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Enabling timely HIV postexposure prophylaxis access in sub-Saharan Africa

Postexposure prophylaxis (PEP) is a World Health Organisation-endorsed approach to prevent HIV acquisition from a recent sexual exposure by initiating an antiretroviral drug regimen, within 72 h after the exposure, but ideally within 24 h, and continuing for 28 days [1]. Nonhuman primate studies suggest that PEP may reduce the risk of acquiring HIV by around 90% [2], with the efficacy likely to be higher the earlier PEP is initiated after sexual exposure. The current recommended regimen for PEP includes TLD (tenofovir/lamivudine/dolutegravir), the same as the recommended first line regimen for treatment of people with HIV. Countries have policies to provide PEP, but these usually require a clinic visit and PEP use is generally low. We hypothesize that providing easy, local PEP access would have a beneficial effect on HIV incidence which outweighs any negative effects.

Our proposal is to consider making PEP (in the form of TLD) widely and freely available without prescription, along with a step change in levels of community education about all aspects of HIV to increase knowledge, limit stigma, increase awareness of PEP and thereby increase population-level motivation to access it when needed. Wherever we distribute free condoms (e.g. free from vending machines in public places such as shops, bars, toilets, workplaces, and through pharmacies and peer outreach workers), we would have 28-day packs of TLD PEP available. The aim would be to ensure that everyone can access PEP within at most 24 h of a sexual HIV risk. Oral contraceptives and postcoital contraception for women would ideally be distributed through the same mechanisms. This would require community ownership with education resources that explain potential benefits and possible harms. The approach is not intended to replace existing clinic services, but rather a complement to those services. Encouraging use of TLD for prevention presents challenges for HIV testing, as has been seen in some cases with cabotegravir used as pre-exposure prophylaxis (PrEP) (e.g. Maxmen [3]), and access to advice on testing and interpretation of test results would be important. The message would be essentially as follows: 'Condom use is the most effective means of prevention of transmission of sexual infections. If any sex that you have is not protected from HIV risk by a condom or by you taking PrEP, make sure it is protected by starting TLD PEP within 24 h, unless you know the partner not to have HIV or to have HIV viral suppression. You should continue PEP for a full 28 days. You may want to consider taking TLD PEP continuously afterwards so you are prepared if you have (another) risk, or you may wish to enrol for PrEP. You are strongly advised to make use of our online counsellors or visit a clinic or a pharmacy to get advice, but if you cannot do this within 24 h of your sexual risk start PEP in any case and then seek advice thereafter. This will include advice on HIV testing. It is important to have an HIV test to check that you did not already have HIV at the time of the sexual exposure – a negative test result while taking PEP does not mean you did not acquire HIV as a result of the exposure. You would not know if you got HIV from a certain exposure until a test at about 12 weeks after'.

Several countries have policies to provide PrEP consisting of tenofovir/FTC but it can be difficult for people to predict their condomless sex and to negotiate access to PrEP and continue with its use, including due to pill size, concern over adverse effects as well as inability to attend clinic on a routine basis to receive an HIV test and renewed PrEP drug supply [4–6]. If the proposed PEP approach is implemented, it could provide a relatively safe bridge to tenofovir/FTC PrEP for individuals who might not consider themselves high risk until a sexual exposure occurs. It would also raise the question of whether existing PrEP services might adapt to also offer continuous TLD PEP as an additional PrEP option for people with recurrent sexual exposures over time. If drugs for HIV prevention are to be widely available without prescription as we describe, the critical advantage of TLD compared with tenofovir/FTC PrEP is that drug resistance risk is much lower and the antiviral effect much greater when a person with HIV takes the drugs [7,8].

The primary potential benefit of this approach is that it provides a realistic means for people to protect themselves from HIV when a sexual risk was unanticipated and it was not possible for them to use a condom. However, we hypothesize that wide TLD availability would also be of benefit people with HIV who have difficulty accessing care, and could decrease late presentation with advanced HIV disease. It would give the opportunity for people with HIV who run out of drug to have access to an emergency supply. It could also lead to some people who suspect they may have HIV, but are afraid to test for it [9], to take TLD to treat their HIV while avoiding the real or perceived stigma they fear with engaging with healthcare, which could be of net benefit, particularly if this leads them subsequently to engage in care. On the other hand, the approach could have a negative effect on engagement with clinical services, including for sexual and reproductive health. Further, while dolutegravir is generally a safe drug, and a similar drug, cabotegravir, is approved as PrEP [10,11], some toxicities do occur. There would also be a risk that some people with HIV who have been under care may default from that care as they know they can access their antiretroviral drugs locally and easily; thus they would be unmonitored. Further, if the approach is introduced in one area and not others there is the possibility of a black market for drugs. We propose that the approach is studied in implementation science projects. Considerations for such studies and thoughts on cost-effectiveness are provided in Table 1.

Table 1. Additional considerations for proposal on easy access TLD PEP.

