

VIEWPOINT

PEP for HIV prevention: are we missing opportunities to reduce new infections?

James Ayieko^{1,§} , Maya L. Petersen², Moses R. Kanya³ and Diane V. Havlir⁴ 

§Corresponding author: James Ayieko, Kenya Medical Research Institute, Center for Microbiology Research, Agoi Road, P.O. Box 614–40100, Kisumu, Kenya. Tel: (+254)720925262. (jimayieko@gmail.com)

Received 7 April 2022; **Accepted** 19 May 2022

Copyright © 2022 The Authors. *Journal of the International AIDS Society* published by John Wiley & Sons Ltd on behalf of the International AIDS Society. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

There is newfound optimism for global efforts to reduce the estimated 1.7 million new HIV infections still occurring every year with expanded pre-exposure prophylaxis (PrEP) access and newer biomedical prevention options on the horizon [1]. The increasing range of antiretroviral-based prevention options, such as the dapivirine ring and long-acting cabotegravir, move the concept of personal “choice” between biomedical HIV prevention options from the theoretical to the actual [2]. Post-exposure prophylaxis (PEP) is not a new option for prevention in adults, but it is one that has been underutilized for decades in low- and middle-income settings, largely being reserved only for high-risk occupational exposures among healthcare workers. We challenge this approach.

The arguments to expand PEP access beyond occupational exposure are three-fold. First, PEP is the only prevention option for adults that can be started after (vs. before) a high-risk exposure. Based on human data and animal models, PEP works after needle stick or sexual exposure and needs to be started within 72 hours [3]. HIV risk exposures are often neither planned nor anticipated. Further, risk is dynamic and varies over time for each individual.

Second, PEP using currently recommended integrase strand transfer inhibitor-based regimens is well-tolerated and can be delivered outside of occupational exposure settings, including in settings, such as rural sub-Saharan Africa (SSA), when operational barriers are addressed [4]. Estimated PEP efficacy is over 90%, which exceeds that of some other prevention options, such as the dapivirine ring [2]. PEP is particularly appealing due to the relatively short period of adherence required (i.e. for a 28-day course). It effectively covers one-time high-risk exposures even among known high-risk groups that do not have continuous ongoing risk, or those who opt to take a “break” from PrEP due to daily pill fatigue. When we offered PEP to persons with high-risk sexual exposures in rural Kenya and Uganda using a patient-centred approach that included offering services outside government clinics, 85% completed the 28-day course and follow-up testing. PEP was well tolerated, and there were no HIV seroconversions. Patients reported high satisfaction having an option that did not require ongoing daily medication [5].

Finally, PEP can be both a gateway to other prevention options for persons with ongoing exposure or a bridge for persons who have needs for short-term protection, inclusive but not limited to occupational exposures [6]. Persons who access PEP have the opportunity to hear about other prevention options, such as PrEP. If they have ongoing risk, they can transition to PrEP with adherence support to overcome the challenge of taking a daily medication. We have found that some clients opt for repeated PEP and then make the self-assessment that they would prefer to be on continuous PrEP only after this experience. We should both expect and embrace different on-ramps and off-ramps for HIV prevention options.

PEP can overcome some, but not all of the challenges of daily oral PrEP. Any daily oral pill started after a sexual encounter or needle sharing can be associated with stigma that can discourage the use of a preventive intervention even if the treatment requires only 28 days [7]. The similarity of PEP to HIV treatment can itself produce stigma of HIV infection that discourages uptake. Just like PrEP, persons can have side effects that make them unwilling to adhere to the regimen. All prevention options need to start with health literacy. Consumer education needs to expand beyond mere knowledge of options available and their side effects. It should include understanding patient goals and application of the knowledge in making choices of appropriate options to match their context [8].

If PEP requires no preplanning, is effective and requires only a short-term 28-day commitment and can potentially increase access to other biomedical options, such as PrEP, then why is it not more widely used? Guidelines per se are not the obstacle. In 2014, the World Health Organization expanded the recommendation for PEP for all persons who have occasional, unanticipated high-risk exposure [9]. Drug supply also does not appear to be the major obstacle now that PEP regimens are the same as first-line Anti-Retroviral Therapy (ART) treatment regimens. Reasons for low uptake appear multi-faceted and vary across settings. Despite being aware of PEP, men-who-have-sex with-men face barriers to access and use of PEP in Africa [10, 11]. Across multiple geographic

contexts, healthcare providers are often unaware or have still not embraced the PEP option outside of the occupational setting or “key populations.” They may convey “judgemental” attitudes to clients seeking PrEP or PEP [8]. They may also view PEP for “emergency use” only, terminology used in the US Centers for Disease Control and Prevention guidelines that may inadvertently discourage PEP use [12].

What needs to happen to reduce barriers to PEP? As countries update HIV prevention guidelines with availability of new products, there needs to be renewed focus on maximizing entry points into HIV prevention. Providers need refresher trainings on prevention that include PEP, and its potential role as an on-ramp or as a bridge to other options. Trainings need to emphasize the important role of providers to reduce stigma with PEP and to resist the temptation to decide what they think is best option for the client. Provision of the full 28-day course of PEP at a single clinical visit, with ongoing remote adherence counselling, can reduce transport and cost barriers to the client [13, 14]. PEP availability needs to be expanded to locations outside the clinics, such as through community-based retail drug shops [15]. Community outreach needs to empower clients to increase consumer demand and PEP delivery systems that meet their needs. Researchers need to evaluate even shorter PEP regimens.

