Is On-Demand PrEP Feasible for Young Gay Men?

Daily dosing or long-acting injectables may be better options for those who have spontaneous sex.

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Young gay and bisexual men may have difficulty predicting when they're likely to have sex, which could make it challenging to use on-demand pre-exposure prophylaxis (PrEP), according to study findings published in the Journal of Acquired Immune Deficiency Syndromes.

"[W]e found that although there was an association between the predicted likelihood of next-day sex and the actual occurrence of sexual encounters in the subsequent 24 hours, almost one third of all sexual encounters were unpredicted and spontaneous, and more than two-thirds of participants experienced such an encounter over the course of two months," the study authors wrote. "These findings suggest that difficulties in predicting sex among young men who have sex with men in particular may reduce the ability of on-demand PrEP to prevent HIV acquisition in this population."

On-demand PrEP (also known as PrEP 2-1-1) involves taking two doses of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC; Truvada or generic equivalents) two to 24 hours before anticipated sex, one dose 24 hours later and a final dose 24 hours after that. Though not approved by the Food and Drug Administration, PrEP guidance from the Centers for Disease Control and Prevention includes off-label use of on-demand PrEP for cisgender men who have sex with men. (This regimen has not yet been adequately studied and is not recommended for other populations.)

Research has shown that on-demand TDF/FTC is as effective as daily dosing, reducing the risk of HIV acquisition by around 99% if used consistently and correctly. In the French PREVENIR trial, more than 3,000 HIV-negative participants, mostly gay and bi men, were offered a choice of daily or on-demand PrEP. HIV incidence rates were low and similar in both groups (1.1 cases per 1,000 person-years).

But to use on-demand PrEP effectively, people need to be able to predict when they will have sex so they can take the first dose in advance.

Bryce Stamp, MPH, of the Gillings School of Global Public Health at the University of North Carolina at Chapel Hill, and colleagues assessed the prediction ability of young gay and bisexual men. Young people ages 13 to 24 have a high HIV incidence rate, accounting for one in five new diagnoses in 2019.

The analysis looked at a nationally recruited prospective cohort of 120 HIV-negative cisgender men who have sex with men, ages 16 to 24. The median age was 21 years, and 47% said they were single. Nearly half were white, a quarter were Latino and 12% were Black. More than a third (37%) lived in the South, and most resided in urban areas and had more than a high school education. More than half (58%) had never taken PrEP, 28% were currently using daily PrEP and 14% had previously used PrEP.

The participants were followed using daily digital surveys sent via text messages for eight weeks. They were asked to predict how likely they were to have anal sex over the next 24 hours (on a scale ranging from "not at all likely" to "very likely") and then reported actual sex acts they engaged in.

The main study outcome was "unpredicted spontaneous encounters," or anal sex that occurred without enough prior knowledge to take on-demand PrEP on time according to dosing guidelines. Encounters that were not expected the previous day ("not at all likely," "somewhat unlikely" or less than 50% likely) were considered "unpredicted," while those that were not expected at least two hours in advance were dubbed "spontaneous."

During the study period, a total of 854 sexual encounters and 952 anal sex acts (some encounters involved more than one act) were reported. Participants said they knew they would have sex at least two hours in advance of 72% of encounters. However, nearly a third of encounters were unpredicted or spontaneous, suggesting that they would not have been protected by on-demand PrEP dosing. More than two thirds of participants (69%) had at least one such encounter over two weeks.

Nearly 40% of sexual encounters involved main partners, 30% involved casual partners and 32% involved anonymous or unknown partners; of the latter, 41% were unpredicted or spontaneous. Men used alcohol or drugs during about a third of encounters, and these were slightly less likely to be unpredicted or spontaneous than those without alcohol or drug use (30% versus 36%). Nearly three quarters of all anal sex acts were condomless.

"On-demand PrEP to prevent HIV acquisition may be challenging for many young men who have sex with men," the researchers concluded. "Clinical and public health approaches that account for patients' predictive abilities alongside their dosing preferences may help to optimize selection of and adherence to PrEP dosing strategies."

"[A]n overarching interpretation of our results is that the temporal precision required by on-demand PrEP may leave many young men who have sex with men at considerable risk of HIV exposure," they wrote in their discussion of the results. "This interpretation is reinforced by our finding that almost three quarters of sex acts were condomless and nearly one-third of sexual

encounters were with an anonymous partner."

The authors suggested that daily TDF/FTC dosing with adherence support might be a better strategy to ensure adequate protection for young gay and bi men during unpredicted or spontaneous sexual encounters. Another option for those who have difficulty predicting when they might have sex could be long-acting Apretude (cabotegravir) injections administered by a health care provider every other month.

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