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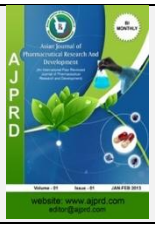

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Review Article

Exploring the Effectiveness of Pre-Exposure Prophylaxis (PrEP) Use for HIV Prevention among High-Risk Populations

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ABSTRACT

Addressing the global burden of HIV requires effective preventative measures that have been shown to have high efficacy rates. PrEP is one of the preventative measures that is effective in preventing HIV. Different clinical trials and population studies have shown PrEPto have an efficacy rate of 40% to 90% when it comes to preventing HIV. Due to its high efficacy, PrEPcan reduce new HIV infections populations considered to be high risk. However, for efficacy to be high, there is a need to increase medication adherence and address the existing barriers that limit uptake. Some of these barriers are lack of knowledge, inadequate access, stigma,lack of trust in service providers, low perception of HIV risk, cost, and fear of side effects. Addressing these barriers can increase PrEP uptake and help in reducing HIV's risk among high-risk populations. Some of the measures that can be put in place to address these barriers are providing education and training, allocating enough resources, leveraging technology, lowering PrEP costs, increasing insurance coverage, and improving communication among the targeted population.

Keywords: PrEP, HIV, high-risk populations, adherence, barriers

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INTRODUCTION

The global incidence of new HIV infections has reduced significantly. The latest UNAIDS report show that new infections have reduced by 59% from 1995 when HIV was at its peak to 1.3 million in 2022.[1]The rate of new HIV infections have almost halved in the last decade. For instance, the total number of new HIV infections in 2010 were 2.1 million which indicates that the rates have reduced by up to 38%.[1] The new HIV infections have reduced because of the preventative measures that have been in place in the last decade. One of these measures is the use of pre-exposure prophylaxis popularly known as PrEP. Findings from different clinical trials show PrEP is effective in preventing one from getting HIV with efficacy rates being as high as 90%.[2,3,4]PrEP is used after one is exposed to HIV and it helps in reducing the risk of HIV acquisition.[5]PrEP entails the use of pre-emptive use of event-based or daily ARTs [tenofovir disoproxil fumurate (TDF) and emtricitabine (FTC)] in reducingHIV acquisition risk after a person's exposure to the virus.[6]Because it is effectivein the reduction of the risk of infection after or before one is exposed, PrEP is effective in the prevention of HIV among high-risk populations. High-risk populations in this case are sex workers, men who have sex with men (MSM), individuals that inject drugs, and transgender women who have sex with men (TWSM).These populations are at highly likely to acquire HIV than the general population. Even with the reduced global incidence and prevalence of new HIV infections, the identified populations remain at high risk with the odds of getting the infection being significantly higher than the general population.[7]As a result, there is a need for preventative measures to reduce the infection risk.

The review aims to explore PrEP's effectiveness in preventing HIV infection among high-risk populations. The study begins by exploring the HIV's prevalence among high-risk populations and the risk factors that make these populations disproportionately affected. The review goes ahead to explore PrEP's effectiveness in preventing HIV infections based on past population studies. The review also explores barriers that make it difficult for high-risk populations to access PrEP and how they can be addressed to optimise positive outcomes.

Prevalence of HIV and Risk Factors among High-Risk Populations

The prevalence of HIV has reduced in the last three decades.Globally 1.3 million new cases were reported in 2022 representing a significant decline.[1] In the US, 36,136 new infections were reported in 2021 (Fig.1).[8] Most of these new infections were reported among high-risk populations including MSM, and individuals that inject drugs. Of the 36,136 new infections, 24,107 were among MSM representing 67% of the total infections.[9]The total number of infections among individuals who inject drugs was 3800 while the number of infections for heterosexual contact was 8,059.[9] Among MSM, the risk was 11 times higher compared to the general population.[10]Sex workers were also greatly affected.The UNAIDS global monitoring report reported HIV prevalence to be four times higher in this group thanit was in the general population. The global median prevalence of HIV among sex workers was 2.5% which was higher than the 0.7% global prevalence reported in the general adult population.[11]In the US, the prevalence of HIV among female sex workers was17.3%.[12] Although the definite number of people affected by HIV in this population group is not known, the infection rates are higher when compared with the general population.

