# Prevalence of *Mycoplasma genitalium* infection among HIV PrEP users: a systematic review and meta-analysis

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## ABSTRACT

**Objectives** To summarise the prevalence of *Mycoplasma genitalium* (MG) and antibiotic-resistant MG infection among HIV pre-exposure prophylaxis (PrEP) users.

**Methods** We searched MEDLINE, Embase, Web of Science and Global Index Medicus up to 30 September 2022. We included studies reporting the prevalence of MG and/or antibiotic-resistant MG infection among PrEP users. Two reviewers independently searched for studies and extracted data. A systematic review with random-effects meta-analysis was performed to quantitatively summarise the results of included studies. The critical appraisal of included studies was conducted with the Joanna Briggs Institute checklist for prevalence studies and the quality of evidence was assessed with Grading of Recommendations Assessment, Development and Evaluation (GRADE).

**Results** A total of 15 studies were included in the systematic review, with 2341 individuals taking PrEP. Studies were conducted in high-income level countries between 2014 and 2019. Median age of participants varied from 23.5 to 40 years. The majority were men (85%) and among them, 93% were men who have sex with men. To identify MG, urine samples were analysed in 14 studies, rectal or anal swabs in 12 studies, oral or pharyngeal swabs in 9 studies, and urethral or vaginal in 3 studies. The pooled point prevalence of MG among PrEP users was 16.7% (95% CI 13.6% to 20.3%; 95% prediction interval (95% PI) 8.2% to 31.1%). The pooled point prevalence of macrolide-resistant infections was 82.6% (95% CI 70.1% to 90.6%; 95% PI 4.7% to 99.8%) and the prevalence of fluoroquinolone-resistant infections was 14.3% (95% CI 1.8% to 42.8%). Individuals taking PrEP have a higher chance of being infected with MG compared with those not taking PrEP (OR 2.30; 95% CI 1.6 to 3.4). The quality of evidence was very low to moderate.

**Conclusion** We observed a high prevalence of MG and its macrolide resistance among PrEP users, highlighting the need to reinforce prevention strategies against sexually transmitted infections in this population.

**PROSPERO registration number** CRD42022310597.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ *Mycoplasma genitalium* (MG) infections are often asymptomatic—a factor that may increase the transmission of the disease. Nevertheless, complications such as epididymitis, prostatitis, infertility and stillbirth are possible outcomes.

⇒ MG is intrinsically resistant to various classes of antibiotics due to the lack of cell wall. Usually, macrolides, quinolones and tetracyclines are the antibiotics of choice. However, it has been observed that the resistance of MG against macrolides and quinolones is rapidly growing.

### WHAT THIS STUDY ADDS

⇒ In our meta-analysis, we identified a pooled prevalence of MG infection of more than 16%; that is, one out of six individuals on HIV pre-exposure prophylaxis (PrEP) was infected with MG. Among the infected, 82.6% had a macrolide-resistant infection, and 14.3% had a fluoroquinolone-resistant infection.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings reinforce the importance of raising awareness among individuals taking PrEP that protection against other sexually transmitted diseases should not be neglected.

## INTRODUCTION

HIV pre-exposure prophylaxis (PrEP) is defined as the use of antiretroviral drugs by HIV-negative individuals at high risk in order to prevent an HIV infection.[1] Some studies show that PrEP is considered a safe prophylaxis and offers up to 99% protection against HIV when used appropriately.[1] Moreover, in places with high uptake of PrEP, population-level effects are being recorded, and the results are promising. Studies have shown reductions from 25% to as high as 58% in the rates of HIV diagnosis over a period of 4–5 years.[2]

However, it has been shown that PrEP users have an increased prevalence of sexually transmitted infections (STIs). A systematic review identified a pooled incidence of chlamydia, gonorrhoea or syphilis of 72.2 cases per 100 person-years among PrEP users.[3] Likewise, a study evaluating approximately 3000 individuals initiating PrEP use in Australia observed an increase in the incidence of chlamydia, gonorrhoea or syphilis from 69.5 cases per 100 person-years before the start of PrEP to 98.4 cases per 100 person-years during PrEP use.[4] One possible explanation is that after starting PrEP, some individuals may frequently engage in risky sexual behaviours, such as having intercourse with

a greater number of partners and neglecting to use condoms.[5–8] Another factor that may be directly related to the increase of STI prevalence among PrEP users is the high frequency of STI screening to which this population is exposed.[5 9]

One of the STIs that can affect this population is caused by *Mycoplasma genitalium* (MG). MG infection has been known as an STI since the bacterium was first isolated in the early 1980s.[10] The pathogen is a slow-growing bacterium without a cell wall[11] that mainly infects the epithelial cells of the genitourinary system and can be transmitted through unprotected sexual intercourse.[11–13] MG infection can cause non-gonococcal urethritis, pelvic inflammatory disease, cervicitis and even leads to infertility.[12 14] Furthermore, the infection is often asymptomatic, which makes diagnosis difficult and contributes to the transmission of the pathogen to other individuals.[14] In the general population, the estimated prevalence of MG infection ranges from 1.3% to 3.9%.[15] Moreover, recent studies have shown that MG is becoming increasingly resistant to macrolides, one of the main classes of antibiotics prescribed; therefore, single-dose azithromycin 1 g therapy is no longer recommended.[16–18] A recently published systematic review reported that the prevalence of mutations associated with macrolide resistance has increased from 10.0% before 2010 to 51.4% between 2016 and 2017.[19]

The increase in cases of antimicrobial-resistant MG, especially in populations with higher exposure to the pathogen, is a public health problem that deserves attention. For this reason, the present systematic review aimed to summarise the prevalence of MG infection and antibiotic-resistant infections among HIV PrEP users.

