LETTER TO THE EDITOR

HIV pre-exposure prophylaxis (PrEP) – are we seeing the end of the HIV pandemic?

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HIV AIDS Rev 2025; 24, 3: 249-251
DOI: https://doi.org/10.5114/hivar/206058

Dear Editor,

FTC/TDF-based (emtricitabine/tenofovir) pre-exposure prophylaxis (PrEP) for human immunodeficiency virus (HIV) infection was registered by the US Food and Drug Administration in 2012 [1], with Poland adopting its own guidelines in 2014 [2]. However, only when generic formulations became available in October 2017 at 25 Euros/30 tablets was PrEP actually launched in Poland [3]. Before this date, patients using patented Truvada for PrEP had been few and far between, with no real impact on the HIV epidemic [4]. The number of newly diagnosed HIV infections has been rising constantly for the last 20 years, with increases due to both migration and regional transmission [4]. Especially among men having sex with men (MSM) engaging in chemsex, a very rapid clustered HIV spread can be seen with onward transmission during 6-18 months [5]. Regular 3-monthly testing as advised by all guidelines for individuals at increased risk of HIV infection has not reduced the incidence [4, 6]. PrEP has proved to be a gamechanger, and countries that have introduced combined HIV and other sexually transmitted infections (STIs) prophylaxis (London UK, New York USA, Melbourne Australia) have been seeing a stable decrease in the number of new HIV infections [7-9].

Sadly, most Central and Eastern European (CEE) countries have not introduced either PrEP or combined prophylaxis in their national programs, leaving large groups of people at risk of HIV infection, no actual access to rapid diagnosis and treatment, let alone prophylaxis. Patients struggle not only with limited or no access to prophylaxis but also stigma among medical professionals, high medication/consultation prices, and sometimes no access to PrEP whatsoever, Croatia and Slovenia being the only exceptions in CEE countries [10-13].

The efficacy of FTC/TDF PrEP (i.e. risk reduction) exceeds 96%, irrespective of whether dosed daily (one tablet once a day) or on demand (2-1-1) [14]. Nonetheless, new HIV infections are still seen among PrEP users, mostly due to non-adherence, dosing mistakes, or stopping PrEP altogether despite ongoing risk [15]. This has been partly addressed in clinical trials of injectable cabotegravir (CAB) dosed intramuscularly every two months. The results have shown higher efficacy compared to oral PrEP; however, it may be due to low adherence and persistence in the oral PrEP arm (74% and 64% during the blinded and unblinded periods, respectively). It is important to note that adherence to the 2-monthly CAB injections also decreased from to 91% in the blinded phase to 80% in the unblinded period [16, 17].

CAB as PrEP has been introduced more widely in the USA and Canada, but due to its cost it has not gained much ground in Europe. Italy and Scotland have been preparing to roll out injectable CAB PrEP but have not implemented it yet in their systems.

Recent PURPOSE-1 and PURPOSE-2 PrEP trials of injectable lenacapavir (LEN) have shown even better results with no incident infections among women [18] and two incident infections among MSM and trans-women [19]. LEN was injected subcutaneously once every 6 months. It surpassed the efficacy of oral FTC/TDF PrEP among women in Africa (trial run in South Africa and Uganda), where adherence to oral PrEP was a major hurdle [20-23]. If accepted by women, LEN PrEP has the potential to increase the currently small numbers of cis women using PrEP.

If PrEP became more easily available among key populations (MSM, migrants, sex workers, incarcerated individuals) and new injectable methods were introduced among hard to reach and non-adherent populations, a rapid fall in new HIV infections could be achieved, as shown in numerous

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Article history:
Received: 06.06.2025
Received in revised form: 08.06.2025
Accepted: 08.06.2025
Available online: 11.07.2025

trials in Australia, New York, and London. However, for this to become a reality, national bodies should address barriers and inequalities to oral PrEP access (like in CEE countries) as well as create incentives for injectable PrEP manufacturers to lower the price and increase the number of PrEP users rather than gains from a single user.

PrEP should be part of combined prophylaxis efforts including regular HIV and STI testing for those at risk with rapid treatment in case of infection. Rapid treatment for HIV leads to undetectable viral load and zero risk of sexual transmission, which has been the base for undetectable = untransmittable (U=U) messaging [24]. Apart from test and treat approach, vaccination for HAV, HBV, HPV, and possibly for *Neisseria meningitidis* should be offered universally.

