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REVIEW ARTICLE

Factors Influencing HIV PrEP Acceptance and Use among At-Risk Populations in Southeast Asia: A Systematic Review

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ABSTRAK

Profilaksis pra-pendedahan (PrEP) merupakan salah satu strategi utama kesihatan awam dalam mengurangkan kadar penularan 'Human Immunodeficiency Virus' (HIV). Pelaksanaan PrEP di rantau Asia Tenggara berhadapan dengan cabaran akibat jurang dalam kaedah pelaksanaan serta kurangnya kesedaran dan kesediaan dalam kalangan populasi berisiko tinggi. Ulasan sistematik ini bertujuan untuk mengenalpasti halangan dan faktor yang memudahkan penerimaan dan penggunaan PrEP di rantau ini. Carian menyeluruh merangkumi pangkalan data PubMed, Scopus dan Web of Science sehingga Oktober 2023 telah menemui 200 artikel yang berpotensi, di mana 16 artikel memenuhi kriteria kemasukan. Tema utama yang dikenalpasti dalam halangan dan faktor yang memudahkan penerimaan dan penggunaan PrEP termasuklah sosiodemografi, psikososial dan sistem kesihatan; seperti kesedaran dan pengetahuan tentang PrEP, persepsi risiko HIV, stigma sosial dan akses kepada perkhidmatan kesihatan. Selain itu, salah faham dan kebimbangan mengenai kesan sampingan PrEP dikenal pasti sebagai faktor penghalang yang signifikan, manakala kesedaran dan pengetahuan tentang PrEP muncul sebagai faktor penggalak utama kepada penerimaan PrEP. Hasil dapatan ulasan ini menekankan kerumitan pelaksanaan PrEP di Asia Tenggara, mencadangkan bahawa intervensi yang disesuaikan dan pelbagai adalah penting untuk meningkatkan penerimaan dan liputan PrEP yang boleh memberikan pandangan berharga kepada pembuat dasar, organisasi kesihatan dan komuniti di Asia Tenggara mengenai strategi intervensi yang efektif untuk meningkatkan penerimaan PrEP dalam kalangan populasi berisiko tinggi, selaras dengan usaha berterusan dalam mencegah penularan HIV.

Kata kunci: *Halangan; kesanggupan; penggalak; profilaksis pra-pendedahan*

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ABSTRACT

Pre-exposure prophylaxis (PrEP) is a critical public health strategy in mitigating human immunodeficiency virus (HIV) transmission. Despite its efficacy, the implementation of PrEP in Southeast Asia faces challenges due to gaps in implementation, awareness and acceptance among at-risk populations. This systematic review aimed to identify the barriers and facilitators influencing PrEP acceptability and uptake in this region. A comprehensive search across PubMed, Scopus and Web of Science databases from 2010 to October 2023 yielded 200 potential articles, of which 16 met the inclusion criteria. Key themes identified within the barriers and facilitators toward PrEP acceptability and uptake included sociodemographic, psychosocial and health system factors; highlighting key factors such as awareness and knowledge of PrEP, perceived HIV risk, social stigma and accessibility to healthcare services. Notably, misconception and worry about side-effects of PrEP emerged as significant barriers, whilst knowledge and awareness of PrEP emerged as critical facilitators. This review highlights the complexity of PrEP implementation in Southeast Asia, suggesting that customised, multifaceted interventions are essential to improve PrEP acceptance and coverage which could give valuable insights to policymakers, healthcare providers, and community-based organisations on effective strategies to increase PrEP uptake among key populations, aligning with the continuous effort to prevent HIV transmission.

Keywords: Barrier; facilitator; pre-exposure prophylaxis; willingness

INTRODUCTION

Human immunodeficiency virus (HIV) has had a significant impact on a large number of individuals globally, particularly in Southeast Asia. Despite strengthened efforts in HIV prevention and control, new HIV infections continue to increase among high-risk populations, including men who have sex with men (MSM), transgender women (TGW) and female sex workers (FSW) (Si et al. 2020). Trends of HIV prevalence in Southeast Asia exceed the global average, with over 0.3% of the population affected, compared to the worldwide prevalence of 0.23% (Challacombe 2020). Worryingly, the incidence of new HIV infections has been documented to be up to 60% in some countries in Southeast Asia (Rosen et al. 2023; Si et al. 2020). Numerous factors have been identified as the primary drivers fuelling the HIV epidemic, including condomless sex, multiple sex partners, substance use (particularly amphetamine-type stimulants; ATS), and co-morbidities such as depression and anxiety (Rosen et al. 2023).

The World Health Organisation approved pre-exposure prophylaxis (PrEP) as an additional biomedical prevention strategy and has released guidelines for PrEP use among all groups at substantial risk of HIV infection (Coukan et al. 2023; Muhumuza et al. 2021). It involves individuals at high risk of HIV taking HIV anti-retroviral drugs, such as tenofovir/emtricitabine (TDF/FTC) (Nabunya et al. 2023; Si et al. 2020). PrEP has been proven to be highly effective in preventing HIV acquisition, with clinical trials demonstrating a decrease in HIV risk by up to 99% when adherence is high (Coukan et al. 2023; Nabunya et al. 2023; Si et al. 2020). 'Uptake' has been defined in multiple ways in the field and is often being used interchangeably with 'acceptability'. In the context of this paper, we have considered both the 'uptake of PrEP' – defined as the initiation of oral PrEP among those offered

PrEP – and 'acceptability of PrEP' – defined as interest or likelihood of taking up or adhering to PrEP (Dunbar et al. 2018; Nakamanya et al. 2022).

Due to its robust efficacy in preventing HIV infection, PrEP is being utilised globally with relatively high degrees of acceptability (Nabunya et al. 2023). In the United States and the United Kingdom, PrEP has been well received and the desirability rate is good. Additionally, studies in Africa, Nigeria and youth in Uganda, Zimbabwe and South Africa have also shown high acceptability for PrEP (Nabunya et al. 2023). While PrEP is recommended as one of the most effective HIV prevention strategies by international agencies, the HIV prevention gap remains high in the Southeast Asian region due to suboptimal PrEP implementation (Rosen et al. 2023; Si et al. 2020). To scale up PrEP beyond current levels, PrEP delivery must be guided by a thorough understanding of the potential barriers to delivery and the opportunities to enhance the acceptability and uptake of PrEP among key populations (Rosen et al. 2023).

