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Determining the screening frequency for sexually transmitted infections for people who use HIV pre-exposure prophylaxis: a systematic review and meta-analysis

Cham-mill Kim[1,#], Victor Zhao[1,#], Maeve Brito De Mello[2], Rachel Baggaley[2], Cheryl C. Johnson[2], Erica Spielman[2], Christopher K. Fairley[3,4], Lei Zhang[3,4,5], Henry de Vries[6,7,8,9], Jeffrey Klausner[10], Rui Zhao[5], Jason J. Ong[3,4,11,*]

[1] Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Melbourne, Australia
[2] Global HIV, Hepatitis and STI Programmes, World Health Organization, Geneva, Switzerland
[3] Central Clinical School, Monash University, Melbourne, Australia
[4] Melbourne Sexual Health Centre, Alfred Health, Melbourne, Australia
[5] China-Australia Joint Research Center for Infectious Diseases, School of Public Health, Xi'an Jiaotong University Health Science Center, Xi'an, China
[6] Amsterdam UMC location University of Amsterdam, Department of Dermatology, Amsterdam, The Netherlands
[7] Amsterdam Institute for Infection and Immunology, Infectious Diseases, Amsterdam, The Netherlands
[8] Center for Sexual Health, Department of Infectious Diseases, Public Health Service Amsterdam, The Netherlands
[9] Amsterdam Institute for Global Health and Development, Amsterdam, The Netherlands
[10] Keck School of Medicine of University of Southern California, Los Angeles, United States
[11] Clinical Research Department, London School of Hygiene and Tropical Medicine, London, United Kingdom

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ABSTRACT

Objectives: Although the World Health Organization recommends 'frequent' screening of sexually transmitted infections (STI) for people who use pre-exposure prophylaxis for HIV, there is no evidence for optimal frequency.

Methods: We searched five databases and used random-effects meta-analysis to calculate pooled estimates of STI test positivity. We narratively synthesized data on secondary outcomes, including adherence to recommended STI screening frequency and changes in STI epidemiology.

Results: Of 7477 studies, we included 38 for the meta-analysis and 11 for secondary outcomes. With 2-3 monthly STI screening, the pooled positivity was 0.20 (95% confidence interval [CI]: 0.15-0.25) for chlamydia, 0.17 (95% CI: 0.12-0.22) for gonorrhea, and 0.07 (95% CI: 0.05-0.08) for syphilis. For chlamydia and gonorrhea, the positivity was approximately 50% and 75% lower, respectively, in studies that screened 4-6 monthly vs 2-3 monthly. There was no significant difference in the positivity for syphilis in studies that screened 4-6 monthly compared to 2-3 monthly. Adherence of clients to recommended screening frequency varied significantly (39-94%) depending on population and country. Modeling studies suggest more frequent STI screening could reduce incidence.

Conclusion: Although more frequent STI screening could reduce delayed diagnoses and incidence, there remain significant knowledge gaps regarding the optimal STI screening frequency.

Introduction

Following a series of successful trials and demonstration studies, the World Health Organization (WHO), together with national and international agencies, has recommended pre-exposure prophylaxis (PrEP) for those at substantial risk of HIV or who would like to use PrEP [1]. People who would benefit most from PrEP often have suboptimal condom use [2], resulting in elevated risk of sexually transmitted infections (STI). Therefore, there is recognition that PrEP programs are a gateway to offering STI services, including screening, treatment, vaccination (for human papillomavirus, hepatitis A and B), or mental health support where needed [3–6].

Although WHO and other national guidelines suggest 3-monthly STI screening for people who use PrEP, there is no cur-

* Corresponding author.
E-mail addresses: Jason.ong@monash.edu, Jason.Ong@lshtm.ac.uk (J.J. Ong).
Equal first coauthors.