## METHODS

### Study design and protocol

We conducted a systematic review with meta-analysis according to the Joanna Briggs Institute (JBI) Reviewer's Manual for Systematic Reviews of Prevalence and Incidence Data[20] and the recommendations from the Prevalence Estimates Reviews—Systematic Review Methodology Group.[21] The protocol of this review was registered at PROSPERO on 15 April 2022 (CRD42022310597). This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (online supplemental material 1).[22]

### Search strategy

We searched MEDLINE (via PubMed), Embase, Web of Science and Global Index Medicus databases from inception up to 30 September 2022. The main search terms were: *Mycoplasma genitalium*, HIV pre-exposure prophylaxis, prevalence and drug resistance. Synonyms were combined with the Boolean operator 'OR'. No restrictions were applied in the search strategies. The complete search strategy for all databases is presented in the online supplemental material 2. In addition, we screened the reference lists of included studies to identify studies that were not retrieved by the database search.

### Study selection and eligibility criteria

We used the EndNote V.20 software to organise references and identify duplicates. After removing duplicates, two independent reviewers (PRS and CBM) identified eligible studies using a two-step approach. First, all titles and abstracts identified in the search were screened. Then, the full texts of potentially eligible studies were retrieved and reviewed. Disagreements between the two reviewers were solved through a consensus or by the third reviewer (MA).

We included studies conducted in any context in which the population (total or partial) was taking PrEP at the time of sample collection for the diagnosis of MG infection. We also included studies that assessed the odds of MG infection in individuals taking PrEP compared with non-PrEP users. There were no restrictions related to participants' characteristics. We excluded studies that presented results by samples (rather than by individuals). Regarding the method used to identify the pathogen, we included studies that used PCR, and there were no restrictions regarding the method used to identify the resistance profile of the bacterium. There was also no restriction about the site of infection or whether the sample was collected by a health professional or self-collected. There were no restrictions concerning the language, date or format (conference abstract or journal article) of the publication of the studies. If more than one article reported data for the same population, we included the most recent one or both, if the data presented were complementary. We excluded reviews, case–control studies and case reports.

### Data extraction

Two independent reviewers (PRS and CBM) performed data extraction using an MS Excel spreadsheet developed for this systematic review prior to the study, and disagreements were solved through a consensus or by the third reviewer (MA). The following data were extracted from each included study: study identification (authors, year of publication, full title, DOI), the country in which the study was conducted, study period, population size, characteristics of included participants (age, gender, sexual orientation), methods used to diagnose the pathogen and antimicrobial resistance profile, and outcomes of interest. Prevalence was defined as the proportion of individuals with MG infection or antibiotic-resistant MG infection. We evaluated the point prevalence (number of current cases at a specified time point) and the period prevalence (number of current cases over a specified period/interval). Since these are different epidemiological frequency measurements, we did not combine them and reported them separately.

### Critical appraisal of included studies and assessment of quality of evidence

The quality of the included studies was assessed using the JBI Critical Appraisal Checklist for Prevalence Studies,[20] which can be considered the most appropriate tool for assessing prevalence estimates.[23] It should be noted, however, that this tool assesses not only the risk of bias but also issues related to reporting and general methods of the studies.

The quality of evidence for point-prevalence estimates was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE).[24] Considering that there is no established guidance for the quality assessment of prevalence estimates, we applied the framework developed for incidence estimates in the context of prognostic studies, as previously conducted in other published systematic reviews.[25]

Critical appraisal of included studies and assessment of the quality of evidence were conducted by two independent reviewers, with discrepancies solved by a consensus.

### Data analysis

Depending on the data availability and heterogeneity of included studies, we conducted random-effects meta-analyses using the inverse variance method and restricted maximum likelihood as the between-study variance estimator to summarise the prevalence estimates or OR of the included studies.

For prevalence estimates, logit was used for the transformation of prevalence data. Considering that there is no consensus in the literature about the most appropriate method for the transformation of proportions,[26] sensitivity analysis using Freeman-Tukey double arcsine transformation was conducted to assess the impact of different data transformation methods in this analysis.[26 27] Results are presented as the summary prevalence estimate and corresponding 95% CI. Moreover, 95% prediction interval (95% PI) was estimated to explore heterogeneity.[28]

In addition, we conducted a random-effect meta-analysis to compare the odds of infection in individuals taking PrEP versus individuals not taking PrEP. We included only adjusted ORs in this analysis considering that raw ORs would be highly susceptible to bias due to confounding. Results are presented as OR with 95% CI. Heterogeneity was assessed using $I^2$.[29]

We did not access publication bias for prevalence meta-analysis because the existing methods (such as funnel plot, Egger's test and Begg's test) are inappropriate for meta-analysis of proportions.[27] In the analysis comparing the odds of infection in different populations, publication bias was not evaluated due to the small number of included studies. To avoid publication bias, we developed a search strategy with enhanced sensitivity and complemented the search by reviewing reference lists of included studies.