Some of the notable barriers to PrEP uptake include lack of knowledge about PrEP, ongoing stigma and discrimination surrounding HIV, challenges in obtaining and affording PrEP medications and services, flaws in the health care system, and cultural and gender norms that restrict access (Moyo & Nunu 2024; Muhumuza et al. 2021; Si et al. 2020). On the other hand, factors that encourage the use of PrEP include supportive laws and regulations, community involvement and the participation of important populations, education and training programs for healthcare professionals, and efforts to make healthcare more affordable and accessible (Moyo & Nunu 2024).

As part of the strategies to attain the 95-95-95 fast-track action to end the AIDS epidemic by 2030 (Frescura et al. 2022), engaging high-risk groups on the acceptance and uptake of PrEP is imperative to successfully reduce the epidemic. Although the barriers and facilitators of PrEP implementation have been reported across various settings (particularly the United State and Canada), epidemiological data on the progress in PrEP uptake and acceptability in this region remains scant. Thus, it becomes crucial to rapidly assess these factors in the local context (Rosen et al. 2023). Therefore, this systematic review sought to identify the barriers and facilitators to PrEP acceptability in high-risk populations in Southeast Asia. This could assist the development of culturally relevant risk reduction strategies for key populations in this region.

MATERIALS AND METHODS

The review method was adopted from Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA 2009) which is specifically designed for systematic review and meta-analysis (Page et al. 2021). The major sections included in PRISMA are identification, screening, eligibility and inclusion as summarised in Figure 1.

Search Strategy

We searched the literature on barriers and facilitators for PrEP acceptability and uptake. The search was conducted using PubMed, Scopus and Web of Science databases to identify relevant papers that described the facilitators and barriers to PrEP acceptability and uptake among at-risk groups in Southeast Asia. The search was conducted using a combination of keywords and subject headings specific to the database, as per Table S1 and following these concepts: (i) Population: Population at risk for HIV, such as men who have sex with men (MSM), transgender (TG),

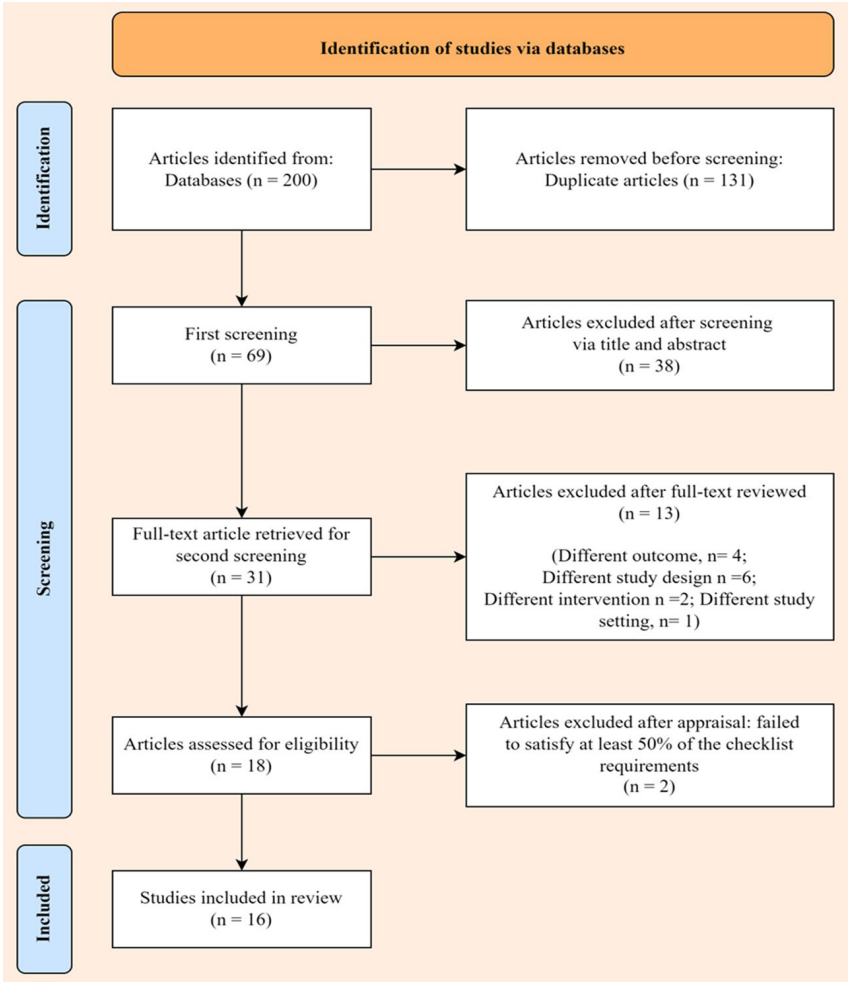

FIGURE 1: PRISMA flowchart diagram

sex worker, etc.; (ii) Exposure: Oral HIV PrEP; and (iii) Outcome: Facilitators and barriers to PrEP acceptability and uptake. In this review, facilitator was defined as any factor that promotes or eases the uptake or acceptability of PrEP, while barrier was defined as any factor or obstacle that may hinder or impede the uptake of PreP.

The search was limited to studies published in English from 2010 until October 2023. References were retrieved from the databases, and duplicate articles were removed using the Deduplicator tool from the Systematic Review Accelerator (Institute for Evidence-Based Healthcare, Gold Coast, Australia) (Clark et al. 2020). Subsequently, the list of references, together with their abstracts, was uploaded to Endnote X (Clarivate Analytics, Philadelphia, USA) for the subsequent screening process.

Study Selection

The title and abstract were initially screened using the following inclusion criteria: (i)

original papers; (ii) quantitative and mixed-method studies; (iii) conducted among individuals at risk; (iv) done in Southeast Asian nations; and (v) described the facilitators and barriers to PrEP uptake. Studies that included other forms of PrEP besides oral administration and qualitative studies were excluded. A total of 31 articles were subsequently retrieved for a second screening based on the eligibility criteria.

Quality Assessment

It is necessary to conduct a critical appraisal of the articles to ensure that they have a strong methodological quality and a minimal risk of bias. The appraisal of each article was done using the Joanna Briggs Institute (JBI) Critical Appraisal Tools that correspond to the study design (Lizarondo et al. 2020; Moola et al. 2020; Tufanaru et al. 2020). The JBI has developed several appraisal tools, each of which is tailored to a specific study design. The JBI tools do not prescribe a particular methodological approach to be used when they are utilised (Barker et al. 2023). On the contrary, they have been deliberately crafted to suit any technique favoured by the review committee. For this evaluation, each article was reviewed by two independent reviewers. Subsequently, the two reviewers convened to discuss their findings. If they were unable to reach a consensus, an unbiased third reviewer was then brought in. From the 18 articles that were examined, two articles were excluded because they failed to satisfy at least 50% of the checklist requirements. The quality of the other articles was considered adequate and, thus, was included in the final review. The results of the quality appraisal is attached in the Supplementary Material Table S2.

