# On-Demand, or 2-1-1, PrEP Prevents HIV Even When Sex Is Infrequent

This PrEP dosing strategy involves taking doses of Truvada only during the days surrounding sex.

December 13, 2019 By Benjamin Ryan

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The on-demand pre-exposure prophylaxis (PrEP) dosing protocol, also known as 2-1-1 PrEP, is highly protective against HIV acquisition among men who have sex with men (MSM) even when they have sex less frequently, according to a follow-up analysis of a key study.

The 2-1-1 strategy is so called because the protocol involves taking two doses of Truvada (tenofovir disoproxil fumarate/emtricitabine) two to 24 hours before anticipated sex; then, if sex does occur, taking one dose 24 hours after the initial double dose and then one final dose 24 hours after that.

In April, the World Health Organization formally endorsed 2-1-1 PrEP for MSM.

It's important to note that this strategy should only be used with Truvada and not with Descovy (tenofovir alafenamide/emtricitabine), the newly approved drug for daily PrEP. The body metabolizes Descovy differently than Truvada; because the on-demand dosing of Descovy has not been studied, it is possible that in this circumstance it would not work as well as Truvada for PrEP.

Research has also not provided guidance for cisgender women and transgender men on the efficacy of 2-1-1 PrEP. Because Truvada is metabolized differently in vaginal tissues compared with rectal tissues, the on-demand protocol may not work as well for vaginal sex as with anal sex.

In 2014, the randomized placebo-controlled IPERGAY trial of the 2-1-1 dosing strategy found that the French and Canadian MSM who received Truvada (on a blinded basis, meaning they didn't know whether they were receiving the drug or a placebo) in the study had an 86% lower risk of contracting HIV compared with the men in the placebo group.

The analysis of that initial study was muddied by the fact that the participants reported a median of 10 sex acts per month and took a median of 15 pills per month. This meant the typical man in the study was taking about four tablets of Truvada per week. Studies of daily use of PrEP among MSM have found that taking four Truvada tablets weekly is apparently as effective as taking daily PrEP.

Therefore, the IPERGAY study authors could not tell for sure whether the specifics of the 2-1-1 dosing protocol were responsible for the high level of protection seen in the Truvada group versus the placebo group or whether the protection was merely a matter of taking about four tablets weekly. Consequently, whether the dosing strategy would prove highly effective among those who followed the protocol correctly and had sex less frequently than 10 times per month remained an open question.

Findings from an analysis of the men in the study reporting less frequent sex were first presented in 2017 at the 9th International AIDS Society Conference on HIV Science in Paris (IAS 2017). Now they have been published in The Lancet HIV by Laurence Meyer, MD, PhD, of INSERM in Villejuif, France, and his colleagues.

The study authors analyzed data on 270 of the IPERGAY participants, including 134 men in the placebo group and 136 in the Truvada group, who had periods during which they took 15 or fewer doses of Truvada per month and reported good adherence to the 2-1-1 dosing protocol. The investigators considered this as high adherence to the dosing strategy with less frequent sex.

There were 134 cumulative years of follow-up of such periods, which accounted for 31% of the total IPERGAY follow-up time.

The men in this new sub-analysis reported a median of five sex acts per month and took a median of 9.5 doses of Truvada per month.

Six of the men in the placebo group contracted HIV during the study's follow-up period, for a diagnosis rate of 9.2 diagnoses per 100 cumulative years of follow-up. None of the men in the Truvada group tested positive for the virus. The difference between these two infection rates was statistically significant, meaning it is unlikely to have been driven by chance.

"A choice between daily or on-demand PrEP regimens could be offered to men who have sex with men who have less frequent sexual intercourse," the study authors concluded.

More research is needed to determine the efficacy of 2-1-1 PrEP for less frequent sex over a longer

period of time and for sex that is even less frequent than seen in this new analysis. How effective would the dosing strategy be, for example, if used only once per month?

To read the study abstract, click here.

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