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rent evidence for the optimal time interval to offer STI screening for people who use PrEP [1,7]. More frequent STI screening could lead to more new infections identified, earlier treatment, and potentially reduce STI incidence at the population level. However, from the public health perspective, it is critical to consider the effectiveness, cost-effectiveness, feasibility, acceptability, and adherence to different time intervals for STI screening, particularly given the financial constraints for providing molecular testing for STIs in resource-limited settings [8]. More frequent STI screening could lead to antibiotic overuse and induce antimicrobial resistance (AMR) [9]. WHO recommends differentiated and simplified approaches to PrEP delivery, which support less frequent clinic visits to increase access, acceptability, feasibility, and coverage. If more frequent STI screening is needed, STI self-tests may be an important approach to lower the frequency of clinic visits; however, affordable and accurate chlamydia/gonorrhea self-tests are not yet available. However, providing online postal STI services integrated into PrEP programs may be a feasible approach [10]. The optimal screening frequency also depends on the natural history of the pathogen, its infectiveness, and the disease burden of each STI by population and setting.

Hence, we conducted a systematic review and meta-analysis to assess the STIs' positivity according to different screening frequencies. Secondary outcomes included the feasibility, client adherence to recommended STI screening frequency, cost-effectiveness, and the changes in STI epidemiology on different STI screening frequencies.

Methods

This review was conducted following the Cochrane Handbook for Systematic Reviews of Interventions, version 6.3 [11]. We searched five databases: Ovid MEDLINE, Ovid EMBASE, Web of Science, GlobalHealth, and CIANHL Econlit with the following inclusion criteria: English language, humans, search starting from 2010 to December 28, 2021. The keywords within our search strategy were words related to HIV, PrEP, STI, and screening. See Appendix A for more details of our search strategy.

Two reviewers independently screened the title and abstracts using Covidence (CK and VZ). Discrepancies were resolved by a third reviewer (JO). Inclusion criteria were primary studies that included data on STI positivity rate (chlamydia, gonorrhea, and syphilis) among people who use PrEP and mentioned the frequency of STI screening (i.e. testing of asymptomatic people). We also included studies that described the effect (if any) on STI epidemiology or the feasibility and client adherence to different STI screening frequencies. We excluded systematic reviews, letters that contained no new data, editorials, duplicated results from the same study, and laboratory studies about STI diagnostic performance. Full texts were screened according to the eligibility criteria, and data were extracted by two reviewers independently (CK and VZ), and discrepancies were resolved by a third reviewer (JO). As positivity may be influenced by the background prevalence of STIs in each study setting and population, we also extracted data related to the latest year of the study, study duration, country income level, study setting, and study population.

We defined the positivity of the three STIs using positivity per person screened over the study duration. We did not distinguish the number of recurrent infections as this data was not commonly reported. For example, if an individual had two positive tests in a year, they would be defined as test positive per person in 1 year (not two positives in the same year). We defined positivity as a positive test result for syphilis, chlamydia, or gonorrhea, independent of anatomic sites where samples were collected. If a study included an interventional arm that could impact the STI positivity, we extracted data from the non-interventional arm.

We used random-effects meta-analysis to calculate across pooled estimates of STI positivity to account for sampling error and heterogeneity. We included studies in the meta-analysis that described STI screening frequency and contained data on positivity for chlamydia, gonorrhea, and/or syphilis. Modeling studies were excluded. Pooled estimates and 95% confidence intervals (CIs) were generated using Freeman–Tukey-type double arcsine transformation to adjust for variance instability [12]. Statistical heterogeneity between studies was assessed using the I^2 statistic. Random-effects meta-regression models were conducted to examine the impact of STI screening frequency, the study duration, country income level, type of study, and latest year of study on the effect size. For the multivariable model, we included all variables with a *P*-value of <0.20 and used the backward elimination process until all variables had a *P*-value of <0.05. A separate multivariable model was developed for each pathogen. Funnel plots were generated to assess the possibility of small study effects which can be caused by publication bias. Egger's test was performed to confirm the presence of this bias [13]. All analyses were conducted using STATA 17.0 (StataCorp LP, College Station, Texas, USA). We evaluated the methodological quality of included studies using the Joanna Briggs Institute's critical assessment tools [14]. This study is registered with PROSPERO (CRD42022300053).

Ethics information

No ethical clearance was required.

Role of funding source

WHO technical staff were involved in the study design and interpretation of results as part of ongoing guideline development.