All analyses were conducted using R (V.4.1.0) and the package meta (V.5.2-0).[30 31]

## RESULTS

### Study selection

The results of study selection are summarised in figure 1. The database search yielded 1964 unique references. A total of 15 studies, reported in 17 publications, fulfilled the inclusion criteria and were included.[32–48] The list of studies excluded after the full-text evaluation is presented in online supplemental material 3.

### Main characteristics of included studies

The main characteristics of included studies and their participants are presented in tables 1 and 2, respectively. Studies were conducted from late 2014 to early 2019 in France (five studies, 33%), Australia (five studies, 33%), Belgium (two studies, 13%), Germany (two studies, 13%) and the USA (one study, 7%). For

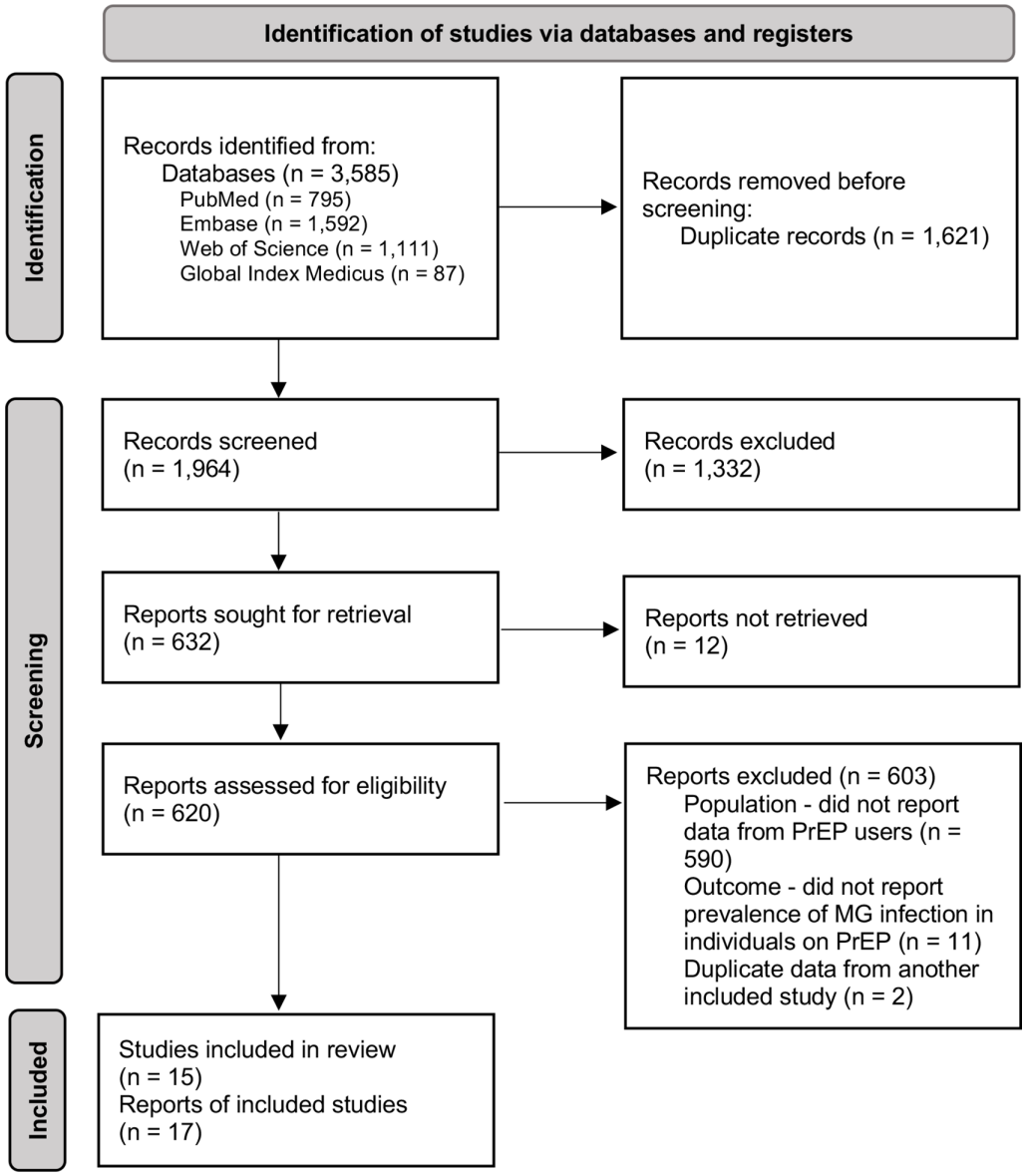


**Figure 1** Flow chart of study selection. MG, *Mycoplasma genitalium*; PrEP, pre-exposure prophylaxis.

**Table 1** Main characteristics of included studies

| Author and year of publication | Country | Study period | Type of samples | Diagnostic methods |
|---|---|---|---|---|
| Berçot *et al*, 2021[32] | France | July 2015–June 2016 | Urine samples, oral and anal swabs | *Mycoplasma genitalium* Real-TM kit (PCR)<br>Cobas TV/MG (PCR)<br>ResistancePlus MG (SpeeDx) (PCR) |
| Bradley *et al*, 2020[33] | Australia | March 2017–May 2017 | Rectal swabs | Bio-Rad CFX96 C1000 (PCR)<br>ResistancePlus MG (SpeeDx) (PCR) |
| Brin *et al*, 2022[34] | France | January 2017–December 2018 | Urine samples, vaginal and anal swabs | Multiplex PCR-Hologic Aptima (PCR) |
| Chambers *et al*, 2019[35] | USA | December 2014–July 2018 | Urine samples and urethral swabs | ResistancePlus MG (SpeeDx) (PCR) |
| Couldwell *et al*, 2018[36]* | Australia | February 2017–May 2017 | Urine samples, oral and anal swabs | ResistancePlus MG (SpeeDx) (PCR) |
| De Baetselier *et al*, 2022[37] | Belgium | 2015–2018 | Urine samples, anorectal and pharyngeal swabs | Accredited in-house real-time PCR |
| Deborde *et al*, 2019 and Ducours *et al*, 2019[38 39] | France | January 2016–February 2017<br>January 2016–December 2017 | Urine samples, anorectal and pharyngeal swabs | Multiplex PCR-Hologic Aptima (PCR) |
| Guiraud *et al*, 2021[40] | France | June 2017–February 2018 | Urine samples, rectal and pharyngeal swabs | S-DiaMGTV kit (PCR) |
| Herms *et al*, 2021[41] | France | January 2017–December 2018 | Urine samples, genital, anal and oral swabs | Cobas TV/MG (PCR) |
| Jansen *et al*, 2020[42] | Germany | February 2018–August 2018 | Urine samples, rectal and pharyngeal swabs | Multiplex PCR-Hologic Aptima (PCR) |
| McIver *et al*, 2019[43] | Australia | April 2017–May 2018 | Urine samples | ResistancePlus MG (SpeeDx) (PCR) |