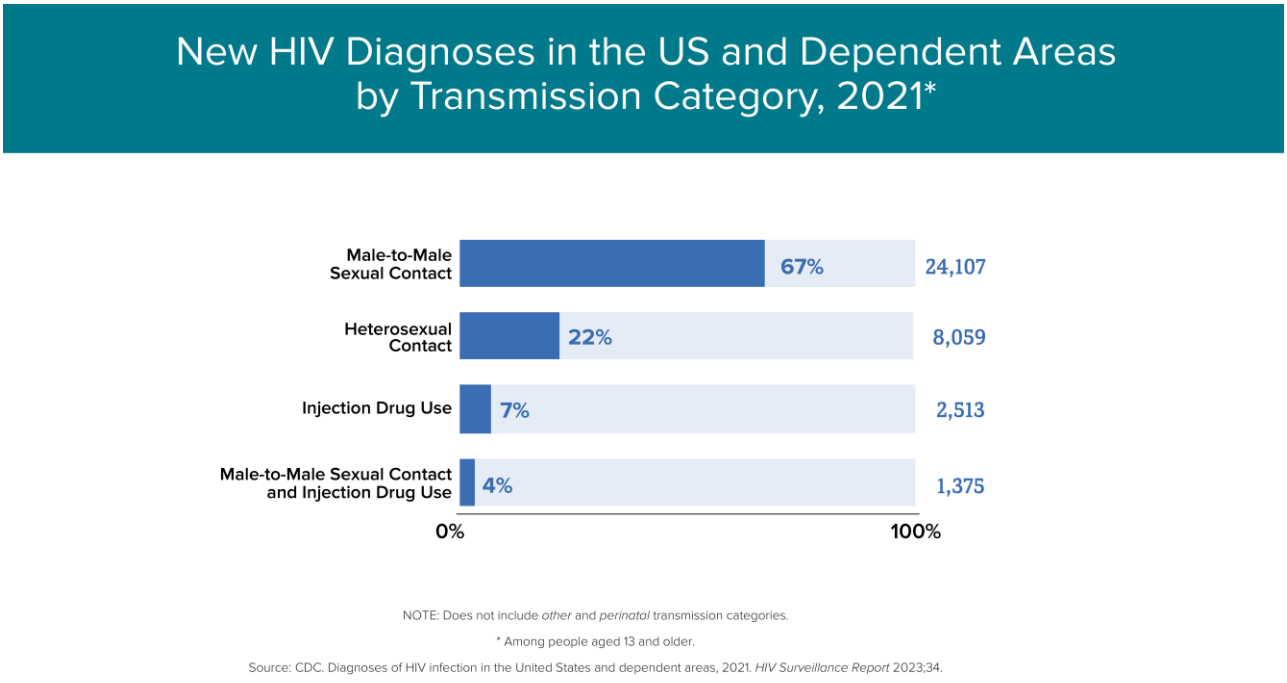

Figure 1: New HIV Diagnoses Reported in the US in 2021

Several risk factors contribute to the increase in number of new HIV infections in thehigh-risk groups. A consideration of female sex workers reveals that there are several risk factors, including having a large number of sex partners, inconsistent condom use, and an increased their likelihood of engagement in high-risk sexual acts, including the engagement in anal sex without a condom contributed to higher risk.[12,13] Sexual workers are also at a high risk because of a history of sexually transmitted infections (STIs). Other risk factors are using drugs and injecting drugs.[14]Injecting drugs itself is a high-risk factor for HIV. When combined with other risk factors mentioned above increases the risk exponentially. Additionally, using drugs impedes one's judgment and decision-making increasing the likelihood of being involved in high-risk behaviour such as exchanging sex for drugs and money.[15]Structural risk factors also increase the risk of getting HIV among this population. Some of these structural risk factors are poverty, stigma, discrimination, the work environment, and criminalization of sex work. In most cases, these factors make it difficult for this population to access prevention services and the necessary HIV care. For instance, stigma and discrimination in care settings increases difficulty of accessing preventative services and HIV-related care.[16,17] The work environment of sex workers also makes them vulnerable and more exposed to HIV infection.

Among MSM, a combination of structural and biological risk factors increases HIV acquisition risk. For this group, anal sex's biologyremains a high-risk factor for HIV infections.[18]Different studies have established that anal sex has a higher risk of transmission than vaginal sex.[19,18]According to Baggaley et al.,the per-act probability of acquiring HIV when it came to anal sex was 1.4% which was 18 times higher than throughvaginal intercourse.[19]Besides the high risk of transmission, the practices associated with anal sex also contribute to the high risk.In most instances, MSM engage in both insertive and receptive anal intercourse; thereby, increasing their probability of getting HIV. Engaging in receptive and insertive anal intercourse increases transmission risk. [20] Receptive anal sex increased prevalence and incidence of HIV.[20]Other risk factors among this group are engaging in sex without using protection, higher rates of sexually transmitted infections, less likelihood of taking antiretrovirals, and reduced access to HIV care.[18,21]All these

factors limit access to preventative services which makes this group disproportionately affected by HIV.