Results

Of 7477 studies identified, we included 46 studies: 38 had data for the meta-analysis, and the remaining studies contained data for secondary outcomes (Figure 1). Table 1 demonstrates that 2- to 3-monthly STI screening (compared to longer screening intervals) appeared more common in studies with data collected after 2015 from high-income countries and for men who have sex with men (MSM).

STI positivity

In total, 38 studies met the inclusion criteria for evaluating STI positivity. Several observations should be noted (Table 2). First, in PrEP programs with 2-3 monthly STI screening, the overall pooled positivity of 0.20 (95% CI: 0.15-0.25) for chlamydia, 0.17 (95% CI: 0.12-0.22) for gonorrhea, and 0.07 (95% CI: 0.05-0.08) for syphilis. Second, in studies that screened 2-3 monthly compared to studies that screened 4-6 monthly for syphilis, there were no significant differences in the positivity. However, for chlamydia and gonorrhea, the positivity was approximately 50% and 75% lower, respectively, in studies that screened 4-6 monthly compared to studies that screened 2-3 monthly. There was large heterogeneity in STI positivity among studies not explained by sampling error. Supplementary Table 1 provides further details of included studies. Supplementary Table 2 presents the pooled positivity according to the study duration, demonstrating the increase of proportion who tested positive over longer observation times. Supplementary Tables 3-5 provide meta-regression analyses. STI screening frequency and latest year of study were significantly associated with chlamydia positivity. STI screening frequency and study duration were significantly associated with gonorrhea and syphilis positivity. Supplementary Figures 1-8 present the Forest plots according

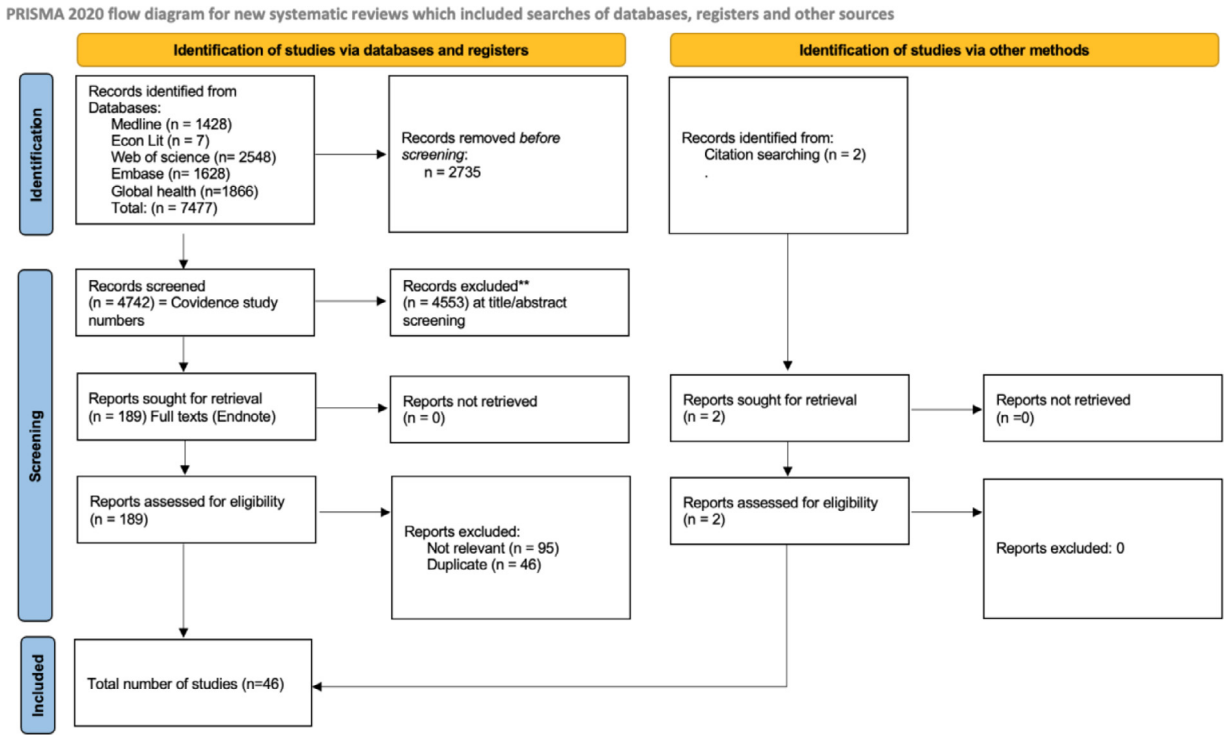

Figure 1. Preferred reporting items for systematic reviews and meta-analyses flow diagram.

