

What barriers do men who have sex with men face for using pre-exposure prophylaxis for HIV? A comparative study between high-, and low- and middle-income countries

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Abstract

In this review the needs and barriers of men who have sex with men (MSM) for pre-exposure prophylaxis (PrEP) implementation in high-income countries (HIC) and low- and middle-income countries (LMIC) are compared. In April 2018 and June 2021, electronic literature searches of Ovid Medline, Embase, AMED, PsychINFO and Cochrane databases were conducted. Studies were screened based on their title and abstract for relevancy, excluding papers that did not focus on MSM, PrEP and human immunodeficiency virus (HIV). Relevant studies were analysed in full, extracting and comparing applicable data. In 2018, 517 studies were identified. Of these, 207 were removed as they were ineligible or duplicates. Of the 310 eligible studies, 72 studies were analysed. It was found that adherence of PrEP must remain high for it to be effective and cost-effective. PrEP is cost-effective and sometimes cost-saving in HICs but the high cost of PrEP, owing to its patent, makes it unfeasible in many LMIC. For maximum effect on the HIV epidemic among MSM, PrEP must be used in conjunction with current HIV prevention methods, which also must be scaled-up. Previous research indicated that awareness of PrEP was low in LMIC, at 29.7%, but willingness to use PrEP was high in these countries, at 64.4%, whilst it was lower in HIC. Stigma and cost were the two greatest barriers to PrEP implementation at individual and government levels in LMIC and HIC. The worldwide rising incidence of HIV among MSM worldwide requires further prevention interventions, such as PrEP in combination with current methods. However, there are many individual- and government-level barriers to its implementation, namely stigma and cost.

Abbreviations

- ARV - Anti-retroviral
- HIC - High-income countries
- HIV - Human immunodeficiency virus
- LGBTQ+ - Lesbian, gay, bisexual, transgender, queer
- LMIC - Low- and middle-income countries
- MSM - Men who have sex with men
- PrEP - Pre-exposure prophylaxis
- QALY - Quality-adjusted life year
- RCT - Randomised controlled trial
- STI - Sexually transmitted infection
- TDF-FTC - Tenofovir/emtricitabine
- UNAIDS - Joint United Nations Programme on HIV and AIDS
- WHO - World Health Organization

Introduction

Despite reductions in incidence of human immunodeficiency virus (HIV) among many heterosexual populations worldwide, men who have sex with men (MSM) are disproportionately affected by HIV.¹ There is a high prevalence of HIV among MSM, averaging 15% worldwide but reaching as high as 25.4% in the Caribbean,¹ which is significantly higher than the general adult HIV prevalence of 1% in the Caribbean.² Prevalence is continuing to expand in most countries among MSM as incidence rates of HIV remain at the same level or increase, particularly in low- and middle-income countries (LMIC).³

MSM are on average 24 times more likely to acquire HIV than the general population,⁴ in part due to the 18 times higher per-act risk of unprotected receptive anal intercourse than unprotected vaginal intercourse.¹

To combat the disproportionate burden of HIV in MSM worldwide the World Health Organization (WHO) recommend a combination of prevention interventions, including testing, counselling, condoms, early anti-retroviral (ARV) treatment and pre-exposure prophylaxis (PrEP).⁵ Consistent condom usage has been declining in high-income countries (HIC)⁶ and LMIC^{7,8} and HIV testing is significantly easier in HIC⁹ than in LMIC.¹⁰ Therefore, to halt and reverse the expanding HIV epidemic among MSM, the WHO strongly recommend PrEP.¹¹

PrEP is a relatively new HIV prevention method that uses ARV drugs to protect people from acquiring HIV.¹² High adherence before and after exposure is required for it to be efficacious.¹³ PrEP is mostly taken as a combination of the ARV drugs, emtricitabine and tenofovir disoproxil fumarate.¹²

The effectiveness of PrEP in preventing HIV acquisition has been determined by 10 studies, 3 of which involved MSM.¹² These three studies found PrEP to be highly effective if adhered to properly, with relative risk reductions of HIV acquisition of 95% (95% CI 70-99%; p<0.001),¹³ 86% (95% CI 40-98%; p=0.002)¹⁴ and 86% (90%CI 64-96%).¹⁵ Before PrEP can be fully implemented for MSM, the barriers must be understood.