Studying the approach in communities	Net benefits are most likely in settings where the population prevalence of unsuppressed HIV is highest. One way to study the effect of the approach would be to select one or more relatively self-contained communities with high HIV incidence and with an inclusive community leadership who are motivated to pilot the approach. A random sample survey would be conducted at baseline (along the lines of the PHIA surveys) [12]. The approach would then be introduced. There would be active surveillance for incidence of drug toxicity. There would follow a second independent (i.e. a new sample) random sample survey after a period of time to study differences from baseline in PEP, PrEP and ART use, viral suppression levels, HIV diagnosis coverage, and other key measures. Any evaluation would need to be accompanied by extensive process evaluation work to monitor acceptability, accessibility, feasibility and unintended consequences of the programme.
Cost-effectiveness considerations	A 28 day course of TLD costs approximately $5, which is similar to the cost of tenofovir/FTC. Risk-informed PrEP has been shown to be likely to be cost-effective [13–15], so this approach is likely to be cost-effective, although assumptions would require verification in pilot implementation and further modelling conducted. There would be a cost to time spent by clinical and pharmacist staff on providing advice, but this would likely be less than in a context where such staff are responsible for managing access as is currently the case for PrEP. Similar approaches to condom distribution could be used for TLD pack distribution. Costs of widespread community education will need to be considered. If moving PrEP entirely to TLD there would be price benefits of extending procurement of TLD compared with separate procurement of tenofovir/FTC PrEP. If PEP could be distributed along with postcoital contraception this would increase the scope of benefits.

PEP, post-exposure prophylaxis; PrEP, pre-exposure prophylaxis; TLD, tenofovir/lamivudine/dolutegravir.

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Conflicts of interest

There are no conflicts of interest.

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Cabotegravir–rilpivirine treatment initiation in a nonvirologically suppressed patient

Currently, there is a single option for a complete parenteral HIV antiretroviral therapy (ART) regimen. Cabotegravir–rilpivirine is a complete HIV ART regimen combining an extended-release injectable integrase strand inhibitor (INSTI) solution (cabotegravir) with an extended-release injectable nonnucleoside reverse transcriptase inhibitor (NNRTI) solution (rilpivirine), which allows for once-a-month dosing.

On the basis of two randomized, open-label, multicenter, multinational, phase 3 clinical trials (ATLAS and FLAIR) a pooled analysis showed noninferiority when virologically suppressed patients were switched from usual therapy to once-monthly dosing of injected cabotegravir and rilpivirine with minimal withdrawal because of adverse events [1]. The combination regimen was approved by the Food and Drug Administration (FDA) in January 2021 for the treatment of HIV-1 infection in adults who are currently virologically suppressed (HIV-1 RNA <50 copies/ml) on a stable ART regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine (https://www.fda.gov/news-events/press-announcements/fda-approves-first-extended-release-injectable-drug-regimen-adults-living-hiv). The therapeutic potential of a long-acting injectable ART regimen as a potential solution for treatment initiation for people with HIV (PWH) who have difficulty with oral regimens has long been recognized [2].

We describe a patient who had failed four different traditional oral HIV ART regimens and had no ART resistance who was initiated on a once-monthly injection of cabotegravir–rilpivirine to circumvent poor pill adherence and gastrointestinal concerns.

A 53-year-old woman with a longstanding history of HIV (diagnosed 2006) and multiple failed ART regimens (Table 1) had been unable to adhere to a daily pill regimen. Genotypes on multiple occasions showed no significant resistance.

On initial presentation, she was noted to have multiple comorbidities and polypharmacy. Baseline labs included normal renal and liver function, an HIV viral load of 178 000 copies/ml, and $CD4^+$ of 211 cells/μl. Despite intensive adherence education and support, reduction of non-HIV medications, and attempt with a new ART regimen (dolutegravir–lamivudine), she failed to achieve viral suppression. A new phenotype to include INSTI showed no significant mutations/resistance to cabotegravir or rilpivirine. The viral load remained elevated at 341 000 copies/ml with a $CD4^+$ of 260 cells/μl.

She was switched to 1 month of oral cabotegravir–rilpivirine with good adherence. She was then prescribed long-acting injectable cabotegravir–rilpivirine administered every 4 weeks to improve adherence and to circumvent any potential gastrointestinal issues that might be affecting absorption/bioavailability. She tolerated the new regimen well; after 3 months, the viral load was undetectable, and $CD4^+$ count improved to 374 cells/μl. At 6 months, the viral load remained suppressed less than 20 copies/ml with improved $CD4^+$ count to 445 cells/μl, and she continued to tolerate the regimen without adverse effects.

Long-acting injectable HIV ART regimens have been sought as an alternative for patients experiencing pill fatigue or who may prefer a regimen that does not require daily pill dosing. There is currently no data in patients who are not virologically suppressed. To date, this regimen has only been FDA-approved as switch therapy for patients already suppressed with oral regimens; treatment initiation or switching unsuppressed patients with injectable cabotegravir–rilpivirine has not been previously described.

We postulate that there may be other situations in which a patient is not able to achieve durable viral suppression because of poor adherence or gastrointestinal issues that prevent obtaining sustained therapeutic levels of daily oral regimens and that these patients amount to a significant portion of unsuppressed patients. These patients could potentially benefit from treatment initiation with an injectable regimen if they have no evidence of significant ART resistance, are willing to receive monthly injections in a medical setting, and potentially have issues with adherence or adequate bioavailability of oral drugs. Further studies are warranted to determine if use of this regimen