to pathogen and STI screening frequency. We found no evidence of publication bias (Supplementary Figures 9-11).

Secondary outcomes

Adherence to recommended STI screening frequency

Seven studies assessed stakeholder adherence to recommended STI screening frequency in people who use PrEP [15–21]. Survey data from the United States (US)-based ARTnet study (N = 631 MSM) found differences in adherence by anatomical site screened, with blood samples having the highest level of consistent screening (87%), followed by a urine sample or urethral swab (78%), rectal swab (57%), or pharyngeal swab (64%). In this study, 'consistent screening' meant participants self-reported 'always' or 'sometimes' receiving screening for STIs at PrEP check-up visits within 12 months, with most people who use PrEP (82%) attending PrEP visits every 3 months. Adherence also varied between age groups; older users disclosed the lowest level of consistent STI screening compared to younger MSM for all anatomical sites. MSM with recent STI exposure reported more consistent STI screening for urogenital and rectal STIs [15].

The Sibanye Health Project conducted in South Africa between 2015 and 2016 reported varying screening rates between anatomical sites. Participants returned for STI and HIV screening 6 and 12 months after PrEP initiation. Of the 201 participants, 193 (96%) attended at least one visit where follow-up STI screening was offered. Acceptance of at least one urethral chlamydia/gonorrhea test (94%) and syphilis (94%) were high, with lower acceptance of rectal screening at 75%. Demographic characteristics, study location, participant characteristics, or behaviors did not influence screening behaviors [19]. A retrospective cohort study conducted on people who use PrEP in Israel found inconsistent adherence to recommended 6-monthly STI screening, and adherence differed by type of test. There was a total of 3.1 chlamydia/gonorrhea tests conducted per person-year follow-up and 2.8 syphilis tests conducted per person-year follow-up [16].

Data from a US commercial insurance claims database between 2011-2015 in 3498 people who use PrEP found that at 6 months, 49% screened for syphilis and 39% screened for chlamydia or gonorrhea. Although screening occurred less frequently than recommended, rates increased over the review period. For example, in 2011, 38.6% had tested for syphilis, and 24.4% had tested for chlamydia and gonorrhea by 12 months after PrEP initiation; this increased in 2015, where 69.7% had tested for syphilis and 60.8% for chlamydia and gonorrhea by 12 months after PrEP initiation [17]. A study from an academic clinic in the US reported that STI screening rates decreased as the duration of time on PrEP increased, which corresponded to an increased rate of STI diagnoses in follow-ups [20]. This same study reported higher adherence levels than others, with STI screening uptake at 6 months at 73%, 72%, and 85% for chlamydia, gonorrhea, and syphilis, respectively. Those diagnosed with an STI at baseline were more likely to meet 6-monthly recommendations for screening than those without an STI at baseline (86% vs 57%). Those enrolled in the medication management program were also more likely to meet guideline recommendations than those who were not (86% vs 52%). Furthermore, self-referred patients had higher adherence than those who had been referred through their primary care physicians or via word of mouth [20]. Other factors also influenced STI screening frequency; a study among 67 people who used PrEP in Hong Kong and who obtained PrEP in Thailand found that participants who perceived that they were at high risk for STIs were more likely to engage in screening during follow-up. Conversely, participants who perceived that testing providers would think they were engaging in risky behaviors due to PrEP use were less likely to take up STI screening. This study had a low adherence rate, with just 47.8% of participants reporting STI screening uptake at 3 months [18].

A US study investigated self-reported rectal STI screening in the prior 12 months among 88 MSM who used PrEP. This study found that 69.3% of people who used PrEP reported being screened for a rectal STI in the last 12 months. MSM who had increased vul-

Table 1
Characteristics of included studies, according to STI test frequency.