This review used the World Bank definitions of HIC and LMIC, where HIC had a gross national income per capita of greater than \$12,536 in 2019.¹⁶ A systematic literature review was conducted to identify the needs and barriers of MSM accessing and using PrEP to prevent acquisition of HIV. It compares the individual-, structural- and government-level needs and barriers to MSM for using PrEP between HIC and LMIC. Themes identified included awareness of PrEP, willingness to use it, associated healthcare costs, stigma and criminalisation of homosexuality.

Literature search

In April 2018, an initial library search was conducted using Cochrane library and Ovid (Ovid Medline, AMED, PsycINFO and Embase) databases to identify literature that analysed PrEP for HIV among MSM. The search used the keywords “PrEP”, “HIV”, “MSM” and their variations and then combined the results using “AND”. Medical Subject Heading terms were used with ‘explode’ to ensure all term variations were covered.

2018 literature search

Ovid search The search terms used with Ovid and the articles found are displayed in **Table 1**. All papers found by search number 15 (n=488) were exported to Endnote, where any duplicates were removed (n=14), leaving 474 articles.

Table 1. Search terms and findings from 2018 Ovid search.

Search number	Search term	Number of articles
1	pre-exposure prophylaxis or preexposure prophylaxis or “PrEP” or HIV pre-exposure prophylaxis or HIV preexposure prophylaxis or pre-exposure antiretroviral prophylaxis or preexposure antiretroviral prophylaxis or pre-exposure chemoprophylaxis or preexposure chemoprophylaxis or anti-HIV prophylaxis	4436
2	MeSH: Pre-Exposure Prophylaxis - explode	1015
3	1 OR 2	4436
4	men who have sex with men or MSM or gay or bisexual or homosexual*	39346
5	MeSH: Homosexuality, Male – explode	13147
6	4 OR 5	39346
7	human immunodeficiency virus or HIV or acquired immunodeficiency syndrome or AIDS	423134
8	MeSH: HIV OR HIV-1 OR HIV-2 – explode	91941
9	7 OR 8	423134
10	3 AND 6 AND 9	726
11	10 limited to English language	716
12	11 limited to years 2010-Current	707
13	10 limited to Humans	552
14	12 AND 13	492
15	14 and ‘Journal Article’ [Publication Type]	488

Cochrane library The MeSH search terms used on Cochrane using ‘explode’ and the articles found are displayed in **Table 2**. All articles found by search number 4 (n=29) were also exported to Endnote, where duplicates were removed (n=26), leaving 3 articles.

Table 2. Search terms and findings from 2018 Cochrane library search.

Search number	Search term	Number of articles
1	Homosexuality, male	331
2	Pre-Exposure Prophylaxis	96
3	HIV	3059
4	1 AND 2 AND 3	29

Analysis The combined articles found by the 2018 searches (n=477) were assessed for eligibility by reading the title and abstract.

Exclusion criteria Studies focussing on non-MSM populations or non-PrEP HIV prevention methods were excluded, as were letters, commentaries, inaccessible papers and studies published before 2012, unless the study was a randomised controlled trial (RCT) assessing PrEP effectiveness (n=1). A total of 167 studies were excluded, leaving 310 eligible studies (see **Figure 1** for flow diagram of search).