| Read *et al*, 2019 and Chua *et al*, 2021[44 45] | Australia | August 2016–September 2017 | Urine samples and rectal swabs | ResistancePlus MG (SpeeDx) (PCR) |
| Richardson *et al*, 2021[46]* | Australia | January 2017–December 2018 | Urine samples | In-house PCR assay and ResistancePlus MG (SpeeDx) (PCR) |
| Streeck *et al*, 2022[47] | Germany | June 2018–July 2019 | Urine samples, anal and pharyngeal swabs | *M. genitalium* assay-Hologic Aptima (PCR) |
| Van Praet *et al*, 2019[48] | Belgium | June 2017–March 2019 | Urine samples, rectal and pharyngeal swabs | TaqMan Array Card (PCR) |

*There is an overlap of participants between the studies of Couldwell *et al* and Richardson *et al*.

MG diagnosis, urine samples were tested in 14 studies (93%), rectal or anal swabs in 12 studies (80%), oral or pharyngeal swabs in 9 studies (60%), and genital (urethral or vaginal) in 3 studies (20%). In all studies, MG infection was detected by PCR methods. The total number of included participants was 12 869; among them, 2341 were taking PrEP. The median age of participants included in the studies ranged from 23.5 to 40 years, and the majority were men (10 900, 85%). Regarding sexual orientation, data were available from 7215 individuals; among them, 6729 (93%) declared themselves as men who have sex with men (MSM). It is important to note that for some studies, these participant characteristics consider the entire study sample and not only the characteristics of PrEP users, since data for this subgroup of included individuals were not available.

## Risk of bias and quality of evidence

The complete assessment of risk of bias for the included studies is presented in online supplemental material 4. Overall, most studies had methodological limitations (such as inappropriate sampling frame, inappropriate sample, low response rate or insufficient sample coverage) that may lead to biases due to differences between the target population and the study sample. On the other hand, most studies used standard and valid methods to identify the outcome of interest—MG infection or antibiotic-resistant MG infection. Therefore, we did not detect any substantial risk bias due to issues in measuring the condition of interest.

The quality of evidence for primary outcomes (point-prevalence estimates) is presented below, and the full assessment can be found in online supplemental material 5. For all outcomes, the quality of evidence was downgraded due to the high risk of bias, as most of the included studies had methodological issues that may lead to bias arising from differences between the sample evaluated and the target population. Also, imprecision was identified in the analyses regarding antibiotic-resistant infections. There was no evidence of inconsistency, indirectness or publication bias in our analyses.