Characteristics	All studies (N = 46) n (%)	Three monthly (or fewer) testing[a] (N = 24)	≥4-6 monthly testing[a] (N = 13)	>6 monthly testing[a] (N = 3)
Latest year of study[b]				
Before 2015	4 (8.7%)	1 (2.2)	3 (6.5%)	0 (0.0%)
After 2015	38 (82.6%)	23 (50.0%)	10 (21.7%)	3 (6.5%)
Modeling study (no real-world data)	4 (8.7%)			
Country income level[c]				
Low	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lower-middle	1 (2.2%)	0 (0.0%)	1 (2.2%)	0 (0.0%)
Upper-middle	3 (6.5%)	1 (2.2%)	1 (2.2%)	1 (2.2%)
High	39 (84.8%)	22 (47.8%)	7 (15.2%)	2 (4.3%)
Mixed	3 (6.5%)	1 (2.2%)	3 (6.5%)	0 (0.0%)
Study setting				
Primary level health facilities	22 (47.8%)	16 (34.8%)	5 (10.9%)	1 (2.2%)
Hospitals	7 (15.2%)	3 (6.5%)	3 (6.5%)	1 (2.2%)
Community organizations	4 (8.7%)	2 (4.3%)	3 (6.5%)	0 (0.0%)
Hospitals and community centers	1 (2.2%)	1 (2.2%)	0 (0.0%)	0 (0.0%)
Other	10 (21.7%)	2 (4.3%)	0 (0.0%)	1 (2.2%)
Unclear	2 (4.3%)	0 (0.0%)	2 (4.3%)	0 (0.0%)
Population				
Men who have sex with men	43 (93.5%)	23 (50.0%)	13 (28.3%)	2 (4.3%)
HIV serodiscordant couples	1 (2.2%)	1 (2.2%)	0 (0.0%)	0 (0.0%)
People who use drugs	3 (6.5%)	2 (4.3%)	1 (2.2%)	1 (2.2%)
Trans and gender diverse	12 (26.1%)	8 (17.4%)	4 (8.7%)	1 (2.2%)
Other[d]	7 (15.2%)	5 (10.9%)	1 (2.2%)	1 (2.2%)
Not specified	2 (4.3%)	1 (2.2%)	0 (0.0%)	0 (0.0%)
Primary outcome				
STI positivity[e]	38 (82.6%)			
Secondary outcomes				
Adherence to STI testing frequency	7 (15.2%)			
Feasibility of STI testing	1 (2.2%)			
Changes in STI epidemiology according to testing frequency	3 (6.5%)			
Cost-effectiveness of STI testing	0 (0.0%)			

STI, sexually transmitted infection.
[a] Only studies with primary patient data were included in this table. Modeling studies were excluded. One study evaluated both 3-monthly and 6-monthly screening.
[b] The latest year of study is defined as the year when the latest observation was reported (not the publication year).
[c] According to World Bank classification.
[d] Populations included in 'other' include cisgender men, women, or adolescents who self-identify as heterosexuals.
[e] Chlamydia, gonorrhea, or syphilis.

Table 2
Pooled test positivity.

Testing frequency	Number of studies	Pooled test positivity (95% confidence interval)	I^2
Chlamydia			
3 monthly	16	0.20 (0.15-0.25)	96.6%
6 monthly	12	0.10 (0.06-0.14)	95.6%
12 monthly	2	0.16 (0.03-0.34)	-
Gonorrhea			
3 monthly	16	0.17 (0.12-0.22)	97.3%
6 monthly	12	0.04 (0.00-0.09)	94.1%
12 monthly	2	0.12 (0.00-0.41)	-
Syphilis			
3 monthly	18	0.07 (0.05-0.08)	81.9%
6 monthly	8	0.07 (0.04-0.11)	93.6%
12 monthly	1	0.10 (0.08-0.13)	-

nerability for STIs, such as a previous syphilis diagnosis and engaging in condomless anal sex with casual partners, were more likely to accept rectal STI screening. Having a provider who offered HIV screening was also found to increase the likelihood of MSM on PrEP being screened for rectal STI [21].