For individuals who inject drugs, some of the risky behaviors that significantly increase the risk of getting HIV are sharing needles, syringes, and other injection equipment. Sharing needles and other injection equipment with a person who is already infected increases the risk of acquiring HIV significantly.[22] Other than sharing needles and other injecting equipment, this group is disproportionately affected by HIV because of engaging in risky behaviors.[23] For instance, this population is highly likely toengage in risky sexual behaviors for drugs. It is also likely to engage in sex without protection. This group is also likely to have multiple sex partners which increases this significantly. The lower likelihood of seeking preventative services such as PrEP also increases the risk. Drugs affect one's judgment and reasoning which could explain why seeking preventative services among this group is lower.

PrEP's Effectiveness in HIV Prevention among High-risk Populations

Research has established that PrEP is effective in HIV prevention with the efficacy rate ranging from 40% to 90%.[3,4]A randomized clinical trial by McCormack et al.involving 544 participants established that PrEP was effective in preventing participants from acquiring HIV.[3]The study participants were divided into two groups with 275 participants being placed in the immediate group and the deferred group having 269 participants.[3]The immediate group were placed on PrEP while the deferred group was placed on PrEP later following early evidence of effectiveness.Following follow-up, the deferred group had 20 HIV infections and the immediate group had three HIV infections.[3] The 20 new infections in the deferred group were reported even after 174 prescriptions. The findings from the study are evidence that PrEP is highly effective in the prevention new HIV infections. The lower rates of new infections that were reported in the group that was immediately placed on PrEP is evidence of the effectiveness of the drug in reducing the risk of new HIV infections. Similar findings were established by Molina et al.[4]The double-blind randomized trial established that PrEP was highly effective in the prevention of HIV infections with the rate of infections reported in the experimental group being lower than those in the placebo group.[4] Among the 400 participants who were enrolled in the study, 16 new infections of HIV were reported during follow-up.[4] Of these, 2 were reported in the group that was placed under TDF-FTC while 14 were reported in the placebo group.[4]The group that was placed under TDF-FTC had lower rates of new HIV infections in comparison to the control group showing the effectiveness of PrEP in reducing HIV acquisition risk.

PrEPalso helps to reduce the risk of new HIV infections in MSM and TWSM. In a randomised study with a total of 2499 participants randomly assigned to the TDF-FTC group or a placebo, lower rates of new infections were reported by up to 44%.[2]Of the 100 cases of new HIV infections reported36 werein the TDF-FTC group while 64 in the placebo group.[2]Another study conducted in France had similar findings regarding PrEP's use inthe reduction of the number of HIV infections. The study established that the use of PrEP accounted for 60% effectiveness in reducing the risk of new HIV infections.[24]The effectiveness reached 93% for the higher amount of PrEP consumption.[24]The group that was using PrEPreported lower HIV cases compared to the controls. Similar findings were established by Liu et al.where using PrEP had 80 to 85.6% protection against HIV.[25] The effectiveness of PrEPhas also been established in systematic reviews and meta-analyses.[5,26]Therefore, PrEP is effective in HIV prevention with the effectiveness rate varying from 40% to 90%.

Although PrEP is ideal in the prevention of new HIV infections among high-risk populations, its effectiveness is dependent on various factors. One of these is adherence. Adherence has been shown to be important when using PrEP with the efficacy of the drug being dependent on a person's adherence.[27]Lack of adherence has been shown to lead to lower efficacy levels while higher levels of adherence have been shown to lead to greater effectiveness. According to Grant et al. the ability to maintain a good adherence was crucial to the success of PrEP intervention in preventing HIV.[2]Similarly, Martin et al. established that the risk of HIV infection reduced as adherence to PrEP improved.[28]The study noted that the risk of infection reduced from 48.9% to 83.5% for individuals who had 97.5% adherence.[28]Different factors contribute to poor PrEP adherence. They include forgetting to take the drugs, the possible side effects, being busy, being incarcerated, and injecting drugs.[28,29] Addressing these factors can increase PrEP adherence and the subsequent effectiveness in preventing HIV infections. Other factors that may affect PrEP uptake and the subsequent effectiveness are accessibility, affordability, perceived effectiveness of the drug, and knowledge about the drug.[30]Dealing with these factors can increase PrEP uptake among populations considered to be of high risk and reduce the risk of infections.