Data Extraction, Synthesis and Analysis

A standardised data extraction sheet was specifically designed for this review. Information collected, if available, included the study characteristics (study title, authors, year of study and publication, study population, location of the study, and study design) as well as the specific data on facilitators and barriers that were found to have a significant association with the uptake or initiation of PrEP. The data extraction method was conducted to specifically collect all pertinent data to answer the research question, and all data were recorded on the data extraction sheet. Thematic analysis was applied to identify recurring themes in the studies that were included. Similar data were pooled thematically, with a total of six themes identified.

RESULTS

Primary Study Characteristics

A total of 16 articles were selected for final review. In general, there were a limited number of studies on PrEP uptake in Southeast Asia, with the majority of studies being conducted in Thailand (n = 12). Other countries include Malaysia (n = 2), Singapore (n = 1) and Myanmar (n = 1). Most studies were conducted among the MSM group and TG populations. Most studies employed a cross-sectional study design. Overall, PrEP acceptance among key populations varied from 15 to 62.8% across the studies in this review. Table 1 summarised the key attributes of the studies that were considered.

TABLE 1: Characteristics of included studies

No.	Author, Year	Country	Study design	Participants	Sample size	Uptake and acceptance of PrEP
1.	Chewanan et al. (2023)	Thailand	Prospective cohort	MSM and TG	803	43.5% started PrEP
2.	Weir et al. (2023)	Thailand	Quasi-experimental study	MSM and TGW	846	62.8% initiated PrEP
3.	Eger et al. (2022)	Malaysia	Cross-sectional	MSM	355	18.3% used PrEP
4.	Rayanakorn et al. (2022)	Thailand	Cross-sectional	Key population *	196	NA
5.	Kawichai et al. (2022)	Thailand	Randomised controlled trial	MSM and TG	200	NA
6.	Auemaneekul et al. (2020)	Thailand	Cross-sectional	MSM and TG	310	31% intended to take daily PrEP
7.	Ramautarsing et al. (2020)	Thailand	Cross-sectional	MSM and TG	7187	43.9% used PrEP
8.	Tan et al. (2018)	Singapore	Mixed methods study	MSM	1339	15% had taken PrEP
9.	Ongwandee et al. (2018)	Thailand	Cross-sectional	MSM and TG	507	46% started PrEP
10.	Lim et al. (2017)	Malaysia	Cross-sectional	MSM	990	39% were willing to take PrEP.
11.	Draper et al. (2017)	Myanmar	Cross-sectional	GM, MSM and TG	434	62% were willing to use PrEP.
12.	Plotzker et al. (2017)	Thailand	Cross-sectional	MSM and TG	297	55% accepted PrEP
13.	Martin et al. (2017)	Thailand	Prospective cohort	PWID	798	61% chose to start open-label PrEP
14.	Anand et al. (2017)	Thailand	Cross-sectional	MSM and TG	316	53.2% started PrEP
15.	Sineath et al. (2013)	Thailand	Cross-sectional	MSM	404	35% indicated interest in PrEP
16.	Yang et al. (2013)	Thailand	Cross-sectional	MSM and TG	238	39% very likely to accept prep

NA= Not Applicable; MSM: men who have sex with men; TGW: transgender women; FSW: female sex workers; TG: transgender; PWID: person who inject drug; GM: gender minority; PrEP: Pre-exposure prophylaxis

Facilitators to the Uptake and Acceptance of HIV Pre-exposure Prophylaxis

- Sociodemographic factors

The outcome of the comprehensive analysis of 16 research articles highlighted various significant socio-demographic characteristics that contributed to the acceptance of PrEP among key populations. The criteria encompassed gender, age, ethnicity, educational attainment, marital status and occupation as summarised in Table 2. A study

TABLE 2: Facilitators to HIV PrEP uptake and acceptance

Theme	Factor	Author, Year	Results
Sociodemographic	Gender	Martin et al. (2017)	Acceptance of PrEP was more likely in male versus female participants (aOR 1.9, 95% CI 1.0 - 3.6); p = 0.04.
	Age	Tan et al. (2018)	Participants aged 30-39 years (aOR 1.54), 40–49 years (1.93), and 50 years (aOR 2.13) were more likely than those ages 18-29 years to take PrEP.
		Martin et al. (2017)	Older participants >30 years old (odds ratio [OR] 1 8; 95% CI 1 4, 2 2) were more likely to choose PrEP.
	Ethnicity	Lim et al. (2017)	Malay ethnicity was significantly associated with willingness to use PrEP (48.6% willing, aOR 1.73, CI 1.12, -2.27).
		Draper et al. (2017)	Mandalay was significantly associated with willingness to use PrEP (adjusted odds ratio (aOR) = 1.79; 95%CI = 1.05–3.03).
	Level of education	Tan et al. (2018)	Those with a postgraduate degree were 2.4 times more likely than those with secondary school education and below to take PrEP.
		Anand et al. (2017)	Higher education 86% (OR 2.30) was significantly associated with PrEP uptake.
	Marital status	Tan et al. (2018)	4/154 (3%) among those who took PrEP and 1/176 (0.6%) among those considering taking PrEP were in a HIV-serodiscordant relationship
Awareness and knowledge	Knowledge regarding PrEP	Chewanan et al. (2023)	Those with high PrEP knowledge scores (aOR 1.5; 95% CI 1.1–2.0) were more likely to start PrEP.
		Plotzker et al. (2017)	PrEP acceptance was positively associated with knowing PrEP is not an ART [OR: 2.1 (1.0-4.3)].
	Awareness of PrEP	Eger et al. (2022)	Those who were aware of PrEP availability and use (22.6% of 287) took PrEP.
		Yang et al. (2013)	Factors associated with acceptability included prior awareness of PrEP (aOR 3.3; 95%CIs 1.2-9.0).
		Lim et al. (2017)	Having heard of PrEP (42.6%) was significantly associated with willingness to use PrEP (aOR 1.4. CI 1.06, 1.86).
	HIV risk perception	Plotzker et al. (2017)	PrEP acceptance was positively associated with HIV risk perception [OR: 4.3 (1.5–12.2), 6.3 (2.1–19.0), and 14.7 (3.9–55.1) for minimal, moderate, and high risk, respectively].
		Draper et al. (2017)	Those who perceived themselves as likely to become HIV positive (aOR = 1.82; 95%CI = 1.10–3.02) were more likely to accept PrEP.
		Tan et al. (2018)	Those who perceived themselves to be at high risk for HIV: - 11/154 (8.2%) were among those that took PrEP.