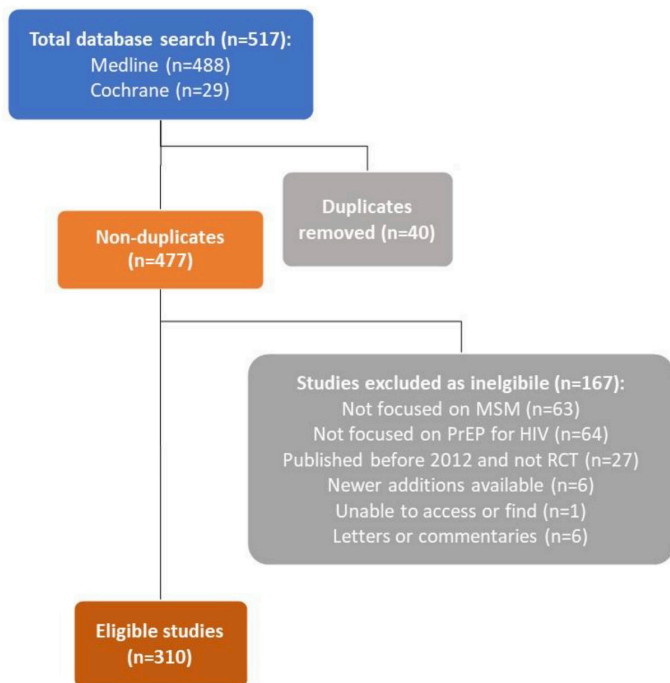


Figure 1. Flow diagram of 2018 library searches

Inclusion criteria Papers published in 2015-2018 (n=218) were initially prioritised for analysis as they were the most recent, giving up-to-date information at the time of the study. They were grouped by geographical region when mentioned in the paper's title or abstract (n=134; **Table 3**), leaving 84 papers that did not have any mention of geographical region.

Table 3. Number of articles per geographical region from 2018 search.

Region	Studies identified as country-specific from title or abstract	Most relevant studies taken as a sample from each region	Studies fully analysed from each region
Africa	7	7	5
Asia	1	9	8
Australia	4	2	2
Canada	6	1	1
Europe	20	15	11
Latin America	6	4	3
Multi region	20	15	15
USA	54	26	11
Total	134	79	56

Meta-analyses and multi-region studies were prioritised to give a better global perspective, cover a greater total geographical distribution and read summaries of many of the other papers found. Due to the far greater number of papers in North America and Europe, only a sample of papers from these regions were analysed and read in full, whereas most studies in LMIC were fully analysed (see **Table 3**). Studies published in 2012-2014 were then screened for themes not covered in the 2015-2018 publications.

WHO and Joint United Nations Programme on HIV and AIDS

Further to the library literature searches, the WHO and Joint United Nations Programme on HIV and AIDS (UNAIDS) websites were searched for publications and guidelines for PrEP in MSM to prevent HIV. There were 3 relevant publications from the WHO website and 4 from the UNAIDS website, which were analysed for relevant ideas.

In total 76 publications were analysed in full, with 56 being discussed in this paper (see **Figure 2**). Publications that were analysed and not discussed extended beyond the scope of this review or lacked relevance to the review question.

2021 library search

An update of this review was conducted in June 2021 via an additional library search, using the same methodology as the 2018 search. This resulted in 929 potentially applicable articles from 2018-2021 being found. The same inclusion and exclusion criteria as in the 2018 search yielded 444 eligible publications, of which systematic reviews (n=20) were fully analysed to extract new themes and to reinforce previous ideas; four of these articles were included in this review.

Awareness of PrEP

Six studies in LMIC assessed the awareness of PrEP among MSM. One meta-analysis analysed 23 articles and found awareness of PrEP to be low in LMIC at 29.7% (95% CI 16.9%-44.3%).³ However, awareness was higher in a few studies (61.3%-72.8% in Brazil, Thailand and China).¹⁷⁻²⁰ Higher awareness was associated with older age, greater education levels, employment¹⁷⁻²¹, and receiving a sexually transmitted infection (STI) diagnosis in the previous 12 months.¹⁷⁻²⁰