It is important to note that PrEP use has been previously connected with rising numbers of other STIs, especially syphilis (TP), gonorrhoea (NG), and chlamydiosis (CT). However, these numbers are rather the result of increased testing and diagnosing previously missed infections as 80% of NG and CT throat and rectal infections are asymptomatic. Only CT incidence has been shown to increase by 17% after PrEP commencement [25]. Additionally, it has been shown in different settings that the number of sexual partners, rather than condom use, correlate with the risk of transmission of TP, NG, and CT because these pathogens are transmitted through direct contact with skin or mucosal lesions [25-27].

Doxycycline post-exposure prophylaxis with 200 mg taken 1-3 days after exposure has been shown to reduce the risk of TP and CT infections by around 80% while NG by 30-40% only [28, 29]. NG risk reduction will most probably diminish further due to rapid resistance spread. Such prophylaxis has been proven to be highly efficacious and acceptable among men and trans women; however, no efficacy has been shown for cis women so far. Nonetheless, doxy-PEP offers an additional choice for people at risk, especially in regions with reduced access to STI clinics. Questions remain about its potential influence on microbiome, potential drug resistance emergence among commensals, and their clinical significance [29]. The same hopes are invested in the gonorrhoeae vaccine utilizing meningococcal serogroup B vaccine, which has been shown to reduce NG incidence by around 20-50% [30-32].

We now live in a period in which numerous prophylactic methods for HIV and other STIs are available. When implemented and combined, they have been shown to be extremely efficacious and reduce incidence at the populational level [33, 34]. The newest injectable PrEP formulations appear to be able to address the needs of different populations as well as non-adherent users. These formulations might easily be offered to women when combined with birth control or hormonal replacement therapy. The price of the new injectable forms has been set extremely high, especially when compared to generic oral forms. The suggested price for one cabotegravir injection exceeds the monthly oral PrEP price by over 10 fold. When considering that over 60-70% of PrEP users in Poland dose PrEP on demand [3, 10, 15], this price difference gets even bigger. Cost studies have shown that despite the price difference, injectable PrEP might be cost-effective, especially if adherence among oral PrEP users is low [35]. However, data show that long-term adherence to two-monthly cabotegravir injections might be decreasing with time, posing additional problems [16]; no such data for 6-monthly LEN have been presented. To achieve stable, long-term HIV incidence reduction, especially among non-adherent PrEP users, injectable PrEP has to be easily accessible, and hence affordable or even cheap. We suggest driving the price of injectable PrEP formulations to levels comparable to that of oral generic FTC/TDF, to reduce financial barriers and include large numbers of individuals at risk. If the price is not reduced, we fear injectable PrEP will remain exclusive and not impact the population meaningfully to the extent it could.

We therefore urge health officials to introduce combined prophylaxis programs that include PrEP, while injectable PrEP manufacturers should rapidly rethink their strategies and move from exclusive to universal access. Otherwise, due to limited funds in health systems and generic oral PrEP being cheap and highly efficacious in most users, there might be no political will to cover the extreme extra costs. Therefore, we will miss the opportunity to swiftly put an end to the HIV epidemic.