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	Awareness of partner's HIV status	Anand et al. (2017)	Being aware of sexual partner's HIV status (38% users) (OR 2.37) was significantly associated with PrEP uptake.
Behavioural	Precautionary measures before engaging in sexual activity	Tan et al. (2018)	20/154 (14.9%) among those that took PrEP and 22/176 (12.5%) among those considering taking PrEP regarded it as extra protection over other current methods of prevention.
		Tan et al. (2018)	13/154 (9.7%) among those who took PrEP and 12/176 (6.8%) among those considering taking PrEP use PrEP to engage in sex without condoms.
		Yang et al. (2013)	Having a prior history of STIs increased uptake of PrEP (AOR 4.6; 95% CIs 1.7-12.6).
		Weir et al. (2023)	Having a history of chlamydia infection was associated with higher initiation of PrEP.
		Chewanan et al. (2023)	Sex workers (aOR 1.7; 95% CI 1.0–2.8) were more likely to start PrEP.
	Compliance with PrEP	Auemaneekul et al. (2020)	MSM and TG with a high level of perceived behavioural control of PrEP adherence had a three times higher chance of developing the intention to take PrEP daily compared with those who had a low level of perceived behavioral control (95% CI 5 1.8–5.2).
	Sexual orientation	Lim et al. (2017)	Identifying as gay or homosexual (39.6% willing).
	Sexual behaviour	Eger et al. (2022)	Involvement in group sex (31.7% from 60 took PrEP).
		Anand et al. (2017)	Seeking sex partners online (39% PrEP users) (OR 2.05).
		Yang et al. (2013)	MSM with regularly planned sex (AOR 2.8, 95% CIs 1.1-7.2), and infrequent sex (AOR 2.9 95% CIs 1.3-6.3).
		Martin et al. (2017)	Participants who reported sex with a casual partner were less likely to take tenofovir than those who did not report sex with casual partners (AOR 0.5, 95% CI 0.3-0.8) p = 0.002.
		Weir et al. (2023)	Recent anal intercourse within 30 days was associated with immediate initiation of PrEP.
		Weir et al. (2023)	Those that use condoms was associated with immediate initiation of PrEP.
		Lim et al. (2017)	Having multiple male sexual partners (44.8% willing, AOR 1.98), having lack of confidence in practicing safe sex (35.7% willing, AOR 1.36), and having paid for sex with male partner (47.7% willing, AOR 1.39) were associated with willingness to take PrEP.
		Draper et al. (2017)	Those who had more than one recent regular partner (aOR = 2.94; 95%CI = 1.41-6.14), no regular partners (aOR = 2.05; 95%CI = 1.10-3.67), more than five casual partners (aOR = 2.05; 95%CI = 1.06-3.99), and no casual partners (aOR = 2.25; 95%CI = 1.23-4.11) were more likely to be willing to use PrEP.

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	Drug use	Eger et al. (2022)	Taking recreational drugs before sex (45.2% from 42) (AOR: 3.37; 95% CI: 1.44-7.89) was associated with use of PrEP
		Martin et al. (2017)	Those who were willing to take PrEP were likely to have injected drugs (723 [52%] of 1399 who did not inject vs 625 [62%] of 1014 who injected; p<0.0001).
PrEP-specific factors	Effectiveness of PrEP	Tan et al. (2018)	80 (59.7%) of 154 that took PrEP and 122/176 (69.3%) among those considering taking PrEP considered the effectiveness of PreP in preventing HIV.
Health system factors	HIV testing	Auemaneekul et al. (2020)	MSM and TGW having a history of HIV testing had a 2.3 times higher chance of developing their intention to take PrEP daily compared with those who never took the test (95% CI 5 1.3–4.1).
		Eger et al. (2022)	Those who had the accessibility to HIV testing and were HIV tested in the last 12 months were more likely to take PrEP (26.5% from 215 took PrEP) (AOR: 2.08; 95% CI: 1.13–3.85).
		Yang et al. (2013)	Previous HIV testing was associated with willingness to take PrEP (AOR 2.4 95%CIs 1.1-5.3).
	Deliverance mechanism	Anand et al. (2017)	Online based enrolment had 45% increased uptake of PrEP (OR 3.79) which may signify a preference to online based recruitment in comparison to community-based sites.
		Kawichai et al. (2022)	Health Technology – a smartphone PrEP adherence support app observed higher proportions of PrEP adherence among frequent app users than among infrequent users (Of the 87 participants, 22 (25%) were classified as frequent users).
	Availability of private insurance	Yang et al. (2013)	Having private insurance (AOR 5.0; 95% CIs 1.3-19.0) was associated with willingness to take PrEP.
	Availability of PrEP	Ongwandee et al. (2018)	235 (65.3%) reported they would definitely use PrEP if it was available.
Psychosocial	Disclosed sexual orientation	Eger et. al. (2022)	Those who had disclosed their sexual orientation to their family were more willing to take PrEP (24.4% from 131 took PrEP) (AOR: 1.85; 95% CI: 1.02–3.34).
	Peer influence	Weir et al. (2023)	Knowing others who had taken PrEP was associated with immediate PrEP initiation.

ART: antiretroviral medication; HIV: human immunodeficiency virus; MSM: men who have sex with men; PrEP: pre-exposure prophylaxis; TG: transgender

conducted by Martin et al. (2017) revealed a significant gender difference, indicating a higher prevalence of PrEP uptake among males compared to females (AOR 1.9, 95% CI 1.0 - 3.6; p = 0.04). Regarding age, Tan et al. (2018) highlighted its importance by demonstrating that those between the ages of 30 and 39 (1.54), 40 and 49 (1.93), and 50 years (2.13) had higher odds and were more inclined to choose PrEP compared to those between the ages of

18 and 29. Consistent with this, Martin et al. (2017) demonstrated that older participants exhibited a heightened likelihood of choosing PrEP ((OR) 1.8 (95% CI 1.4-2.2)). Two studies have highlighted a significant correlation between ethnicity and the adoption of PrEP in the community. In a study done in Malaysia, Lim et al. (2017) found a significant correlation between Malay ethnicity and a desire to use PrEP with 48.6% of individuals expressing readiness (AOR 1.73, CI 1.12, 2.27). Draper et al. (2017) conducted a study in Myanmar and found a strong link between Mandalay ethnicity and readiness to use PrEP (AOR = 1.79; 95% CI = 1.05–3.03). Tan et al. (2018) discovered a direct relationship between higher education and the uptake of PrEP. Their findings indicated that people with postgraduate degrees were 2.4 times more inclined to select PrEP. Anand et al. (2017) found a significant correlation, where individuals with higher education had a PrEP uptake rate of 86% (OR 2.30). Tan et al. (2018) observed that a mere 3% of individuals involved in HIV-serodiscordant relationships expressed a willingness to adopt PrEP, whereas 0.6% were contemplating its utilisation. In addition, Cheewanan et al. (2023) provided evidence indicating that sex workers had a greater probability of initiating PrEP (aOR) of 1.7 (95% CI 1.0-2.8).