Feasibility

Ryan et al. described the impact of PrEP implementation during the PrEPX study on healthcare delivery, including STI screening, on existing health services in Victoria, Australia [22]. Victorian sexual health and primary care services had high feasibility to accommo-

date the increased demand for 3-monthly STI screening after rapid PrEP implementation in a large cohort (over 2000 participants in under 3 months). This was achieved through close collaboration with various stakeholders, including community members, clinicians, pharmacists, and researchers. However, it should be noted that this study was limited to five large clinics, and this high feasibility may not reflect the ability of smaller clinics to respond to increased STI screening demand for people who use PrEP [22].

Cost-effectiveness

Although we did not identify cost-effectiveness analyses as part of our search strategy, during the review of the paper, it was brought to our attention that a study from the Netherlands among MSM PrEP users demonstrated that 3-monthly screening for chlamydia and gonorrhea was not cost-effective compared to 6-monthly screening [23].

Change in STI epidemiology according to different STI screening frequencies

Two modeling studies and one demonstration project (prospective, open-label cohort study) investigated the change in STI epidemiology according to different STI screening frequencies. A US mathematical modeling study investigated the impact of STI screening frequency on gonorrhea and chlamydia incidence in MSM after PrEP initiation. They report combined gonorrhea and chlamydia observed incidence would decrease with increasing STI screening frequency: from 1.85 per 100 person-years (6-monthly screening) to 0.93 per 100 person-years (3-monthly screening) [24]. The change of STI screening frequency from 6 months to 3 months would detect more incident infections so that earlier treatment could reduce population-level incidence. A Canadian modeling study that investigated the change in gonorrhea prevalence according to STI screening frequency suggested that STI screening every 3 months as per Canada's public health guidelines was insufficient to prevent increased gonorrhea levels after PrEP initiation. Their model showed that screening once every 2 months minimized gonorrhea prevalence while allowing for flexibility in other parameters influencing STI levels, such as lower condom use. Furthermore, screening every 2 months with a 10-25% reduction in risky behavior worked synergistically to maintain gonorrhea levels at pre-PrEP levels. However, the authors acknowledged that 2-monthly screening might not be feasible due to low adherence by users and financial constraints of health providers. Their models also indicated that as condom usage decreased, the benefits of high STI screening frequency were counteracted. When longer screening intervals were modeled, gonorrhea prevalence increased dramatically (5-yearly screening: 60%, biannual screening: 50%), reinforcing the importance of regular monitoring [25].

A study that examined STI incidence in the US PrEP Demonstration Project suggested that quarterly STI screening was superior to biannual screening for detection of asymptomatic STIs for people who use PrEP in this cohort. In total, 557 MSM and transgender women received STI screening every 3 months over 48 weeks in US STI clinics. Had screening been done every 6 months rather than 3 months, identification of 62/181 (34.3%) gonorrhea, 84/210 (40.0%) chlamydia, and 11/54 (20.4%) syphilis cases would have been delayed by up to 3 months, thus prolonging the period of infectivity for each case [26].

Discussion

This systematic review consolidates the evidence within the published literature regarding the STI positivity, client adherence to STI screening frequency recommendations, feasibility, cost-effectiveness, and modeled impact on STI epidemics of screening at different frequencies. We found that increasing screening frequency was generally associated with increased positivity. However, adherence to recommended STI screening frequency varied significantly, including substantial variations in anatomical testing sites. More data is needed regarding the feasibility of healthcare clinics to accommodate the increased offer of STI screening with the scaling up of PrEP. From modeling studies, we found that increased STI screening could reduce STI incidence, and one cost-effectiveness analysis from the Netherlands reported that 3-monthly screening for chlamydia and gonorrhea was not cost-effective compared to 6-monthly screening. There were no studies that provided data on AMR induced by more frequently diagnosed infections that required treatment.

