On-Demand PrEP Works as Well as Daily Pills

The PrEP 2-1-1 regimen offers an option to take HIV prevention pills before and after sex instead of every day.

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On-demand pre-exposure prophylaxis (PrEP) taken before and after sex—known as PrEP 2-1-1—was as effective and well tolerated as daily pills, according to the latest findings from the French PREVENIR study recently published in The Lancet HIV.

Daily PrEP using tenofovir disoproxil fumarate/emtricitabine (TDF/FTC, sold as Truvada or generic equivalents) reduces the risk of HIV acquisition by around 99% when taken consistently and correctly, according to the Centers for Disease Control and Prevention (CDC).

But for those who do not wish to take pills every day, on-demand (also called intermittent or event-driven) PrEP offers another option. PrEP 2-1-1 involves taking two doses of TDF/FTC between two and 24 hours before anticipated sex, one dose 24 hours after the initial double dose and a final dose 24 hours after that.

Jean-Michel Molina, MD, of Université de Paris Cité, and colleagues have conducted two major studies to evaluate on-demand PrEP. Results from the Ipergay study, first presented in 2014, showed that on-demand TDF/FTC PrEP reduced the risk of HIV among gay and bisexual men by 86% compared with a placebo. A follow-up analysis found that the 2-1-1 regimen is also highly effective for those who have sex less frequently.

The PREVENIR study (NCT03113123) enrolled more than 3,000 HIV-negative adults, almost all of whom were men who have sex with men (MSM), at 26 sites around Paris between May 2017 and May 2019. They were considered to be at high risk for HIV, and they could either be starting PrEP for the first time (44%) or already using PrEP. The median age was 36 years, most were white, 45% had a regular sex partner and 17% said their main sex partner was living with HIV.

Men and transgender women who have sex with men could opt to either take TDF/FTC as one pill each day or use the PrEP 2-1-1 schedule. About half chose each option (1,540 and 1,509 participants, respectively). They were allowed to switch between the regimens, and many did so. Men who opted for on-demand PrEP were older and had fewer sex partners, on average.

The participants were tested for HIV at study entry and every three months thereafter. PrEP adherence was assessed by self-report and tenofovir concentrations in dried blood spots.

Preliminary results, presented in 2018, revealed no new cases of HIV among men who consistently used either on-demand or daily PrEP.

The new larger analysis included data through September 30, 2020. After a median follow-up period of about 22 months, there were three HIV seroconversions in the daily PrEP group and three in the on-demand PrEP group. This worked out to an HIV incidence of 1.1 cases per 1,000 person-years in both groups.

Adherence was generally good, and tolerability was similar in both groups. Two people using daily PrEP and two using on-demand PrEP discontinued due to treatment-related adverse events, including nausea, vomiting, diarrhea and lower back pain.

“In this study, which enrolled mainly MSM, HIV-1 incidence on PrEP was low and did not differ between participants using daily PrEP and those using on-demand PrEP,” the researchers concluded. “On-demand PrEP therefore represents a valid alternative to daily PrEP for MSM, providing greater choice in HIV prevention.”

All of the participants who seroconverted were men who have sex with men. The study enrolled too few cisgender women (13), transgender women (12) or trans men (two) to do separate analyses for these groups.

Of note, the PrEP 2-1-1 regimen has not yet been studied in cisgender women or transgender men who have vaginal or frontal sex. And on-demand PrEP study results for cisgender gay and bisexual men apply only to TDF/FTC, not the newer tenofovir alafenamide/emtricitabine (TAF/FTC, sold as Descovy). Descovy was approved in 2019 as a second daily PrEP option, but not for people who are exposed to HIV via vaginal sex, due to a lack of research.

“Additional studies are needed to assess whether on-demand PrEP could be used in other populations at high risk of HIV infection, or with other antiretroviral drug combinations within the PrEP pill,” the study authors wrote.

On-demand PrEP for men who have sex with men is not yet approved by the Food and Drug Administration. Nonetheless, the World Health Organization has endorsed it. The CDC’s 2021 PrEP clinical practice guidance outlines information about off-label prescription of PrEP 2-1-1, and some cities—including New York City and San Francisco—offer it as an option.

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