- Knowledge and awareness

Cheewanan et al. (2023) highlighted the significant importance of information, stating that persons with strong PrEP knowledge levels had a 1.5 times greater likelihood of starting PrEP. In addition, Plotzker et al. (2017) emphasised a direct correlation between recognising the difference between PrEP and antiretroviral medication (ART) and a higher level of acceptability of PrEP [OR: 2.1 (1.0-4.3)]. In addition, Eger et al. (2022) emphasised the subject of awareness, stating that 22.6% of those who used PrEP were conscious of its availability and utilisation. Yang et al. (2013) revealed that prior awareness played a crucial role, showing that those who received information about PrEP were 3.3 times more likely to accept treatment. This discovery was consistent with the research conducted by Lim et al. (2017), which highlighted that being aware of PrEP was strongly linked to a willingness to take it (AOR 1.4, CI 1.06, 1.86).

Plotzker et al. (2017) demonstrated a correlation between the acceptance of PrEP and the perception of HIV risk, emphasising the influence of knowledge on the formation of attitudes towards risk. Anand et al. (2017) proposed the concept of awareness of a sexual partner's HIV status being strongly linked to the use of PrEP, with 38% of users reporting such awareness (OR 2.37). In addition, Sineath et al. (2013) revealed the correlation between knowledge and interconnectedness, suggesting that those who were knowledgeable about the availability of free condoms were 4.5 times more likely to be familiar with PrEP.

- Behavioural factors

In a study conducted by Cheewanan et al. (2023), it was found that sex workers were more inclined to initiate PrEP as a precautionary measure before engaging in sexual activity ([aOR] 1.7; 95% [CI] 1.0-2.8). Additionally, 14.9% of PrEP users and 12.5% of individuals who were contemplating using PrEP considered it to provide additional protection compared to other methods of prevention. A total of 9.7% of individuals who took PrEP and 6.8% of individuals who were contemplating using PrEP were those who performed sexual intercourse without using condoms (Tan et al. 2018). Individuals who had previously contracted sexually transmitted infections (STIs) also showed a higher rate of using PrEP (Weir et al. 2023; Yang et al. 2013).

According to a study by Auemaneekul et al. (2020), MSM and TG individuals who had strong sense of control over their behaviour were three times more likely to have the intention to use PrEP consistently. In addition, MSM who engaged in sex regularly ([AOR] 2.8) and those who had infrequent intercourse ([AOR] 2.9) were three times more likely to express willingness to embrace PrEP according to a study by Yang et al. (2013). Being identified as gay or homosexual was linked to a 39.6% inclination to use PrEP (Lim et al. 2017). Furthermore, it had been observed that engaging in group sexual activities and actively searching for sexual partners on the internet were factors that contributed to a higher adoption rate of PrEP (Anand et al. 2017; Eger et al. 2022). Two studies found a correlation between intravenous drug usage and higher likelihood of accepting PrEP (Eger et al. 2022; Martin et al. 2017). Engaging in substance abuse prior to sexual activity was found to be linked to a significantly increased likelihood of accepting PrEP use, with an AOR of 3.37 and a 95% CI ranging from 1.44 to 7.89, according to a study conducted by Eger et al. in 2022.

- PrEP-specific factors

The primary motivation (59.7%) for initiating PrEP was the awareness of its efficacy in preventing HIV transmission (Tan et al. 2018). This study also observed that a majority (69.3%) of individuals who were aware of PrEP but had not yet initiated its use expressed an intention to start using it. This decision was mostly influenced by the perceived effectiveness of PrEP in reducing HIV transmission (Tan et al., 2018). An additional study revealed that those who had previously undergone any PrEP treatment were 2.46 times more inclined to initiate PrEP compared to those who had not received PrEP (Anand et al. 2017).

- Health system factors

Three studies examined the impact of HIV testing on the commencement of PrEP and revealed that individuals with a prior history of HIV testing were approximately twice as likely to begin PrEP (Auemaneekul et al. 2020; Eger et al. 2022; Yang et al. 2013). Two further studies found that participants expressed a preference for being enrolled in PrEP programs outside of conventional government or commercial healthcare facilities (Anand et al. 2017; Lim et al. 2017). They had a preference for alternative organisations or internet platforms for PrEP recruitment. A further study observed that the utilisation of a mobile application in the management of a PrEP programme enhanced the level of adherence to treatment among its users (Kawichai et al. 2022). In locations where PrEP was funded through personal expenses, having medical insurance was correlated with a fivefold increase in the likelihood of accepting PrEP, compared to those without insurance (Yang et al. 2013). A study conducted in Thailand found that a significant majority (65.3%) of individuals who were aware of the benefits of PrEP were prepared to take it, even if they had to bear the cost themselves (Ongwandee et al. 2018).

- Pyschosocial factors

According to Eger et al. (2022), individuals who openly shared their sexual orientation with their family members were twice as likely to start PrEP compared to those who kept it hidden. Knowing individuals who had commenced PrEP was also found to be correlated with initiation of PrEP upon enrollment (Weir et al. 2023). Table 2 illustrated facilitating factors towards PrEP acceptance and uptake, based on identified themes.

Barrier to the Uptake and Acceptance of HIV Pre-Exposure Prophylaxis

- Sociodemographic, knowledge and awareness factors

Being single was perceived as a barrier to acceptance of PrEP (Cheewanan et al. 2023). A lack of information about PrEP resulted in a decline in the use of PrEP (Tan et al. 2018). Moreover, those who had no prior knowledge of PrEP had a reduced inclination to initiate PrEP (Sineath et al. 2013). The perception of low risk of acquiring HIV was identified as a major barrier to initiating PrEP. Two studies, by Ramautarsing et al. (2020) and Tan et al. (2018), found that individuals who regarded themselves to be at low risk of HIV infection were less likely to start using PrEP.

- Behavioural factors

The lack of adherence to PrEP (Cheewanan et al. 2023; Plotzker et al. 2017) and worries about sexual conduct (Sineath et al. 2013; Tan et al. 2018) were the behavioural elements linked to reduced PrEP uptake. Non-compliance can occur when individuals neglected to adhere to the prescribed tablet regimen (Cheewanan et al. 2023), or when they had a personal distaste to pills and are hesitant to start PrEP (Plotzker et al. 2017). Populations vulnerable to HIV infection who engaged in consistent condom use during sexual intercourse (Tan et al. 2018) or were aware that their partner tested negative for HIV (Sineath et al. 2013) were also less inclined to use PrEP.