## Prevalence of MG infection

A total of 12 studies involving 2135 individuals were included in the meta-analysis of the point prevalence of MG in PrEP users.[32–38 41–44 47] The pooled point prevalence of MG infection among the PrEP users was estimated at 16.7% (95% CI 13.6% to 20.3%), as presented in figure 2. The 95% PI for this analysis was 8.2% to 31.1%, indicating that we expect that the prevalence of MG infection in PrEP users to vary within this interval in different settings that can be evaluated in future studies. The quality of evidence was moderate due to serious risk of bias (online supplemental material 5). Sensitivity analysis using Freeman-Tukey double arcsine transformation yielded similar results (online supplemental material 6).

Results from the study of Richardson *et al*[46] were not included in our meta-analysis to avoid double-counting of individuals, due to the overlap of participants in the studies reported by Richardson *et al* and Couldwell *et al*.[36 46] According to Richardson *et al*,[46] the point prevalence of MG infection in MSM PrEP users with concomitant symptomatic gonococcal urethritis was 9.7% (95% CI 2.0% to 25.8%).

We also evaluated the prevalence of MG according to the site of infection (online supplemental material 7). Anorectal and

**Table 2** Main characteristics of participants from included studies

| Author and year of publication | Population | N (on PrEP/not on PrEP) | Gender and sexual orientation* | Age median (IQR)* |
|---|---|---|---|---|
| Berçot *et al*, 2021[32] | Asymptomatic MSM from the ANRS IPERGAY trial (which evaluated on-demand PrEP) that were enrolled in an RCT of PEP with doxycycline | 210 (210/0) | Men: 210 (MSM: 210) | 38 (32–46) |
| Bradley *et al*, 2020[33]* | Asymptomatic MSM who were having a rectal swab for NG, CT and MG collected as part of their routine care (screening) | 742 (170/572) | Men: 739 (MSM: 739)<br>Transgender: 3 | 31 (27–39) |
| Brin *et al*, 2022[34]* | Patients vising the hospital for routine STI screening, possible STI symptoms or follow-up for PrEP or HIV infection | 5586 (207/5379) | Men: 3649 (MSM: NR)<br>Women: 1884<br>Transgender: 8 | Women: 23 (21–28)<br>Men: 29 (23–39) |
| Chambers *et al*, 2019[35]* | Symptomatic MSM >16 years with NGU from an STI clinic | 103 (18/85) | Men: 103 (MSM: 103) | 30 (27–39) |
| Couldwell *et al*, 2018[36]*† | Symptomatic and asymptomatic MSM attending a sexual health centre for STI testing | 508 (169/339) | Men: 508 (MSM: 508) | 33 (NR) |
| De Baetselier *et al*, 2022[37] | Symptomatic and asymptomatic MSM from the Be-PrEP-ared cohort study, in which STIs were tested every 3 months | 179 (179/0) | Men: 179 (MSM: 179) | NR |
| Deborde *et al*, 2019 and Ducours *et al*, 2019[38 39] | Patients on PrEP | 148 (148/0) | Men: 145 (MSM: 145)<br>Woman: 1<br>Transgender: 2 | 35 (NR) |
| Guiraud *et al*, 2021[40]* | Men from an STI clinic | 78 (16/62) | Men: 78 (MSM: 60) | 34 (20–58) |
| Herms *et al*, 2021[41]* | Symptomatic and asymptomatic patients undergoing STI testing | 249 (13/236) | Men: 224 (MSM: 85)<br>Women: 22 | Mean 34 (range 15–76) |
| Jansen *et al*, 2020[42]* | Symptomatic and asymptomatic ≥18 years MSM | 2303 (283/2020) | Men: 2303 (MSM: 2303) | 39 (range 18–79) |
| McIver *et al*, 2019[43]* | Men >16 years presenting symptoms of acute NGU | 588 (102/486) | Men: 588 (MSM: 306) | 30 (26–37) |
| Read *et al*, 2019* and Chua *et al*, 2021[44 45]* | Asymptomatic MSM from the MnM Study that reported receptive anal sex in the preceding year | 1001 (142/859)<br>94 (14/80) | Men: 1001 (MSM: 1001)<br>Men: 94 (MSM: 94) | 29 (24–34)<br>27 (23–32) |
| Richardson *et al*, 2021[46]*† | MSM with symptomatic gonococcal urethritis | 184 (31/153) | Men: 184 (MSM: 109) | 31 (24–38) |
| Streeck *et al*, 2022[47]* | MSM at the screening visit for the BRAHMS Study | 1043 (553/490) | Men: 1042 (MSM: 959) | 33 (28–39) |
| Van Praet *et al*, 2019[48] | MSM on PrEP screened for STIs | 131 (131/0) | Men: 131 (MSM: 131) | 40 (20–79) |

*For studies that also included not only individuals on PrEP.
†There is an overlap of participants between the studies of Couldwell *et al* and Richardson *et al*.
CT, *Chlamydia trachomatis*; MG, *Mycoplasma genitalium*; MSM, men who have sex with men; N, number of participants; NG, *Neisseria gonorrhoeae*; NGU, non-gonococcal urethritis; NR, not reported; PEP, post-exposure prophylaxis; PrEP, pre-exposure prophylaxis; RCT, randomised clinical trial; STI, sexually transmitted infection.

genital infections were the most prevalent, with a point prevalence of 9.6% (95% CI 4.9% to 18.0%) and 8.2% (95% CI 5.1% to 13.0%), respectively. The prevalence of oropharyngeal infection was 1.2% (95% CI 0.2% to 5.3%).