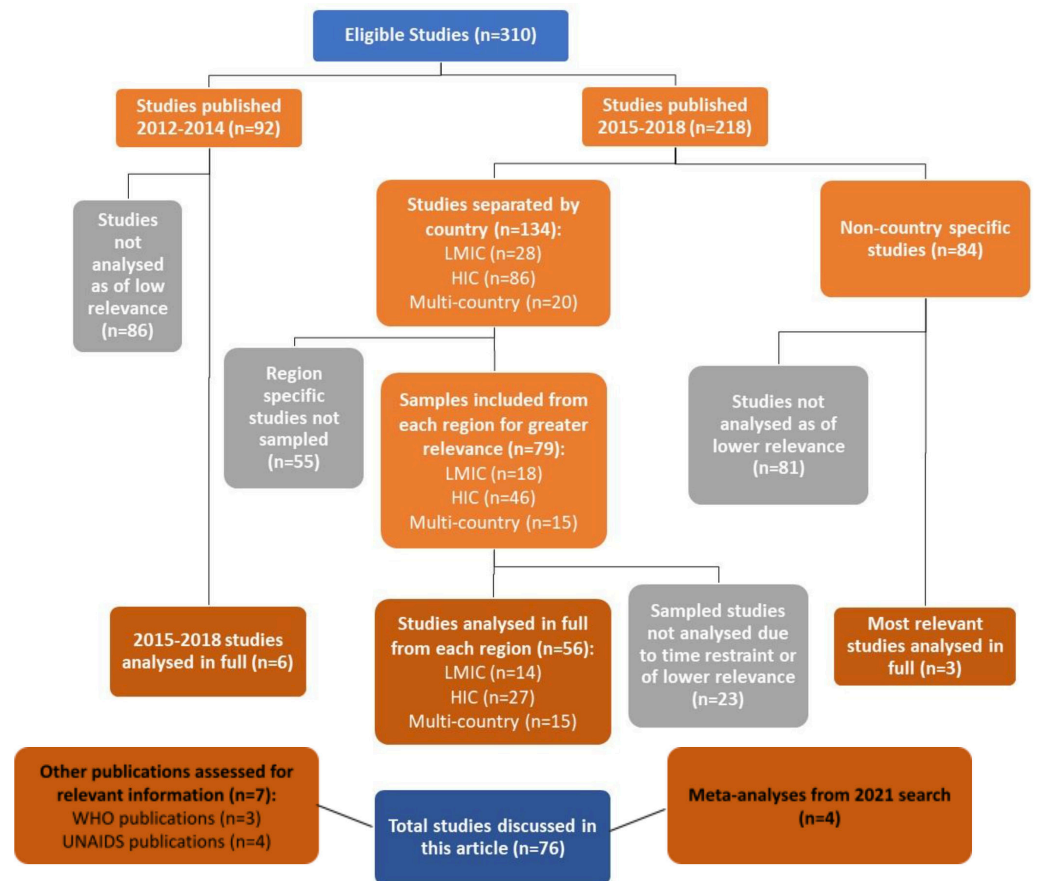
Seven studies assessed the awareness of PrEP among MSM in HIC, which was generally higher than in LMIC. One US study found that 86% of MSM were aware of PrEP.²² However, low awareness was found in Canada (20.9%)²³ and Spain (28.7%).²⁴

Willingness to use PrEP

Nine studies mentioned the willingness of MSM to use PrEP in LMIC. A meta-analysis of 20 studies in LMIC showed high hypothetical willingness to use PrEP once participants were made aware of it, at 64.4% (95% CI 53.3%-74.8%).³ Higher self-perceived risk of HIV acquisition and engaging in higher risk activities (including increased number of partners and sex with HIV-positive partners) were found to have a positive association with being willing to use PrEP.^{7,25-28} Older MSM were more likely to be willing to use PrEP in China,^{19,29} whereas some studies reported willingness to use PrEP was higher among MSM with lower income.³⁰

Six studies discussed willingness to use PrEP in HIC, which was generally lower than in LMIC.³¹ High willingness to use PrEP was found in Spain (57.6%)²⁴ and in²⁰ American cities (61%).³² Moreover, in an open-label US study, 60.5% of eligible participants joined the tenofovir/emtricitabine (TDF-FTC) arm of the study.³³ Willingness to use PrEP was lower in the Netherlands (only 13% had high intention to use),³⁴ Australia (31.7%)³⁵ and Hong Kong (7.7% were willing to use PrEP if they had to pay, whilst 45.2% if it was free).³⁶ A meta-analysis found overall acceptability of PrEP to be 57.8% and to not differ greatly between developing and developed countries; instead, acceptability of PrEP was found to depend on an individual's understanding of PrEP's high effectiveness and cost.²⁷