- PrEP-specific factors

The most frequently reported barrier to initiating PrEP was the concern about potential side effects, as indicated by Cheewanan et al. (2023), Draper et al. (2017) and Tan et al. (2018). Individuals who expressed reservations over the adverse effects and extended duration of PrEP usage had a 0.7 times higher likelihood of being unwilling to start PrEP (Draper et al. 2017). Moreover, Cheewanan et al. (2023) emphasised that over half of the participants expressed reluctance to use PrEP because of its adverse effects. PrEP was often misunderstood in several ways, such as questioning its effectiveness in preventing HIV infection, viewing it as inconvenient, and expressing concerns about the development of resistance to anti-retroviral drugs (Rayanakorn et al. 2022; Tan et al. 2018). The prevalence of these misconceptions regarding PrEP resulted in a significant reluctance among the majority of participants to commence PrEP.

- Health system and other factors

The primary obstacle to the implementation of PrEP at a health system level was perceived to be its cost (Cheewanan et al. 2023; Tan et al. 2018). Nevertheless, Sineath et al. (2013) observed that over 20% of individuals showed reluctance to accept PrEP, even when it was offered at no cost. In addition, Rayanakorn et al. (2022) emphasised that the limited duration of PrEP counselling and the lack of support from the National Health Security Office and the Ministry of Public Health were obstacles to the adoption of PrEP in Thailand. Not being circumcised, or refusing to disclose circumcision status was cited as a barrier in a study by Plotzker et al. (2017). Table 3 illustrated factors identified as barriers to PrEP acceptance.

DISCUSSION

This systematic review has found various sociodemographic characteristics that impact the acceptability of PrEP among at-risk groups in Southeast Asia. It highlights the intricate relationship between socio-cultural, economic, and healthcare system

TABLE 3: Barriers to HIV PrEP uptake and acceptance

Theme	Factor	Author, Year	Results
Socio-demographic	Relationship status	Chewanan et al. (2023)	Those who were single were less likely to start PrEP than those who were living with a partner (aOR 0.6; 95% CI 0.5-0.9).
Awareness and knowledge	Knowledge on PrEP	Tan et al. (2018)	Lack of information about PrEP resulted in reduced acceptance of PrEP: 7/129 (5.4%).
	HIV risk perception	Ramautarsing et al. (2020)	No or low-risk perception was key barrier to PrEP acceptance among MSM (46.7%) and TG (41.9%) who met PrEP eligibility criteria
		Tan et al. (2018)	Low perceived susceptibility of HIV 37/129 (28.7%) was associated with reduced PrEP uptake.
Behavioural	Non-compliance with PrEP	Chewanan et al. (2023)	Likelihood of forgetting to take PrEP (383 [47.7%]) was associated with reduced preference to take PrEP.
		Plotzker et al. (2017)	Participants who reported an aversion to pills were much less likely to accept PrEP [OR: 0.11 (0.06-0.50)].
	Sexual behaviour	Tan et al. (2018)	Those who preferred sex with condoms: 8/129 (6.2%) were less likely to take PrEP.
		Sineath et al. (2013)	Respondents indicating disinterest in using PrEP most commonly ascribed this to having an HIV-negative partner.
PrEP-specific factors	Drug resistance	Rayanakorn et al. (2022)	Residual concern regarding antiretroviral drugs resistance was noted among those who preferred not to take PrEP.
	Misconceptions of PrEP	Tan et al. (2018)	Doubts on the efficacy of PrEP (16/129-12.4%) and regarding PrEP as inconvenient (7/129-5.4%) were reasons for not taking PrEP.
	Side effects	Tan et al. (2018)	Being worried of the side effects of PrEP: 15/129 (11.6%) was given as a reason for not initiating PrEP.
		Draper et al. (2017)	Gay men who reported concerns about the side effects and long-term use of PrEP were less likely (aOR = 0.35; 95%CI = 0.21-0.59) to be willing to use PrEP.
		Chewanan et al. (2023)	405 (50.4%) of participants reported being unwilling to take PrEP due to side effects.
Health system factors	Cost	Chewanan et al. (2023)	The cost of PrEP was seen as a barrier from willingness to initiate PrEP (296 [36.9%]).
		Tan et al. (2018)	Cost & accessibility of PrEP were barriers to PrEP uptake 23/129 (17.8%).
		Sineath et al. (2013)	Approximately 24% of respondents were unwilling to take PrEP even if it was free.
	Lack of support	Rayanakorn et al. (2022)	Limited PrEP counselling time and the need for support from the National Health Security Office/ Ministry of Public Health were identified as challenges to PrEP uptake in Thailand.

components. Age is found to be a key factor, as our analysis shows that individuals over the age of 30 are more likely to adopt PrEP. This may be due to their increased awareness and knowledge of HIV/AIDS prevention techniques, including PrEP. This level of awareness frequently develops as individuals grow older and gain knowledge about health through the accumulation of information over time (Olilo et al. 2019). However, these findings contradict with Kabaghe et al. (2023) and Zhou and Assanangkornchai (2022), who found that younger age groups, especially among MSM and TGW were more open to using PrEP.

Gender disparities also influence the adoption of PrEP, as indicated by a study conducted by Martin et al. (2017), which reveals a greater propensity for PrEP usage among males. This trend may be attributed to lower levels of awareness among females, as evidenced by a population study conducted in Malawi by Kabaghe et al. (2023). Another aspect that has an impact is ethnicity. For example, Tan et al. (2018) observed that the Malay community in Malaysia showed a greater inclination to take PrEP compared to other ethnic groups. The inclusion of PrEP in national health services has a significant impact on the acceptance of PrEP across both the general population and minority ethnic groups (Coukan et al. 2023; Mwaturura et al. 2021).

The degree of education is also crucial, as higher educational attainment is associated with a higher uptake of PrEP (Anand et al. 2017; Tan et al. 2018). The correlation may exist because those with greater levels of education are more likely to have the financial means to acquire PrEP (Tan et al. 2018). An individual's occupation, especially if it involves risk-taking behaviours, has a substantial impact on the acceptance of PrEP. This was demonstrated in a study in Thailand that establishes a connection between sex workers and increased adoption of PrEP, with sex workers having a twofold higher likelihood of using PrEP (Cheewanan et al. 2023). This could be attributed to their heightened vulnerability to sexual health risks associated with their profession, as well as their greater awareness of the sexual health services available, including PrEP. This finding aligns with the results of Zhou and Assanangkornchai (2022), which indicates that labourers, migrant workers, farmers, and government employees are more likely to commence PrEP. These findings provide valuable information for HIV prevention programmes targeting specific groups, highlighting the importance of educating them about PrEP. Consequently, this may increase their willingness to use PrEP, as they are already aware of the risks of HIV transmission owing to their occupational exposure.