Barriers to Access and/or Uptake of PrEP

Several barriers make it difficult for high-risk populations to access PrEP which limits its uptake. Some of these barriers include inadequate accessto PrEP services, fear of PrEP's side effects, lack of knowledge, lack of trust in service providers, misinformation about the drug, stigma, cost, and low perception of HIV risk.[31-36] Barriers have a significant impact on access and overall uptake of PrEP which affects overall patient outcomes. They act as obstacles that make it difficult for these high-risk populations to access the drug in a timely manner hence affecting the efficacy of the drug.

Inadequate Access to PrEP Services

A notable barrier to PrEP uptake is inadequate access. Several studies reported inadequate access to PrEP services as a barrier that limited uptake.[35,36,37]Different factors contributed to inadequate access to PrEP services. For some, the geographical location of care and sexual health resources limited access to PrEP.[36] Participants who resided in rural and conservative states for instance reported difficulty accessing PrEP and providers who were willing to prescribe the drughad difficulty prescribing it.[36,37]Seeking PrEP through different practice settings was also a barrier. Having to seek PrEP services through different providers of different specialities was also a barrier that made uptake a

problem.[37]In some instances, there was no existing PrEP infrastructure in lower health facilities making it hard for participants to access medication.[35]In other instances, healthcare systems were not structured to support certain populations such as MSM, with most services being tailored to provide support to women.[38]Therefore, addressing accessibility barriers can increase uptake of PrEP more so for high-risk populationsdisproportionately affected by HIV.

Stigma

Stigma was a notable barrier that made it difficult for high-risk populations to access PrEP.In most studies, stigma was reported in two ways. One was the stigma surrounding PrEP use and the second was the stigma from healthcare providers. Different studies reported stigma that was associated with PrEP use as a barrier to uptake.[39,40]This type of stigma contributed to low uptake because people were not willing to take PrEP for fear of being stigmatized.[35]In most cases, stigma emanated from social and sexual networks. For men who had sex with men, the hostile social context surrounding having sex with other men played a crucial role in building stigma.[36] In one study, participants reported lack of comfort when it came to discussions abouttheir sexual identities with several doctors because of the stigma associated with the fact that they were men having sex with men.[38] The participants indicated that they were more comfortable in developing a relationship with their provider and seeing that provider consistently. Seeing different providers contributed to stigma in most cases perceived stigma which made most of them not seek PrEP services.[38]

Stigma from healthcare providers is also a significant barrier that limits PrEP uptake. Different studies have reported the role that stigma from healthcare providers plays is one of the most notable barriers to PrEP uptake.[41-45]Stigma from healthcare providers makes it difficult for at-risk populations to access PrEP services. In most cases, it becomes difficult to build a patient-provider relationship which is key in ensuring medication adherence. For high-risk populations, the fear of being judged by healthcare providers for their lifestyle or risky sexual behaviorscan inform their decisions not to seek PrEP services. It can also affect adherence to PrEP.

Fear of Side Effects

Another notable barrier that is considered to affect PrEP uptake is the fear of its side effects. Various studies have established that fear of PrEP side effects had an impact on service uptake as well as some people' willingness to use the pill.[34,35]The fear was mainly attributed to safety concerns and medical interaction concerns.[46] The fear that PrEP could cause adverse effects created fear and hence low uptake. However, in one study, some side effects were reported. They include nausea, dizziness, poor appetite, vomiting, and having a stomach-ache.[47]Although there are no known adverse effects associated with PrEP use, fear and safety concerns are major barriers that can limit PrEP uptake. As a result, there is a need to address these concerns to increase uptake.

Costs

Another common barrier that was reported in relation to PrEP use was cost. Many patients reported concerns overPrEP costs and the ability to pay for the drugs.[48]In some instances, the lack of insurance coverage and concerns over whether insurance could cover PrEPacted as a barrier.[41] In another study, the uptake and distribution of the drug was significantly affected by the lack of resources for routine screening and medication.[34] Not having to pay for PrEP was reported as vital in ensuring accessibility, acceptability, and adherence. Addressing the cost barriers attributed to PrEPis vital in HIV prevention. For most high-risk populations, the affordability of preventative services such as PrEP can be difficult. As such, there is a need to address the cost barrier to increase access. Besides, the cost-effectiveness of PrEP is associated with better outcomes including the reduced burden of dealing with HIV.[48]