Disclosures

1. Institutional review board statement: Not applicable.
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

References

1. https://www.fda.gov/files/drugs/published/Truvada-for-PrEP-Fact-Sheet--Ensuring-Safe-and-Proper-Use.pdf [Accessed: 30.05.2025].
2. Horban A, Podlasin R, Cholewińska G, Wiercińska-Drapało A, Knysz B. Zasady opieki nad osobami zakażonymi HIV. Zalecenia PTN AIDS 2014. Warszawa: Polskie Towarzystwo Naukowe AIDS; 2014.
3. Szetela B, Cielniak I, Kubicka J, Rojewski T, Katafias A, Jakubowski P, et al. Pre-exposure prophylaxis (PrEP) in Poland 2017 to 2021: lessons from a country with no national PrEP programme. Journal of the International Aids Society 2022; 25. Supplement: HIV.
4. Raport o zdrowiu, HIV/AIDS. Warszawa: Narodowy Fundusz Zdrowia; 2022.
5. Parczewski M, Leszczyszyn-Pynka M, Witak-Jędra M, Szetela B, Gąsiorowski J, Knysz B, et al. Expanding HIV-1 subtype B transmission networks among men who have sex with men in Poland. PLoS One 2017; 12: e0172473. DOI: https://doi.org/10.1371/journal.pone.0172473.
6. Narodowy Instytut Zdrowia Publicznego – Państwowy Zakład Higieny. Zakażenia HIV i zachorowania na AIDS w Polsce. 2022. Available at: https://wwwold.pzh.gov.pl/oldpage/epimeld/hiv_aids/index.htm (Accessed: 10.03.2024).
7. Samra R, Fairley C, Ong J, Aung ET, Chow EP. Changes in HIV post-exposure prophylaxis prescriptions before and after the introduction of HIV pre-exposure prophylaxis at a sexual health clinic in Melbourne, Australia, 2011-2021. Aust N Z J Public Health 2024; 48: 100179. DOI: 10.1016/j.anzjph.2024.100179.