A survey conducted in Singapore revealed that the primary motivation for considering PrEP is its effectiveness in preventing HIV. On the other hand, the main reasons for not considering PrEP are associated with concerns about its cost, doubts regarding its efficacy, potential side effects, and the inconvenience it may cause (Tan et al. 2018). Dang et al. (2022) reported that in the United States, there is a lack of PrEP initiation among TGW due to concerns about potential interactions between PrEP and their gender-affirming hormone therapy. This reliability concern has resulted in a decreased readiness to use PrEP among TGW. Hence, it is crucial to widely distribute information on the efficacy and safety of PrEP through counselling and social media platforms, with a particular focus on key populations.

The adoption of PrEP is greatly impacted by several health system elements, such as the ease of access, the presence of the service and the method of delivering it. Ongwandee et al. (2018) highlights the significance of availability

whereby a majority of participants indicated their readiness to utilise PrEP when it was easily obtainable, and as a result, almost half of them commenced PrEP. This suggests that the sheer presence or accessibility of something might serve as a powerful catalyst or enabler. Mwaturura et al. (2021) specifically examined African immigrants residing in affluent nations and found that cost was a predominant barrier to PrEP uptake. The results indicated a strong inclination to utilise PrEP among participants if it was provided with free of charge, underscoring the importance of cost-free availability in encouraging PrEP adoption. In addition, Yang et al. (2013) found that having private insurance increases the acceptance of PrEP, indicating that insurance coverage could play a crucial role in facilitating its use. These studies demonstrate how the functioning of the healthcare system, including issues such as the availability of services, cost and insurance coverage, significantly impact the acceptance and use of PrEP among populations at risk.

The acceptance and utilisation of PrEP is strongly correlated with many facets of sexual conduct. Various studies have observed a connection between sexual activity, with PreP users exhibiting higher levels of sexual risk-taking behaviour compared to non-users (Eaton et al. 2018). A longitudinal study in the Netherlands found that those using PrEP were more prone to having a higher number of casual sexual partners, engaging in unprotected anal intercourse, using substances during sexual activity, and being at a higher risk of contracting STIs, in comparison to a control group (Coyer et al. 2022; Draper et al. 2017; Eger et al. 2022; Lim et al. 2017). Similarly, Anand et al. (2017) found that individuals who actively sought sexual partners using online platforms had a twofold higher likelihood of utilising PrEP. These findings indicate that individuals who engage in high-risk sexual behaviours may possess a heightened insight of their elevated risk of acquiring HIV, and hence, are more likely to utilise PrEP.

Recent sexual activity and adherence to safe sex practices are crucial factors in determining the choice to utilise PrEP (Weir et al. 2023). Lim et al. (2017) found that individuals who lacked confidence in practicing safe sex and engaged in paying for sex with male partners were more likely to use PrEP. Additionally, recent anal intercourse and the use of condoms was linked with better acceptance of PrEP (Yang et al 2013). PrEP is often perceived as an additional safeguard in addition to other preventive measures, or even as a means to engage in unprotected sexual activity while still mitigating the risk of HIV transmission. Mcmanus et al. (2020) suggested that the utilisation of PrEP may decrease fear and anxiety, perhaps resulting in a modification of sexual conduct. These findings underscore the significance of consistent screening and ongoing sexual health education among key populations. Interestingly, cessation of PrEP use has been found to result in a subsequent reduction or cessation of sexual encounters (Hong 2023).

Eger et al. (2022) have identified a correlation between the consumption of recreational drugs before sexual activity and the willingness to initiate PrEP. Martin et al. (2016) corroborated this observation, highlighting a proclivity for PrEP utilisation among people who inject drugs (PWID). This link highlights the intricate interaction between drug use patterns, perceived danger, and risk-taking behaviour while making decisions regarding the use of PrEP. Comprehending these dynamics is crucial for implementing successful intervention measures, considering the present stigma and marginalisation key populations may face when accessing healthcare.

Yang et al. (2013) and Wier et al. (2023) highlighted the crucial influence of an individual's personal sexual history on the uptake of PrEP, whereby individuals who previously had STIs are nearly five times more inclined to start PrEP. Eger et al. (2022) observed that individuals with a prior history of STIs were more inclined to use PrEP. This may indicate that firsthand experience of the consequences of unprotected sex serves as a motivating factor for adopting preventive measures against other diseases.

The significance of knowledge in influencing the initiation of PrEP has been demonstrated in multiple studies (Cheewanan et al. 2023; Plotzker et al. 2017). These studies have shown a statistically significant correlation, indicating that individuals with a high level of knowledge about PrEP are twice as likely to begin taking and accepting PrEP (Cheewanan et al. 2023; Plotzker et al. 2017). This aligns with conclusions drawn from other comprehensive analyses in the United States (U.S), which revealed that awareness of PrEP and HIV has a substantial influence on its level of acceptance (Coukan et al. 2023; Dang et al. 2022).

Awareness regarding PrEP is also crucial for the willingness to initiate PrEP. Eger et al. (2022), Yang et al. (2013) and Lim et al. (2017), have examined different aspects of awareness and found that it increases the likelihood of accepting PrEP. The presence of characteristics such as extensive information, heightened awareness, and prompt disclosure of HIV risk was found to be substantially correlated with the inclination to utilise PrEP. This is corroborated by Chan et al. (2022) and Shamu et al. (2021), who demonstrated that the extensive dissemination of PrEP health promotion campaign materials through social media and social networks significantly increases awareness and knowledge about PrEP, consequently influencing the decision to take PrEP due to the perceived risk of HIV infection. An extensive media effort should be launched to educate young people and at-risk groups about HIV prevention strategies like PrEP, to raise awareness and encourage its adoption.

Eger et al. (2022) and Weir et al. (2023) examined the psychological factors that affect the decision to start PrEP. Eger et al. (2022) established that revealing one's sexual orientation has a crucial role in their willingness to start PrEP. Individuals who disclosed their sexual orientation to family members were twice as likely to initiate PrEP compared to those who concealed their sexual orientation. The authors further highlighted that creating a supportive environment and promoting open communication can have a favourable effect on the adoption of PrEP. Weir et al.'s (2023) study examined the social factors that influence the introduction of PrEP. The correlation between awareness of peers commencing PrEP and rapid uptake indicates the presence of a social contagion phenomenon. This behaviour could be attributed to social norms, wherein individuals are susceptible to the impact of their peers' actions and choices. Psychologically, the idea of social influence corresponds with ideas like social identity and conformity, highlighting the significance of interpersonal interactions in moulding decisions connected to health (Weir et al. 2023).

