

Long-Term Study Results Support On-Demand PrEP

With good adherence, HIV acquisition remained very low for users of either daily or on-demand prevention pills.

March 9, 2026 By [Liz Highleyman](#)

On-demand [pre-exposure prophylaxis \(PrEP\)](#) taken before and after sex, also known as PrEP 2-1-1, remained as effective for HIV prevention as once-daily pills—as long as it was used as directed, according to long-term study results presented at the [Conference on Retroviruses and Opportunistic Infections \(CROI 2026\)](#) in Denver. Over eight years of follow-up, many participants switched between daily and on-demand PrEP according to their current needs.

Daily PrEP using tenofovir disoproxil fumarate/emtricitabine (TDF/FTC; Truvada or generic equivalents) reduces the risk of HIV acquisition by around 99% when taken consistently. PrEP uptake remains suboptimal, however. [Only around a third](#) of people who could benefit have been prescribed PrEP, with substantial racial/ethnic disparities, according to the Centers for Disease Control and Prevention. Having more options could boost uptake.

For people who don't wish to take pills every day, on-demand PrEP (sometimes called intermittent or event-driven PrEP) might be preferable. 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.

Back in 2014, Jean-Michel Molina, MD, of University of Paris Cité, and colleagues reported results from the [IPERGAY study](#), showing that on-demand TDF/FTC PrEP reduced the risk of HIV acquisition among gay and bisexual men by 86% compared with a placebo.

In 2017, they started the PREVENIR trial to compare once-daily and on-demand PrEP use in more than 3,000 HIV-negative gay and bisexual men and transgender women (0.4%) in Paris. The median age was 36 years, and most were white (85%) and born in France (83%). They reported a median of two condomless sex acts during the past month and a median of 10 sex partners in the prior three months. Participants opted for daily or on-demand PrEP and could switch back and forth; about half (47%) initially chose on-demand PrEP.

As reported in [The Lancet HIV](#) in 2022, HIV incidence (new cases) was low and comparable in both groups (1.1 cases per 1,000 person-years). The study ended in May 2025, allowing long-term

assessment of HIV incidence and safety.

Over time, about half of study participants used daily PrEP, and half used on-demand PrEP, but a majority switched from one regimen to the other at least once (59% from daily to on-demand and 52% from on-demand to daily). According to Molina, people who started on-demand PrEP were older, and people tended to switch from daily to on-demand use when they were having less sex. The number of sex partners decreased over time, but the number of condomless sex acts increased.

The participants were therefore divided into three groups: those who used daily PrEP for more than 75% of follow-up time (38%); those who used on-demand PrEP 75% of the time (38%); and those who switched (23%). In the latter group, they used daily PrEP half the time. The likelihood of study discontinuation at eight years was similar across groups: 66% for consistent daily users, 61% for consistent on-demand users and 56% for those who switched.

During follow-up, HIV incidence remained low overall, at 0.99 cases per 1,000 person-years (PY). There were 14 new cases: three in the consistent daily PrEP group (0.6 per 1,000 PY), seven in the consistent on-demand group (1.5 per 1,000 PY), three in the switch group (0.9 per 1,000 PY) and one person who did not properly consent and was excluded from the analysis. Because the numbers were small, the difference did not reach statistical significance. Importantly, however, nine were not currently taking PrEP at the time of HIV acquisition, and four showed evidence of poor adherence.

Both PrEP regimens were safe and well-tolerated over time. The most common side effects were gastrointestinal, reported by 2% to 5%. This was reported more often by on-demand users even though they spent less total time on PrEP—not surprising, as side effects tend to occur soon after starting the meds. Less than 1% of people who discontinued the study did so due to PrEP-related side effects.

One goal of the PREVENIR trial was to see whether PrEP would contribute to reducing new HIV diagnoses among men who have sex with and trans women in the Paris region. Overall, it did not. However, HIV incidence did decline by 33% among gay and bisexual men born in France. Over the same period, incidence rose by 73% among those born elsewhere, underscoring the need for improved PrEP access for people born abroad.

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