Our overall STI positivity was consistent with the baseline STI prevalence among people who use PrEP in another systematic review [27], reflecting the high STI burden among people who use PrEP. So, optimizing STI screening frequency to improve the detection and treatment of STIs for people who use PrEP may reduce their overall burden of STIs. Interestingly, we observed that studies with 2-3 or 4-6 monthly frequencies of syphilis screening did not significantly differ in positivity. However, for chlamydia and gonorrhea, the positivity was 50% and 75% lower, respectively, in studies with 4-6 monthly compared with 2-3 monthly screenings. The larger difference in gonorrhea positivity may be due to the possibility for gonorrhea to naturally clear faster than chlamydia [28,29]. Thus, our findings suggest that screening more frequently would be ideal if the aim is to identify chlamydia and/or gonorrhea more quickly [26].

Although using 3-monthly rather than 6-monthly STI screening could detect more infections [30], an important consideration for recommending frequent STI screening is the increased need for antibiotics. An analysis of national and sentinel surveillance data in England (2015-2019) indicated that there was increasing gonococcal AMR, especially among MSM populations compared to heterosexual couples [31]. In an age where antibiotic stewardship is increasingly critical, it is important to limit antibiotic use to only when necessary. It is theorized that intensive STI screening has been linked to AMR within the United Kingdom and US [31]. So, an alternate approach might be to vary STI screening frequency for people who use PrEP depending on subpopulations with different levels of risk for STIs. There is also evidence that a minority of people who use PrEP contribute to most STIs detected [32]. Thus, improving better identification of those at higher risk for STIs may allow for a targeted approach to STI screening to optimize resource use and reduce the overuse of antibiotics.

Particularly for 3-monthly screening, there are significant client-, provider- and service-level barriers to complying with this common recommendation. Regarding client-level barriers, a study from Hong Kong showed that STI screening uptake at 3 months was low (47.8%). The study also found that participants who perceived that providers of STI screening would think they were engaging in risky behaviors due to PrEP use were less likely to take up STI screening [18]. Those who used PrEP informally (i.e. users who obtained PrEP via non-prescription sources such as online, abroad, friends, or other sources) may face unique challenges such as unawareness of the location of testing facilities. Additionally, people who use PrEP intermittently may be less likely to screen frequently for STIs as they may not attend PrEP services on a regular basis. Out-of-pocket costs for increased frequency of STI screening and treatment or transportation when the frequency of screening is shorter than the PrEP follow-up visits [33] can add to the challenges of frequent screening [34]. Interviews from a younger group of people who would benefit from PrEP also indicated that participants were unwilling to be screened every 3 months due to perceptions that follow-ups would be time-consuming and inconvenient [35].

In contrast, sex-positive and knowledgeable providers were shown to encourage engagement in PrEP-related healthcare, which included STI screening [18,21,36]. Additionally, people who use PrEP who had higher vulnerability for STIs were more accepting of frequent STI screening, such as those with positive baseline STI tests [18,20], a previous syphilis diagnosis [15,21], or users who engage in condomless sex with casual partners [15]. Other factors associated with more recent STI screening included younger age, White race, college education, and greater parental support [15,35]. Specific measures that encouraged adherence to 3-monthly STI screening also assisted in overcoming barriers to attendance, such as counseling, appointment reminders, and assistance from pharmacy staff [20].

PrEP programs can also facilitate frequent STI screening by acting as a gateway to engagement with the healthcare system, especially among clients at higher risk of infection who may not otherwise access such services [37,38]. Initiating PrEP can also have a positive psychological effect, allowing users to feel in control of their sexual health care and helping build rapport with healthcare providers [36]. However, this effect may wane over time, as suggested by one study, which showed that users who took PrEP for over one year were far less likely to meet the STI screening recommendations compared to those who had been taking PrEP for a shorter time [20]. People who use PrEP are a heterogeneous group, so further research should focus on subgroups of clients to better understand and address their unique challenges. Efforts should be made to train PrEP providers in providing inclusive and non-stigmatizing sexual health care.