In conclusion, a combination approach to preventing HIV infection, including behavioural, biomedical and structural approaches tailored to those at greatest need, must be adapted to realize the effectiveness of different HIV prevention options and reduce new infections [16]. Collectively, including more options can enhance the success of the overall prevention armamentarium. PEP is an efficacious HIV prevention option that has largely been underutilized. This defines a missed opportunity to prevent HIV infection associated with high-risk exposures in high-burden disease settings. A shift in thinking around the use of PEP by policy makers and implementing programs is needed as we move to one of the most exciting eras in HIV prevention.

AUTHORS' AFFILIATIONS

¹Kenya Medical Research Institute, Center for Microbiology Research, Kisumu, Kenya; ²School of Public Health, University of California, Berkeley, California, USA; ³Makerere University, College of Health Sciences and the Infectious Diseases Research Collaboration, Kampala, Uganda; ⁴Division of HIV, Infectious Disease and Global Medicine, University of California, San Francisco, San Francisco

COMPETING INTERESTS

All authors research support from NIH. DVH received non-financial support from Gilead Sciences to her institution for research studies.

AUTHORS' CONTRIBUTIONS

JA was the lead author and compiled the first draft. DVH, MLP and MRK reviewed and edited the manuscript. All authors read and approved the content of this Viewpoint.

ACKNOWLEDGEMENTS

We acknowledge the support from NIAID and Gilead (non-financial support) in conducting studies (NCT0186403) where we have offered PEP and PrEP to participants.

DISCLAIMER

The contents of the Viewpoint represent the views of the authors and not necessarily the views of their affiliated institutions.

REFERENCES

1. UNAIDS. Seizing the moment: tackling entrenched inequalities to end epidemics. Global AIDS Update 2020. Geneva (Cited 15 March 2022) https://www.unaids.org/sites/default/files/media_asset/2020_global-aids-report_en.pdf.
2. Bekker LG, Pike C, Hillier SL. HIV prevention: better choice for better coverage. *J Int AIDS Soc*. 2022;25(1):e25872.
3. Irvine C, Egan KJ, Shubber Z, Van Rompay KK, Beanland RL, Ford N. Efficacy of HIV postexposure prophylaxis: systematic review and meta-analysis of nonhuman primate studies. *Clin Infect Dis*. 2015;60(Suppl 3):S165–9.
4. Mayer KH, Gelman M, Holmes J, Kraft J, Melbourne K, Mimiaga MJ. Safety and tolerability of once daily co-formulated bicitgravir, emtricitabine, and tenofovir alafenamide for post-exposure prophylaxis after sexual exposure. *J Acquir Immune Defic Syndr*. 2022;90(1):27–32 PMID:34991141.
5. Ayieko J, Petersen ML, Kabami J, Mwangwa F, Opel F, Nyabuti M, et al. Uptake and outcomes of a novel community-based HIV post-exposure prophylaxis (PEP) programme in rural Kenya and Uganda. *J Int AIDS Soc*. 2021;24(6):e25670.
6. Marcus JL, Levine K, Grasso C, Krakower DS, Powell V, Bernstein KT, et al. HIV preexposure prophylaxis as a gateway to primary care. *Am J Public Health*. 2018;108(10):1418–20.
7. Golub SA. PrEP stigma: implicit and explicit drivers of disparity. *Curr HIV/AIDS Rep*. 2018;15(2):190–7.
8. Sun Z, Gu Q, Dai Y, Zou H, Agins B, Chen Q, et al. Increasing awareness of HIV pre-exposure prophylaxis (PrEP) and willingness to use HIV PrEP among men who have sex with men: a systematic review and meta-analysis of global data. *J Int AIDS Soc*. 2022;25(3):e25883.
9. WHO. 2015. https://apps.who.int/WHO_HIV_2015.48_eng.pdf. Accessed March 16, 2022.
10. Hugo JM, Stall RD, Rebe K, Egan JE, Jobson G, De Swardt G, et al. Knowledge, attitudes and beliefs regarding post exposure prophylaxis among South African men who have sex with men. *AIDS Behav*. 2016;20(Suppl 3):350–6.
11. Isano S, Wong R, Logan J, El-Halabi S, El-Khatib Z. Barriers to post exposure prophylaxis use among men who have sex with men in sub-Saharan Africa: an online cross-sectional survey. *Prev Med Rep*. 2020;19:101100.
12. Centers for Disease Control and Prevention. CDC HIV risk and prevention: HIV post-exposure prophylaxis (PEP). [Cited 26 Mar 2022] <https://www.cdc.gov/hiv/risk/pep/index.html>.
13. Beanland RL, Irvine CM, Green K. End users' views and preferences on prescribing and taking postexposure prophylaxis for prevention of HIV: methods to support World Health Organization Guideline Development. *Clin Infect Dis*. 2015;60(Suppl 3):S191–5.
14. Ford N, Venter F, Irvine C, Beanland RL, Shubber Z. Starter packs versus full prescription of antiretroviral drugs for postexposure prophylaxis: a systematic review. *Clin Infect Dis*. 2015;60(Suppl 3):S182–6.
15. Tubert J, Packer L, Hunter LA, Mfaume R, Njau P, Ramadhani AA, et al. HIV prevention at drug shops: awareness and attitudes among shop dispensers and young women about oral pre-exposure prophylaxis and the dapivirine ring in Shinyanga, Tanzania. *AIDS Res Ther*. 2021;18(1):21.
16. Stover J, Glaubius R, Teng Y, Kelly S, Brown T, Hallett TB, et al. Modeling the epidemiological impact of the UNAIDS 2025 targets to end AIDS as a public health threat by 2030. *PLoS Med*. 2021;18(10):e1003831.