Four studies presented estimates for period prevalence for different time frames—6, 12, 18 and 24 months.[32 37 39 48] The period prevalence varied from 15.2% (95% CI 10.7% to 20.8%) in 6 months to 18.9% (95% CI 13.0% to 26.2%) in 24 months, with the highest estimate in 18 months (39.1%; 95% CI 31.9% to 46.7%).

Two studies, with a total of 1250 individuals, reported adjusted estimates comparing the odds of being infected with MG among PrEP users versus non-users.[33 36] The variables used for adjustment were history of STIs, age and HIV infection in the study reported by Bradley *et al*,[33] and condom use, number of male partners in the last 3 months, age, other urethral or anal infection, and HIV infection in the study reported by Couldwell *et al*.[36] As shown in figure 3, individuals taking PrEP have an odds 2.3 times higher of being infected with MG (95% CI 1.6 to 3.4; p<0.0001) compared with non-PrEP users.

### Prevalence of macrolide-resistant MG infection

Three studies, with 63 participants, reported the point-prevalence estimate for macrolide-resistant MG infection in PrEP users.[36 43 44] As shown in figure 4, the summary prevalence estimate was 82.6% (95% CI 70.1% to 90.6%). The 95% PI was 4.7% to 99.8%, indicating that we expect a high heterogeneity in the prevalence of macrolide-resistant MG infections between different settings. The quality of evidence was low due to serious risk of bias and serious imprecision (online supplemental material 5). Sensitivity analysis using Freeman-Tukey double arcsine transformation yielded similar results (online supplemental material 6).

The period prevalence of macrolide-resistant MG infection in PrEP users was reported in three studies with three different time intervals. One study reported a 6-month prevalence of 69.6% (95% CI 47.1% to 86.8%)[32]; another study reported a 9-month prevalence of 75.0% (95% CI 47.6% to 92.7%)[40]; and the third study reported a 24-month prevalence of 75.0% (95% CI 55.1% to 89.3%),[39] as can be seen in figure 4A.

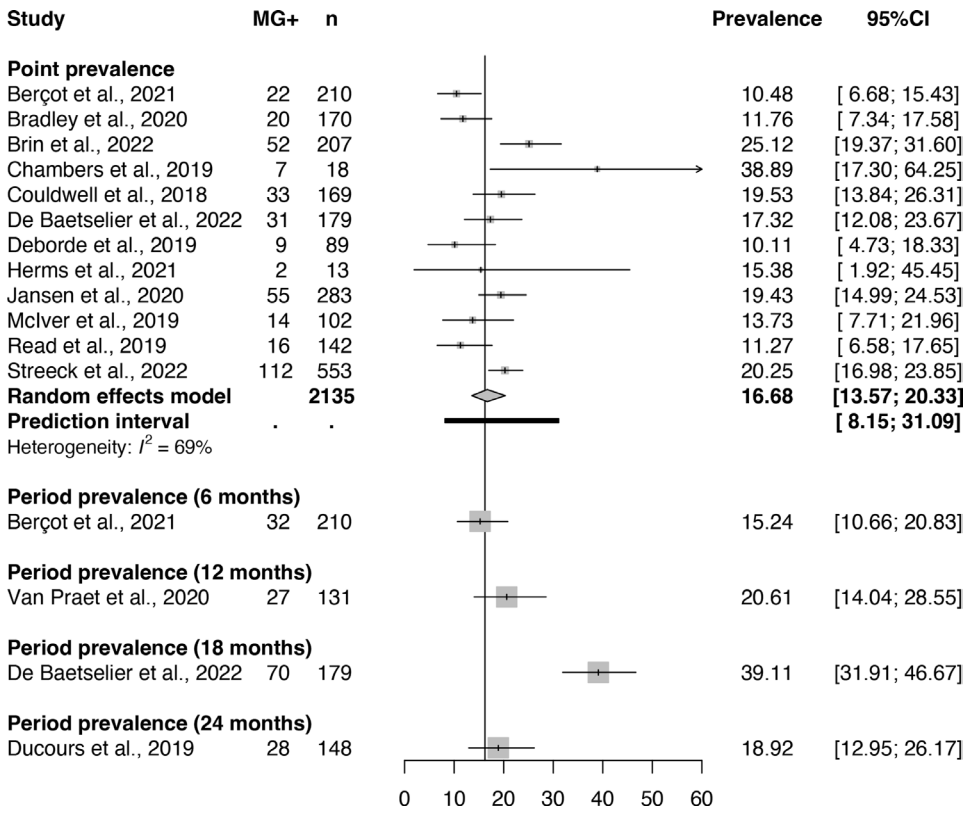


**Figure 2** Prevalence of MG infection among PrEP users. MG, *Mycoplasma genitalium*; PrEP, pre-exposure prophylaxis.

### Prevalence of fluoroquinolone-resistant MG infection

One study with 14 participants evaluated the point prevalence of fluoroquinolone-resistant MG infection (figure 4B).[45] The estimated prevalence was 14.3% (95% CI 1.8% to 42.8%). The quality of evidence was as very low due to serious risk of bias and very serious imprecision (online supplemental material 5).

