Insight Brief

Exploring HIV Research in the PrEP Era: Challenges and Opportunities

Vaccine needed to protect increasing global at-risk population

Introduction

The landscape of HIV research continues to evolve amid widespread adoption of pre-exposure prophylaxis (PrEP) as the standard of care for HIV prevention. When taken as prescribed, PrEP is 99% effective in preventing infections following exposure to the virus, making it challenging to demonstrate the efficacy of new approaches in people already receiving PrEP.[1]

Yet, development of a vaccine to prevent HIV infection remains a high priority as the global at-risk population increases in size, with more young people at risk of HIV acquisition. Reasons for this include lack of awareness of HIV risk and the high levels of stigma that still surround HIV/AIDS. In the U.S., many new infections occur in high-risk people who do not perceive themselves to be at high risk and so do not take appropriate preventive measures. Globally, there has been slow uptake of PrEP. The Joint United Nations Program on HIV/AIDS (UNAIDS) goal of reaching 3 million PrEP users by 2020 was not met; the updated target for 2025 is 10 million.[2]

This insight brief looks at the unique challenges and opportunities for clinical trials evaluating new prevention strategies in this environment, a topic discussed on a recent IQVIA webcast.

Current research focuses on improved efficacy, reduced side effects

Current HIV treatment research is focused on developing regimens with improved efficacy and less severe side effects than existing therapies, with the ability to reduce viral loads to undetectable levels. A key goal is to reduce transmission rates and increase worldwide accessibility.[3] Antiretroviral therapy increases life expectancy but must be taken for life; broadly neutralizing antibodies (bnAbs) are in development as a potential therapy that may have reduced toxicity, require lower doses and generate a broader immune response to deliver sustained viral control.

Vaccines to completely prevent HIV infection have been a goal for 30+ years, but have faced multiple setbacks. For example, a trial in Uganda, Tanzania and South Africa was halted in late 2023 due to lack of proof of efficacy. This trial of two different combinations of experimental HIV vaccines was initiated in December 2020 as part of a broader initiative, PrEPVacc, with enrollment of 1,500 healthy adults.[4] Another HIV vaccine study, in South Africa, was halted in 2020 after analysis found no evidence of efficacy. The challenge in proving efficacy in a vaccine lies in the ability of PrEP to reduce the overall rates of new infection. Without an accepted correlate of immunity, proving the efficacy of a vaccine in the era of PrEP will be near impossible.

Phase III study success reported for lenacapavir

In addition to the approved, long-acting injectable PrEP option, cabotegravir[5] (approved in 2021[6]), other candidates are in the pipeline for prevention, including lenacapavir, which is also approved for HIV treatment.[7]

In a development that may reset the prevention landscape for the coming years, Gilead recently announced the success of the Phase III, PURPOSE 1 trial with lenacapavir, the company's twice-yearly injectable HIV-1 capsid inhibitor.[8] This demonstrated 100% efficacy for the investigational use of HIV prevention in cisgender women. Based on these results, the independent Data Monitoring Committee (DMC) has recommended that Gilead stop the trial's blinded phase and offer open-label lenacapavir to all participants.

In a second pivotal trial, PURPOSE 2, Gilead is studying the effectiveness in lenacapavir in cisgender men who have sex with men, transgender men, transgender women and gender non-binary individuals who have sex with partners assigned male at birth. Gilead expects results in late 2024 or early 2025. Other types of long-acting HIV prevention are also in development and testing: intravaginal rings, injectable drugs, implants, and antibodies.[9]