8. Xia Q, Edelstein ZR, Katz B, Bertolino D, Berry A, Tsoi BW, Torian LV. Impact of HIV preexposure prophylaxis prescriptions on HIV diagnoses in New York City. AIDS 2024; 38: 1412-1423.
9. Sullivan A, Saunders J, Desai M, Cartier A, Mitchell HD, Jaffer S, et al. HIV pre-exposure prophylaxis and its implementation in the PrEP Impact Trial in England: a pragmatic health technology assessment. Lancet HIV 2023; 10: e790-e806. DOI: 10.1016/S2352-3018(23)00256-4.
10. Szetela B. PrEP – what we have achieved in CEE and what needs to be done. EACS Standard of Care for HIV and Co-infections in Europe meeting, Brussels, 13-14 October 2022.
11. European Centre for Disease Prevention and Control. HIV stigma in the healthcare setting. Monitoring implementation of the Dublin Declaration on partnership to fight HIV/AIDS in Europe and Central Asia. Stockholm: ECDC; 2024.
12. Dashti AS, Joulaei R, Amiri S, Joulaei H. Knowledge, attitude, and practice of blood-borne diseases among healthcare providers in two selected educational hospitals in Southwest Iran. HIV AIDS Rev 2022; 21: 256-260.
13. Bohdziewicz A, Goździalska M, Mikuła T, Wiercińska-Drapało A. What do Polish students know about HIV infections after 35 years of the first confirmed case? HIV AIDS Rev 2022; 21: 284-289.
14. Molina JM, Ghosn J, Assoumou L, Delaugerre C, Algarte-Genin M, Pialoux G, et al.; ANRS PREVENIR Study Group. Daily and on-demand HIV pre-exposure prophylaxis with emtricitabine and tenofovir disoproxil (ANRS PREVENIR): a prospective observational cohort study. Lancet HIV 2022; 9: e554-e562. DOI: 10.1016/S2352-3018(22)00133-3.
15. Szetela B, Serwin K, Bozejko M, Zinczuk A, Zielinska K, Lapinski L, et al. HIV incident infections during pre-exposure prophylaxis (PrEP) use in Wroclaw, Poland, 2017–2023: a real-life experience. Sex Transm Infect 2025. DOI: 10.1136/sextrans-2024-056329.
16. Landovitz R, Donnell D, Clement M, Hanscom B, Cottle L, Coelho L, et al. Cabotegravir for HIV prevention in cisgender men and transgender women. N Engl J Med 2021; 385: 595-608.
17. Delany-Moretlwe S, Hughes J, Bock P, Ouma SG, Hunidzarira P, Kalonji D, et al. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. Lancet 2022; 399: 1779-1789.
18. Bekker LG, Das M, Abdool Karim Q, Ahmed K, Batting J, Brumskine W, Gill K, et al. Twice-yearly lenacapavir or daily F/TAF for HIV prevention in cisgender women. N Engl J Med 2024; 391: 1179-1192.
19. Kelley C, Acevedo-Quiñones M, Agwu A, Avihingsanon A, Benson P, Blumenthal J, et al. Twice-yearly lenacapavir for HIV prevention in men and gender-diverse persons. N Engl J Med 2025; 392: 1261-1276.
20. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. N Engl J Med 2012; 367: 411-422.
21. Marrazzo J, Ramjee G, Richardson B, Gomez K, Mgodi N, Nair G, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. N Engl J Med 2015; 372: 509-518.
22. Baeten J, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med 2012; 367: 399-410.
23. Eshun SN, Tampah-Naah AM, Udor R, Addae D. Awareness and willingness to use pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) among sexually active adults in Ghana. HIV AIDS Rev 2023; 22: 329-336.
24. Rodger A, Cambiano V, Bruun T, Vernazza P, Collins S, Degen O, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet 2019; 393: 2428-2438.
25. Traeger MW, Cornelisse VJ, Asselin J, Price B, Roth NJ, Willcox J, et al. Association of HIV preexposure prophylaxis with incidence of sexually transmitted infections among individuals at high risk of HIV infection. JAMA 2019; 321: 1380-1390.
26. Biała M, Mączyńska B, Starzyński K, Rurańska-Smutnicka D, Secewicz A, Szuba P, Szetela B. Antimicrobial resistance of Neisseria gonorrhoeae isolates among men who have sex with men in Lower Silesia, Poland. Pathogens 2024; 13: 890. DOI: 10.3390/pathogens13100890.
27. Szetela B, Łapiński Ł, Giniewicz K. Very high incidence of Chlamydia trachomatis, Neisseria gonorrhoeae, and Treponema pallidum among low-risk MSM in an Outpatient Clinic in Wroclaw, Poland in 2019-2020. Int J Environ Res Public Health 2023; 20: 2582. DOI: https://doi.org/10.3390/ijerph20032582.
28. Luetkemeyer AF, Donnell D, Dombrowski JC, et al. Postexposure Doxycycline to prevent bacterial sexually transmitted infections. N Engl J Med 2023; 388: 1296-1306.
29. Palacios R, Gómez-Ayerbe C, López-Jodar M, Martín-Cortés S, Pérez-Hernández I, Prolo A, et al. Post-exposure prophylaxis with doxycycline (DoxyPEP) in a cohort of men who have sex with men (MSM) in high risk for sexually transmitted infections (STI): the PRIDOX study. Abstract Supplement HIV Glasgow 10-13 November 2024, Glasgow, UK/Virtual. J Int AIDS Soc 2024; 27 Suppl 6: e26370. https://doi.org/10.1002/jia2.26370.
30. Bruxvoort K, Lewnard J, Chen L, Tseng HF, Chang J, Veltman J, et al. Prevention of Neisseria gonorrhoeae with meningococcal B vaccine: a matched cohort study in Southern California. Clin Infect Dis 2023; 76: e1341-e1349. DOI: https://doi.org/10.1093/cid/ciac436.
31. Wang B, Giles L, Andraweera P, McMillan M, Almond S, Beazley R, et al. Effectiveness and impact of the 4CMenB vaccine against invasive serogroup B meningococcal disease and gonorrhoea in an infant, child, and adolescent programme: an observational cohort and case-control study. Lancet Infect Dis 2022; 22: 1011-1020.
32. Molina JM, Charreau I, Chidiac C, Pialoux G, Cua E, Delaugerre C, et al. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. Lancet Infect Dis 2018; 3: 308-317.
33. Estcourt C, Alana Y, Rakb N, Goldberg D, Cullen B, Steedman N, et al. Population-level effectiveness of a national HIV preexposure prophylaxis programme in MSM. AIDS 2021; 35: 665-673.
34. Traeger MW, Leyden WA, Volk JE, Silverberg MJ, Horberg MA, Davis TL, et al. Doxycycline postexposure prophylaxis and bacterial sexually transmitted infections among individuals using HIV preexposure prophylaxis. JAMA Intern Med 2025; 185: 273-281.
35. Adelakun A, Dolph M, Matthews E, Oglesby A, Campbell K, Davis A, et al. Cost-effectiveness and public-health impact of cabotegravir long-acting injectable for HIV pre-exposure prophylaxis in Canada. Abstract Supplement HIV Glasgow 10-13 November 2024, Glasgow, UK/Virtual. J Int AIDS Soc 2024; 27 Suppl 6: e26370. DOI: https://doi.org/10.1002/jia2.26370.