Figure 2. Flow diagram of 2012-2018 study selection for this article



Cost of PrEP

Four studies in the USA and 1 in Canada demonstrated the cost of PrEP ranged from being cost saving to costing 298,000 US dollars per quality-adjusted life year (QALY) gained,³⁷⁻⁴¹ depending on the effectiveness of PrEP.⁴² PrEP was also found to be cost-effective in the Netherlands³⁴ and France.⁴³ Maximum financial benefit was found when PrEP was used in conjunction with other HIV prevention programmes.⁴⁴ Conversely, in Australia PrEP was not cost-effective at a population level,⁴⁵ and the cost of PrEP initially prevented widescale implementation in England and Wales,⁴³ though it is now available free of charge, on the NHS, for high-risk individuals.⁴⁶

PrEP would be cost-effective in Peru,⁴⁷ however, the total cost of PrEP has been prohibitive to its implementation. Generic PrEP may be too expensive for large-scale implementation in Myanmar, where the HIV prevention budget is very low.⁸

Stigma and criminalisation

Removal of stigmatising barriers is essential for effective PrEP uptake.¹ Criminalisation of same-sex activity was identified in 6 studies, all of which are LMIC: Myanmar,⁸ Kenya,⁴⁸ Malaysia,^{29,49} Senegal⁵⁰ and Nigeria.³¹

Seven studies discussed stigma being a significant barrier to PrEP in HIC, listing homophobia, lack of 'outness' and service provider discrimination as being factors in reducing access to HIV and PrEP services.^{25-28,31,51} The USA population were found to particularly suffer from stigmatising barriers due to greater community prejudices that meant that PrEP was viewed as only being 'used by whores' and promoted unsafe sex.^{25-28,51} This stigma was perpetuated by healthcare professionals, who were condescending, dismissive or lacking in lesbian, gay, bisexual, transgender, queer (LGBTQ+)-specific knowledge.²⁵⁻²⁸

Individual barriers

Current prevention methods are failing to contain the rising

HIV epidemic among MSM. Therefore, there is a need for further intervention, such as the addition of PrEP.^{1,5,11} Significant barriers exist to PrEP implementation worldwide at individual and government level, including stigmatisation of HIV and sexual orientation, cost to individuals and governments, low awareness of PrEP, and the requirement of high willingness to maintain adherence.

Utilisation of an intervention requires the prerequisites of awareness of the intervention, willingness to use it and sufficient adherence.³ Therefore, low awareness of PrEP among MSM in LMIC (29.7%) presents a significant barrier to PrEP's implementation and demonstrates an international inequality, acting as a greater barrier to implementation in LMIC than HIC.³

Conversely willingness to use PrEP is higher in LMIC (64.4%) than HIC,³ which could be due to larger inadequacy of HIV services in LMIC compared to HIC.³¹ MSM who engage in high-risk sexual behaviours and have higher risk perception are more likely to be willing to use PrEP for greater protection from HIV in both HIC and LMIC.^{7,8,25-28} However, there is poor accuracy of predicting actual uptake based on willingness. For example, in the USA, 58% of participants expressed willingness to use PrEP but uptake was only 15%.^{26,32} A range of individual circumstances and the way in which PrEP is provided may affect actual uptake,³ including perceived or experienced side effects.²⁶ Further research is required to examine the broken link between hypothetical willingness, actual uptake and maintained adherence.²⁶

Low willingness to use PrEP presents a considerable barrier to its uptake and adherence; stigma and cost are the primary barriers to willingness to use PrEP in both LMIC and HIC.³ Perception of or the actual cost of PrEP reduces willingness for its use among MSM and discriminates against those who are unable to pay, creating inequality and reducing the overall effectiveness of PrEP.^{25-28,52} Stigma provides barriers at individual, community, healthcare and structural levels.²⁵⁻²⁸ High-risk sexual activity, such as unprotected sex, can lead to internalised stigma.²⁵⁻²⁸ Fear of peers and family assuming the user is gay,²⁵ HIV+,^{7,25} promiscuous,^{25,28,29,49} engaging in high-risk sexual activity, careless about STIs or being labelled a 'Truvada whore' also

reduces willingness to use PrEP.²⁵⁻²⁸ PrEP providers can perpetuate stigma with patronising and disdainful remarks regarding 'condomless sex' or perceived promiscuity.²⁵⁻²⁸ Community-level stigma provided barriers in 5 LMIC^{7,8} but in only 1 HIC (the USA).⁵³ Wider reduction of homophobia and condemnation of sexual promiscuity are required to reduce the anticipated and received stigma for PrEP users.