These studies highlight the significance of several elements, such as the health system, education, awareness, behaviour, and psychosocial aspects, in influencing individual choices about the use of PrEP as an intervention against the transmission of HIV. It is essential to focus on filling information gaps and comprehending the social and psychosocial factors involved to develop successful public

health measures to increase the adoption of PrEP.

Strengths and Limitations

This review analyses the acceptability and uptake of PrEP specifically in Southeast Asia. Based on the region's unique socio-cultural and health system factors, the review provides important insights as to barriers and facilitators that may be different and underappreciated from studies in Western or African contexts. As outlined in the discussion part, the understanding of determinants that can influence acceptance of PrEP is complex and multilayered. Using a structured approach by categorising findings into specific domains of sociodemographic, psychosocial, health system, behavioural, and PrEP-specific factors enables researchers and policymakers to target interventions in all these domains. The findings also lend additional support to the need for multifaceted, culturally tailored interventions and highlight the need for region-specific research in HIV prevention. Findings from this review may inform what would be crucial in using policies and community-based strategies to increase the uptake of PrEP and align with global HIV prevention goals. Included studies in this review are up to 2023, and serve to provide the most up-to-date landscape of PrEP program adoption challenges and opportunities in Southeast Asia. As HIV incidence rates rise in Southeast Asia PrEP programs face an urgent need to scale up rapidly, this review provides timely and actionable knowledge. However, several limitations must be acknowledged. As this review focuses on Southeast Asia, the findings may not be generalisable to other regions, especially regions that have different socio-cultural and healthcare contexts. Furthermore, the representation from countries other than Thailand is relatively limited, thus there may be a geographical bias, which will limit the applicability of the findings for Southeast Asia at large. This bias could be due to the region's early stage of PrEP implementation, reflecting certain nation's limited awareness and availability. The varied research methodologies across the studies further challenge the comparability of results. Additionally, barriers such as high costs, societal stigma, discrimination, and strict regulatory frameworks are among the factors that hinder the broader study of PrEP in Southeast Asia, emphasising the necessity for region-specific research and interventions (Zablotska et al. 2016).

CONCLUSION

This systematic review examines the facilitators and barriers that individuals encounter when making personal decisions on the initiation of PrEP as a preventive treatment for HIV in Southeast Asia. Factors that stand out include the sociodemographics of individuals, the importance of the health system, awareness, as well as behavioural and psychosocial elements. An in-depth comprehension of these determinants within key populations can aid in the development, surveillance and assessment of targeted public health interventions for these groups. However, to develop effective public health interventions to tackle these problems, it is necessary to have a thorough understanding of the theory of behaviour change. To effectively decrease the occurrence of HIV among key populations at risk, it is imperative to examine these factors beyond MSM and TGW, who dominate in terms of at-risk people studied. Furthermore, most of the attributes identified in this analysis were focused on individuals. Widening the scope to include barriers and facilitators at the national and regional level could help

to inform policies and decisions to ensure the successful uptake of PrEP among at-risk populations and reduce the transmission of HIV. Overall, this review highlights the need for a localised, evidence-based roadmap to enhance PrEP accessibility and service uptake for Southeast Asia prevention efforts.

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Table S1: Search string used for each database

Database	Search string
PubMed	("men who have sex with men" OR msm OR gay OR bisexual OR "sex worker" OR "key population*" OR pwid) AND (PreP OR "pre exposure prophylaxis" OR chemoprevention OR chemoprophylaxis OR "pre exposure prophylaxis") AND (hiv OR "human immunodeficiency virus") AND (barrier* OR facilitator* OR challenge* OR uptake* OR acceptance*) AND ("south east asia" OR SEA OR Cambodia OR Indonesia OR Laos OR "lao pdr" OR Malaysia OR Myanmar OR Philippines OR Singapore OR thai* OR "timor leste" OR Vietnam OR ASEAN)
Web of Science	TS= (("men who have sex with men" OR msm OR gay OR bisexual OR "sex worker" OR "key population*" OR pwid) AND (PreP OR "pre exposure prophylaxis" OR chemoprevention OR chemoprophylaxis OR "pre exposure prophylaxis") AND (hiv OR "human immunodeficiency virus") AND (barrier* OR facilitator* OR challenge* OR uptake* OR acceptance*) AND ("south east asia" OR SEA OR Cambodia OR Indonesia OR Laos OR "lao pdr" OR Malaysia OR Myanmar OR Philippines OR Singapore OR thai* OR "timor leste" OR Vietnam OR ASEAN))
Scopus	TITLE-ABS-KEY (("men who have sex with men" OR msm OR gay OR bisexual OR "sex worker" OR "key population*" OR pwid) AND (prep OR "pre exposure prophylaxis" OR chemoprevention OR chemoprophylaxis OR "pre exposure prophylaxis") AND (hiv OR "human immunodeficiency virus") AND (barrier* OR facilitator* OR challenge* OR uptake* OR acceptance*) AND ("south east asia" OR sea OR cambodia OR indonesia OR laos OR "lao pdr" OR malaysia OR myanmar OR philippines OR singapore OR thai* OR "timor leste" OR vietnam OR asean))

Table S2: Critical appraisal results of the included articles

No.	Author, Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Overall appraisal
Randomised controlled trials															
1	Kawichai et al. (2022)	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Quasi- esperimental study															
2	Weir et al. (2023)	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	Yes	NA	NA	NA	NA	Include
Prospective cohort															
3	Chewanan et al (2023)	Yes	Unclear	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	NA	NA	Include
4	Martin et al. (2017)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	No	No	No	Yes	NA	NA	Include
Cross-sectional															
5	Eger et al. (2022)	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include
6	Rayanakorn et al. (2022)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	NA	NA	NA	NA	NA	Include
7	Auemaneekul et al. (2020)	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include
8	Ramautarsing et al (2020)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include
9	Tan et al. (2018)	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	NA	NA	NA	NA	NA	Include
10	Ongwandee et al. (2018)	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include
11	Lim et al. (2017)	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include
12	Anand et al. (2017)	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include
13	Draper et al. (2017)	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include
14	Plotzker et al. (2017)	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	NA	NA	NA	NA	NA	Include
15	Sineath et al. (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include
16	Yang et al. (2013)	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	NA	NA	NA	NA	NA	Include

*NA = not applicable since JBI appraisal tool is based on study design