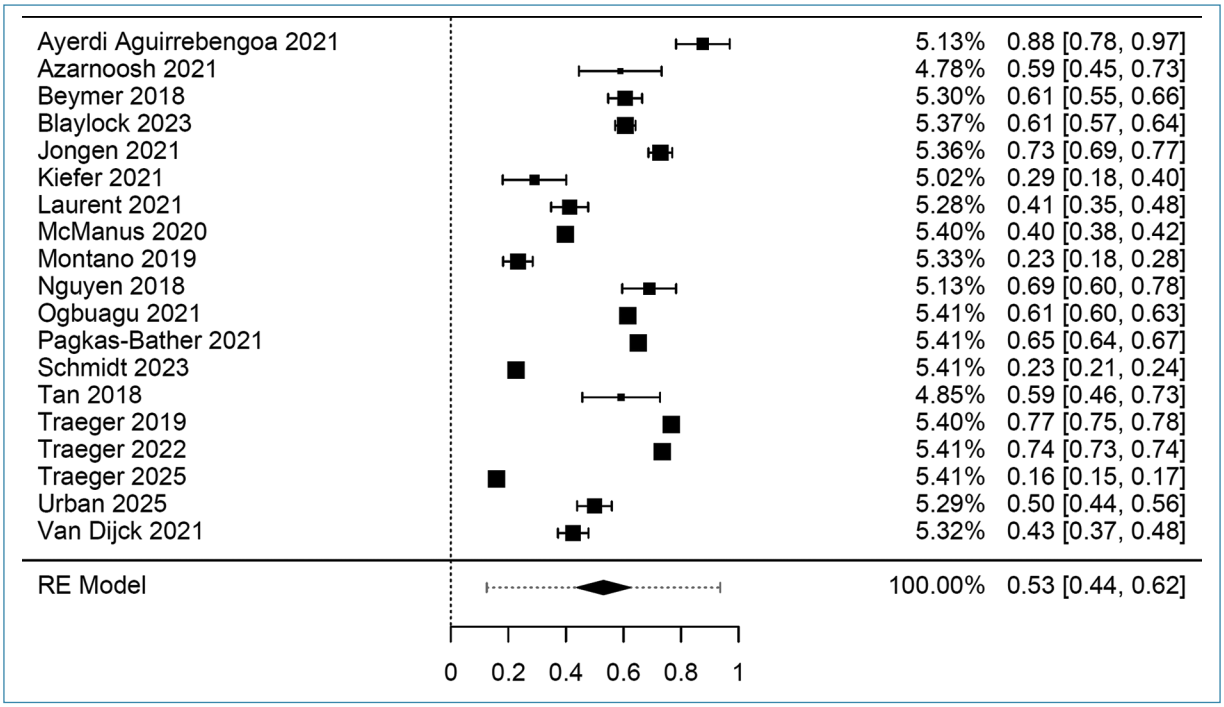

Figure 6. The pooled incidence of chlamydia infection after at least of 6 months of AIDS pre-exposure prophylaxis in men who have sex with men subgroup.

incidence of chlamydia infection in the post-PrEP phase[29], which was also supported by other Australian studies[34,35]. The American studies also revealed the increased incidence of chlamydia infection in the post-PrEP phase[30,33]. The Hawaii study reported the increased incidence of chlamydia infection after 6 months of AIDS PrEP[12]. A Canadian study suggested the increased incidence of chlamydia infection in the post-PrEP phase might be due to the frequent screening intensity[39]. A Germany study suggested the decline of chlamydia infection incidence after AIDS PrEP[3]. However, the previous study of female subjects with AIDS PrEP reported the decrease in the incidence of chlamydia infection during the post-PrEP phase[7]. The results of the present meta-analysis suggested that clinicians should consider the holistic and augmented approach to decrease the increased incidence of chlamydia infection before AIDS PrEP. In addition, the increased incidence of chlamydia infection reminds the clinicians that the present AIDS PrEP might need the provision or augmentation of oral doxycycline in the subjects with multiple sexual partners, which may reduce the infections of chlamydia, treponema, and gonococcus[43]. More efforts should be warranted to decrease the chlamydia infection during the PrEP implementation, especially for MSM subjects.

The present findings should be examined in light of several limitations. First, the selection bias should not be ignored, such as the high incidence of chlamydia due to the inclusion criteria of the included studies. Second, the selection bias of the included studies might also influence the meta-analysis results. This kind of significant heterogeneity may skew the findings. Third, the more frequent screening test intensity and more anatomic sites of chlamydia infection in the included studies might lead to the increased pooled incidence of chlamydia infection in the present meta-analysis. Fourth, not all PrEP studies will report the chlamydia infection status, which might bias our findings. Finally, it is noteworthy that most of the studies were conducted in Europe and America. The data of Asian regions were limited. The ethnicity-related influences should not be ignored in the present findings.

Conclusion

In the updated systematic review and meta-analysis of AIDS PrEP studies after 2018, the pooled incidence of chlamydia infection before PrEP seems relatively high. Chlamydia infection incidence seems to become higher after the implementation of PrEP. In addition, the MSM subgroup is associated with the higher incidence of chlamydia infection in the pre-PrEP and post-PrEP phases.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence (AI). The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

Supplementary data

It can be obtained from the corresponding author under a reasonable request.

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