Lack of Knowledge

Lack of knowledge and awareness about PrEP were also barriers that limited the uptake of the drug. In one study, about half of the respondents reported never hearing about PrEP or its existence.[35] In another study, populations that were at higher risk of acquiring HIV reported that they were not aware of the existence of PrEPand others had reported limited knowledge.[46] Lack of awareness and knowledge was also reported among healthcare providers.[49,50] Other issues that were reported were limited knowledge of PrEP services. Lack of knowledge and awareness and knowledge about PrEP is a key barrier because it means that people are not aware of its existence and hence cannot request it. Among healthcare providers, a lack of knowledge about PrEP means that they cannot help those affected in terms of prescription or referral to PrEP services. Therefore, there is a need to address this barrier to increase uptake.

Low Perception of HIV Risk

Low perception of HIV risk among high-risk populations is an additional barrier that limits PrEP uptake. Some individuals perceive themselves to have a lower risk of HIV.[46] Such perceptions can inform their decisions to not take PrEP even with evidence suggesting their risk to be high. Low perceptions of risk can lower the rate of PrEP uptake.

Lack of Trust in Service Providers

Another barrier which is commonly reported is the lack of trust that people have in service providers. For most high-risk populations, provider bias can inform one's decision not to take PrEP. In other cases, lack of trust in healthcare service providers and the healthcare system in general can affect PrEP uptake.[46] In most cases, lack of trust is informed by past experiences. For instance, if an individual has experienced stigma before in the hands of a service provider, then they are less likely to trust these providers. Establishing trust with individuals who are at high risk of acquiring HIV is vital because it helps to build a provider-patient relationship. Such a relationship is vital in ensuring drug adherence and ensuring people at risk seek care services.

Potential Solutions to Identified Barriers

Addressing the barriers that limit PrEP uptake is vital. Effectiveness of the drug is synonymous with uptake more so in high-risk populations which means there is a need to find solutions to the barriers identified above. One of the

most notable solutions to the barriers identified above is providing education and training to high-risk populations and PrEP service providers.[46] Providing education is a sure way to raise knowledge and increase awareness about the drug. Education can be provided in care settings or any other settings that provide HIV-preventative services. Training can also be done through provision of online resources. Providing training to healthcare providers can reduce incidents of stigma and increase trust among service seekers. Such measures are likely to increase PrEP uptake.

Another potential solution to barriers that limit PrEP uptake is allocating enough resources across different HIV care settings to increase access to PrEP.[7] A clear access to the PrEP pathway is lined to increased access. However, in some instances, this pathway is affected by a lack of resources in some care settings. Therefore, ensuring these resources are available can increase access and uptake. Access can also be improved by having proper referral routes to populations at high risk.

Leveraging technology to make PrEP more accessible can also help to address barriers related to access. For instance, app delivery models such as TelePrEP have been shown to be effective in increasing access to the drug.[51] Such technology has been shown to increase uptake and adherence to the medication.

Other potential solutions that can be implemented to address barriers related to uptake are reducing the cost of the drug, increasing insurance coverage, improving communication with targeted populations to ensure they are knowledgeable on where to get PrEP, and integrating PrEP interventions into the existing prevention programs.[7,46]Reducing cost and increasing insurance coverage can help to address cost-related barriers. Improving communication can make the targeted population more knowledgeable. Integrating PrEP with other prevention programs such as condom use can also address barriers related to access.

CONCLUSION

This review establishes that PrEP is effective in reducing the burden of HIV among high-risk populations. The efficacy is established by different population studies with the rate ranging from 40% to 90%. However, the efficacy of PrEP in preventing HIV infections is dependent on a number of factors. One of these factors is ensuring adherence. PrEP's effectiveness in the reduction of the risk of acquiring HIV is dependent on adherence to the drug. Lack of adherence has been shown to lead to poor effectiveness in HIV prevention. Addressing barriers is one way that can increase uptake and adherence to PrEP. Some of the barriers that lower uptake levels are inadequate access to PrEP services, lack of knowledge, low perception of HIV risk, misinformation about the drug, stigma, fear of side effects, cost, and lack of trust in service providers. Addressing these barriers is vital in increasing the uptake of PrEP and subsequent adherence. Some of the potential solutions that can help to address these barriersproviding education and training to high-risk populations and healthcare providers, allocating enough resources across different HIV care settings, leveraging technology, reducing cost, increasing insurance coverage, improving communication, and integrating PrEP interventions into the existing prevention programs.

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