The period prevalence of fluoroquinolone-resistant MG infection was reported in two studies: 11.1% (95% CI 2.4% to 29.2%) in 6 months[32] and 37.5% (95% CI 15.2% to 64.6%) in 9 months.[40] These results are shown in figure 4B.

Regarding the mechanism of resistance against fluoroquinolones, the studies by Chua *et al*[45] and Guiraud *et al*[40] reported mutations in the parC gene of the samples, specifically changes in the amino acid S83I, while the study by Berçot *et al*[32] reported mutations in the amino acid position S83I and D87Y. These mutations are associated with resistance against fluoroquinolones.[49 50]

### Prevalence of tetracycline-resistant MG infection

Berçot *et al*[32] reported a 6-month prevalence of mutation in the 16S rRNA in 2 out of 14 individuals (14.3%; 95% CI 1.8% to 42.8%). Although some studies associate this mutation with resistance against tetracyclines in some bacteria,[51 52] it is still not entirely clear whether this mechanism is, in fact, responsible for promoting resistance against tetracyclines in MG.[53]

## DISCUSSION

In our study, the pooled prevalence of MG infection in PrEP users was 16.7%, an estimate higher than what has been observed in other populations.

For example, a meta-analysis published in 2018 sought to identify the prevalence of MG infection in different populations and settings. In this study, the authors reported a prevalence in the general population of 1.3% in countries with higher levels of development and 3.9% in countries with lower levels of development. In populations at higher risk of STIs, the prevalence was 3.2% among MSM and 15.9% among sex workers.[15]

We further observed that 82.6% of MG infections were macrolide resistant. Only one study with 14 patients reported that the point prevalence of fluoroquinolone-resistant MG infections among PrEP users, which was 14.9%.[45] By contrast, a recent systematic review that included studies evaluating mainly symptomatic or high-risk patients identified a proportion of

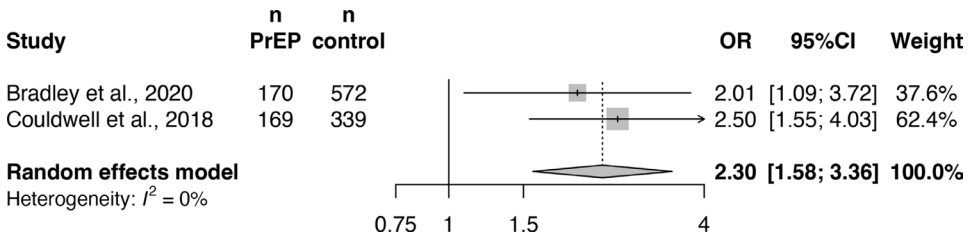


**Figure 3** Odds of MG infection among PrEP users in comparison with individuals not on PrEP. MG, *Mycoplasma genitalium*; PrEP, pre-exposure prophylaxis.