Remaining challenges for trials and public education

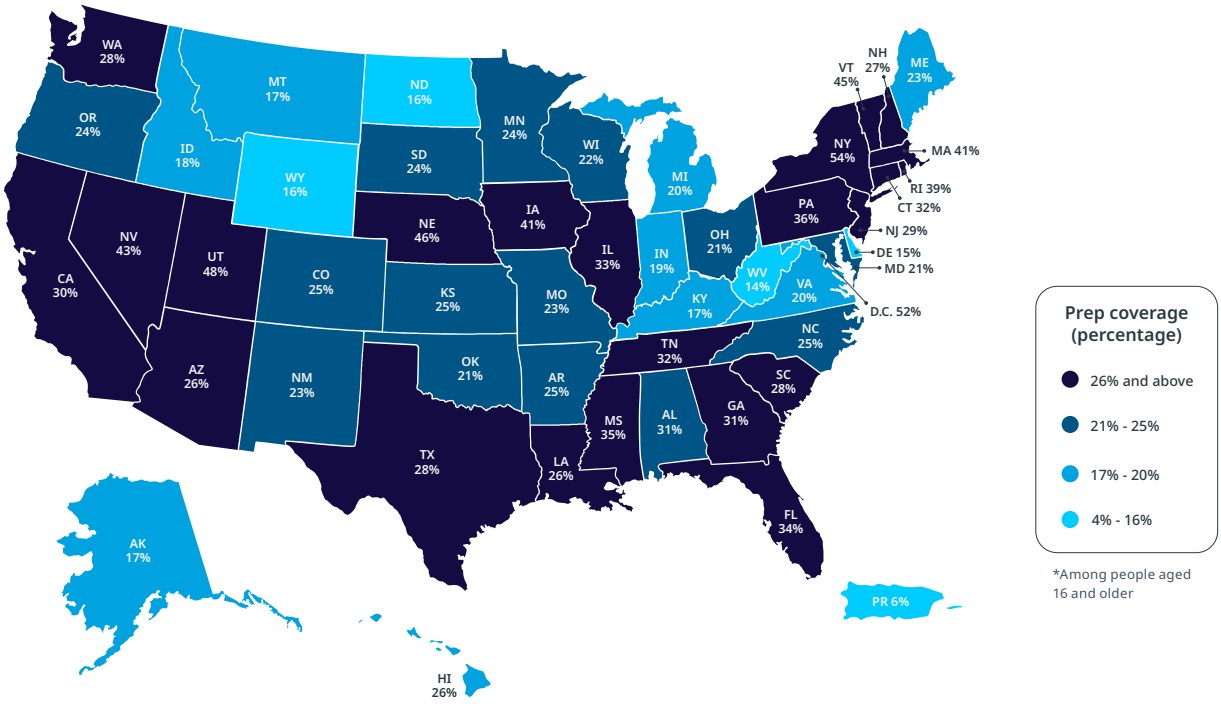
With PrEP as standard of care, researchers conducting trials of new prevention strategies must navigate challenges in study design and endpoint selection, participant recruitment and retention, and ethical considerations. As noted in a blog, trial implementation and adherence monitoring present additional challenges, including: differential access to PrEP depending on access to healthcare or financial resources, which can affect enrollment and reduce the generalizability of study findings; adherence to study interventions, which is more complex when participants are already on PrEP, requiring monitoring and counseling to avoid potentially confounding effects; and participant engagement and retention, requiring clear communication of the benefits and limitations of the investigational intervention, regular follow-up visits, and support services for participants.

There remains a need to educate the public about HIV prevention to address the inability of many individuals to accurately gauge their risk of acquiring HIV. In the US, systems and tools providing access to PrEP are in place (see Figure 1), yet HIV is still not controlled. Innovative approaches are needed to reach the people who can benefit from HIV prevention. These might be based on remote options that advanced during the COVID-19 pandemic, such as telehealth and mobile clinics for administration of injectables. These approaches should be tailored to at-risk populations, which may differ by region or country. Promoting PrEP should be an ongoing effort, requiring sustainable approaches, and ultimately being included as part of primary care.

Progress with PrEP*

In the U.S., significant advances have been made in the use of PrEP as an HIV prevention strategy. Data from the Centers for Disease Control and Prevention (CDC) show that in 2021, PrEP was prescribed to about 30% of the 1.2 million people who could benefit from it, compared to only about 13% in 2017 (Figure 1). [13]

Figure 1: PrEP coverage in the U.S. and Puerto Rico by area of residence, 2021[14]



In the U.S., PrEP can be taken as tablets – Truvada® (emtricitabine + tenofovir disoproxil) and Descovy® (emtricitabine + tenofovir alafenamid) – or an injectable, Apretude (capotegravir).[15]

Conclusion

At a global level, the World Health Organization (WHO) Global HIV program has supported PrEP implementation,[10] with recommendations that are followed by many countries. However, others lack policies supporting HIV control. Sustained efforts are needed to advance access by educating stakeholders such as government officials and community leaders in these countries about the benefits and safety of PrEP. Funding for PrEP implementation is sorely needed in areas of the world where the incidence and prevalence of HIV remains high. The Coalition to Accelerate Access to Long-Acting PrEP has been set up with the goal of bringing together leading donors, agencies, and advocates to ensure an "accelerated, equitable, sustainable and collaborative approach to optimizing access to new long-acting PrEP options."[11] The Coalition includes Unitaid, WHO, UNAIDS, Global Fund and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), with the AIDS Vaccine Advocacy Coalition (AVAC) acting as the secretariat. Continued support for these and other efforts will be fundamental to success in reducing the burden of HIV globally over the next decade.

"Looking ahead, addressing the challenges of HIV research will require additional collaboration between stakeholders, including affected communities, researchers, healthcare providers and policymakers" [12]

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