Regarding healthcare worker-level barriers, inadequate STI-related training and competency of PrEP providers have been a challenge in implementing STI screening [6]. Another study described providers stating time constraints, cultural and language barriers, and difficulty obtaining a sexual history affected their ability to conduct routine STI screening [15]. Providers' adherence to recommended frequency of screening can also be suboptimal, with one study finding that providers only ordered STI screening in 67% of clients every 6 months [39]. They were also less likely to order STI screening in older users, HIV serodiscordant couples, and African Americans compared to White patients. Differences in competence also exist between primary care providers and specialists, with a higher proportion of participants receiving more comprehensive care under specialist treatment than in primary care [40].

Regarding service-level barriers, a recent systematic review of STI screening in PrEP programs found that providers commonly identified that cost was a barrier to implementation of regular STI screening [6]. They also stressed that greater funding would allow them to increase their capacity to screen people who use PrEP. Indeed, high-income countries and countries that have no direct user fee for STI services, such as Australia, the United Kingdom, and France, offer more comprehensive STI services than lower-resourced countries which rely on syndromic case management [6]. While logistical challenges exist [6], PrEP programs in Australia have shown that integrating quarterly STI screening in existing sexual health networks is feasible and effective [22]. At the programmatic level, it is also important to consider the different costs and time to provide test results for syphilis tests, particularly lateral flow rapid tests (treponemal or duo treponemal/non-treponemal tests), when compared to molecular tests for gonorrhea and chlamydia.

The strength of our study is that it systematically reviewed the extant literature to understand the evidence regarding STI screening frequency among people who use PrEP. We also collated data regarding the adherence to recommended STI screening frequency, feasibility, impact on STI epidemics, and cost-effectiveness of STI screening at different frequencies, settings, and populations. Our study should be read considering some limitations. First, most studies were from high-income countries. More research is needed from low- and middle-income countries where access to STI services beyond syndromic case management is not ubiquitous, and epidemiology might differ significantly. Second, there was substantial between-study heterogeneity for pathogen positivity, some of which could be explained by STI screening frequency, latest year of study, and study duration. There are other important factors to explain the observed heterogeneity, such as differences in offer of triple anatomical site screening for those at risk (e.g., MSM), background STI positivity, sexual risk behaviors, and sexual network structures. Third, almost all studies related to MSM using PrEP, with little data from other populations. Thus, our findings may not be generalizable to non-MSM populations using PrEP and low- and middle-income countries. Fourth, there remains uncertainty regarding the impact of screening frequency on STI incidence as current evidence arises from modeling studies. Large, multi-country studies will be needed to determine this. Fifth, it was not possible to determine the impact of unscheduled visits when an individual became symptomatic; thus, our pooled estimates of positivity are likely to underestimate the true test positivity. For example, one sexual health center in Australia reported that a substantial proportion of primary (58%) and secondary (44%) syphilis among PrEP users were made at interim STI clinic attendances [41]. This may also explain the observation of the apparent no statistically significant difference in syphilis positivity in studies screening every 3 months compared with screening every 6 months. However, as defined in our methods, the focus of our review is on STI screening (of asymptomatic people). Last, additional research is needed to determine the benefits and costs associated with more frequent rectal and pharyngeal chlamydia and gonorrhea on a population level, as well as the impact on AMR.

In conclusion, although frequent STI screening could reduce delayed diagnoses and potentially decrease incidence, there remain significant knowledge gaps regarding optimal STI screening frequency for different STIs among people on PrEP to guide recommendations. The increased costs and low adherence to screening for STIs more frequently than every 6 months need to be balanced against possible benefits, including implementation feasibility and AMR. However, improving the identification of people who use PrEP that is at higher risk for STIs for more frequent STI screening can optimize resource use and reduce the overuse of antibiotics.

Declaration of Competing Interest

None of the authors has any competing interests to declare. Some of the authors are present or former staff members of the World Health Organization. The authors alone are responsible for the views expressed in this publication, and they do not necessarily represent the views, decisions, or policies of the institutions with which they are affiliated.

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Author contributions

MM, RB, CC, and JO conceived the idea. CK and VZ did the screening and data extraction. JO conducted the statistical analysis. All authors contributed to the interpretation of the results and

subsequent edits of the manuscript and had final responsibility for the decision to submit for publication.

Data sharing statement

Data will be made available upon request made to the corresponding author.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2023.01.007.

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