Structural barriers

The cost of PrEP proves to be significantly prohibitive to its implementation worldwide for high-risk populations through health policy. However, PrEP can be cost-effective/saving in America,^{37,41,42,54} the Netherlands³⁴ and the UK.⁴⁶ Studies that found PrEP to lack cost-effectiveness failed to account for reduced onward transmission⁴⁰ or did not prioritise key populations, reducing their real-world relevance.³⁹ However, proven cost-effectiveness and availability of funds in HIC demonstrate there are other factors at government-level that contribute to the lack of PrEP implementation. Even generic PrEP, which costs 1 US dollar per month, may not be financially feasible in Myanmar due to the low budget for prevention interventions.⁸ The price of PrEP must be reduced for viability of implementation in LMIC and HIC.

Criminalisation of same-sex activity, as found in 6 of the included LMIC,⁸ prevents governments from targeting healthcare interventions for MSM and further fuels individual-, structural- and community-level stigma, hindering access to HIV services.¹ These countries lack dedicated policies to prevent HIV among MSM generally, let alone expensive PrEP.¹ Despite a lack of criminalisation of same-sex activity, structural-level stigma also persists as a considerable barrier to HIV prevention and PrEP uptake in HIC, thus stigma is exceptionally damaging to HIV prevention efforts worldwide.

Clinical relevance and recommendations

Current HIV prevention methods, such as consistent condom usage, must be scaled-up to reverse the growing HIV epidemic among MSM. PrEP has shown to be effective when used in conjunction with other prevention methods.⁵⁵ PrEP contributed to the 32% fall in HIV diagnoses among MSM at 5 London clinics in 2015-2016 ($p=0.014$), with diagnoses among heterosexuals remaining constant.⁵⁵ Education of PrEP must also be used to improve the awareness of and willingness to use PrEP among MSM, helping to reduce stigma, particularly in LMIC. The high cost of PrEP may be overcome through generic manufacturing in Europe once the patent expires, and through compassionate trade deals in LMIC, which may serve to improve political will to implement PrEP. Furthermore, same-sex activity must be decriminalised or else the stigmatisation and marginalisation that drives the HIV epidemic will continue among MSM. However, such significant legal changes require considerable cultural shifts.

Strengths and limitations

The findings of this literature review build upon the myriad of studies available relating to PrEP for HIV among MSM. A unique asset of this review is the comparison of HIC and LMIC in the needs and barriers of PrEP among MSM, while most previous reviews have focused on effectiveness, willingness to use and awareness.

Time restraints and word limits prevented analysis of all relevant papers, in particular those found by the literature search in 2021, meaning themes may have been missed. The majority of studies were published in the USA and there were many more studies in HIC than LMIC. Moreover, none of the studies focussed on MSM in the Middle East or Caribbean. The greater concentration of studies in HIC and the requirement to sample papers may add unintentional selection bias to this review. Differences between MSM populations within the same country may be underreported, but this is outside of the scope of the review.

Conclusions

PrEP represents an additional preventative intervention against HIV and has been shown to reduce the incidence of HIV among MSM.^{55,56} However, there are many barriers to implementation of PrEP for MSM. Primarily, societal and governmental stigma presents the greatest barrier by preventing willingness to use PrEP,^{1,3} driven by criminalisation of same-sex activity,³¹ and interpersonal and medical perceptions.^{25-28,31} Low awareness among many individuals in LMIC inhibits MSM from accessing PrEP, but the high willingness to use among the same cohort demonstrates a requirement of PrEP. Conversely, higher awareness and lower willingness to use PrEP in HIC demonstrates more realistic expectations for use versus hypothetical willingness for use. The focus on willingness and awareness of PrEP in LMIC demonstrates the infancy of PrEP implementation in LMIC, whereas the focus on effectiveness, adherence and cost-effectiveness in HIC shows PrEP to be further along the implementation continuum. Motivating governments to provide PrEP proves to be a barrier for its implementation due to the high and additional costs of PrEP, despite its cost-effective and even cost-saving abilities.

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