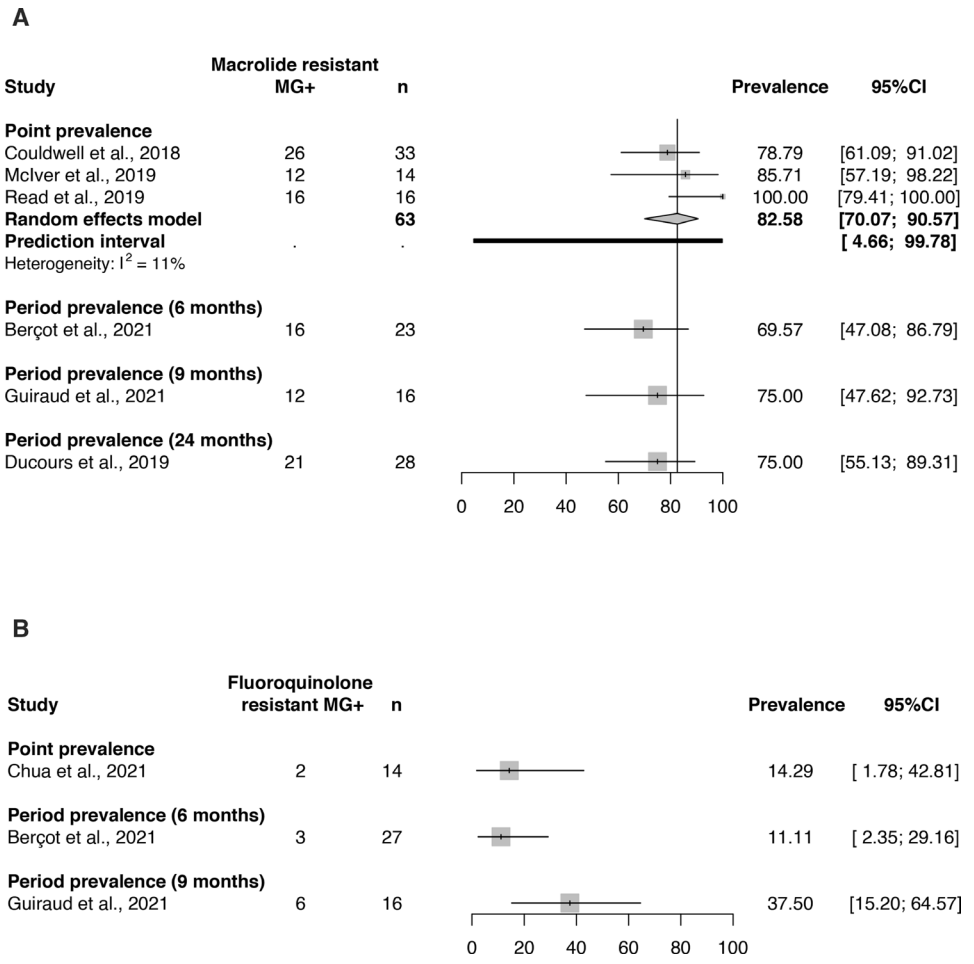


**Figure 4** Prevalence of (A) macrolide and (B) fluoroquinolone-resistant MG infection among PrEP users. MG, *Mycoplasma genitalium*; PrEP, pre-exposure prophylaxis.

35.5% and 7.7% of macrolide and fluoroquinolone-resistant MG infections, respectively.[19]

To our knowledge, our study is the most comprehensive and up-to-date systematic review evaluating the prevalence of MG and antibiotic-resistant MG infection in individuals taking PrEP. Most of the previous studies have assessed either the prevalence of other STIs in PrEP users or the prevalence of MG and MG-resistant infection in different populations.[3 8 19] A previous systematic review conducted in 2018 aimed at estimating the prevalence of STIs in PrEP users.[3] The authors identified only one study, which reported a prevalence of 17.2% (95% CI 12.2% to 23.2%) of MG in this population, a similar finding to ours. We identified 14 new studies in a relatively short period of 4 years, highlighting MG's growing relevance, particularly in high-risk populations such as PrEP users.

In line with our findings, an increased incidence of STIs was observed during follow-up in studies comparing patients before and after PrEP initiation.[5 8] The high prevalence of MG infection and its antibiotic resistance among PrEP users can be explained by changes in sexual behaviour after PrEP initiation—which includes reduced condom use and an increased number of sexual partners.[8 54]

The high proportion of MG infection and its antibiotic resistance among PrEP users might also be related to the high frequency of routine STI screening and, therefore, frequent diagnosis and use of antimicrobials.[5 9] For this reason, some guidelines recommend that screening and treatment for MG should be performed only for symptomatic patients or those with specific indications.[55 56] Screening for MG in asymptomatic patients may induce unnecessary prescription of antimicrobials, contributing to the increase in bacterial resistance.[55–57] It is also highly recommended evaluating the macrolide resistance of positive MG samples, whenever possible, to avoid prescribing inappropriate antibiotics.[55] Therefore, healthcare policies must focus not only on diagnosing and treating infections but also on preventing transmission.

It is essential to point out that results indicating a higher prevalence of STIs in individuals taking PrEP should not discourage the prescription or the use of this important and effective intervention. Rather, they should highlight the need of more effective STI prevention strategies in this high-risk population. To answer the question about how this could be achieved requires further investigations.

Our study has potential strengths and limitations. Among the strengths of our study, we conducted a broad search by applying a search strategy not only in large and traditional databases but also in local databases, a practice that is important for systematic reviews of prevalence. Additionally, we followed a robust methodology for study selection, data extraction and data analysis, based on the best methodological recommendations available in the literature and predetermined in a registered protocol.

Regarding limitations, most of the studies identified were conducted in Occidental Europe and Australia, and all of them were conducted in high-income countries. Therefore, our results

may have limited generalisability for low-income and middle-income regions. It is important to emphasise that the three studies that reported the prevalence of macrolide-resistant MG were conducted in Australia.[36 43 44] According to a previous meta-analysis conducted by Machalek *et al* in 2020, the country had a high prevalence of macrolide-resistant MG compared with other countries.[19] Therefore, our study may contain data that do not necessarily represent the reality in other countries. For this reason, further prevalence studies are required to address these limitations. Moreover, 2 studies tested only urine samples,[43 46] and 11 studies tested urine and anorectal samples to diagnose MG.[32 34 36–41 44 45 47] However, anorectal swabs are especially relevant for MSM, and not testing this site may result in an underestimation of MG prevalence by up to 70%.[44 58] A positive aspect is that no study tested only oropharyngeal samples since this practice is not recommended due to the rare transmission of MG through this site.[59] Other limiting points were the small number of studies comparing the odds of MG infection in PrEP users versus non-PrEP users, as well the scarcity of studies reporting the prevalence of fluoroquinolone-resistant MG.

In conclusion, we observed a high prevalence of MG infection and a high proportion of antibiotic-resistant MG infections in individuals taking PrEP. These results reinforce the need of more effective STI prevention and control programmes to better support this population in achieving overall sexual health.

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# Correction: *Prevalence of Mycoplasma genitalium infection among HIV PrEP users: a systematic review and meta-analysis*

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