Q/ Is event-driven PrEP dosing for HIV as effective as daily dosing?

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EVIDENCE-BASED ANSWER

A/ **PROBABLY,** although there are no head-to-head trials comparing the 2 dosing regimens. Event-driven pre-exposure prophylaxis (PrEP) dosing reduces HIV conversion by 86% compared to placebo (strength of recommendation [SOR]: **B**, large randomized controlled trial [RCT]). Daily PrEP reduces HIV conversion by 44% to 86% (SOR: **B**, based on open-label RCTs).

Event-driven PrEP regimens may be associated with lower adherence when compared with daily PrEP regimens (average of 70% for event-driven PrEP vs average of 92% for daily PrEP) (SOR: **B**, based on open-label and cohort trials). Event-driven PrEP regimens have lower medication costs, and they are associated with no difference in the rate of sexually transmitted infections (STIs) (SOR: **B**, based on prospective cohort studies). Patients may prefer them to daily regimens (75% choose event-driven PrEP vs 25% choose daily PrEP) (SOR: **B**, based on the preponderance of prospective cohort studies with conflicting results).

EVIDENCE SUMMARY

Event-driven PrEP is effective for prevention of HIV transmission

An RCT evaluating the effectiveness of event-driven PrEP in 400 patients at high risk for HIV found that it reduced HIV incidence by 86% compared to placebo. Researchers recruited HIV-negative men or transgender women who had sex with men, who'd had condomless anal sex with at least 2 partners in the previous 6 months, and followed them for a median of 9.3 months for HIV acquisition.[1]

Patients randomized to event-driven PrEP took tenofovir-emtricitabine (300-200 mg) on the following schedule: 2 pills 2 to 24 hours before intercourse (or 1 pill if they had taken it within the past week), followed by a third pill 24 hours later, and a fourth pill 24 hours after that. When patients had multiple consecutive episodes of intercourse, daily use was continued until 2 days after the last episode. Patients in the control group took placebo pills.[1]

Event-driven PrEP reduced HIV incidence vs placebo (2 infections vs 14 infections; 0.91 vs 6.6 per 100 person-years; relative risk [RR] = 0.86; P = .002). PrEP produced more gastrointestinal (14% vs 5%; P = .002) and renal (18% vs 10%; P = .03) adverse effects than placebo. Participants took a median of 15 pills per month.[1]

A post-hoc analysis of the above study, evaluating 270 patients, found that event-driven PrEP reduced HIV incidence by 100% during periods of less frequent sexual encounters. Selected participants had a median of 5 sexual encounters per month (range, 2-10), used a median of 9.5 pills per month (range, 6-13), and represented 134 person-years of follow-up. No HIV infections (0 per 100 person-years; 95% CI, 0-5; P = .013) were diagnosed in the PrEP group and 6 HIV infections (9.2 per 100 person-years; 95% CI, 3.4-20.1) were diagnosed in the placebo group, with a relative reduction of HIV incidence of 100% (95% CI, 39-100).[2]

CONTINUED

In 2019, the USPSTF published a recommendation that clinicians offer PrEP with effective antiretroviral therapy to patients at high risk for HIV acquisition.

For comparison, 2 large open-label trials evaluating daily PrEP found that it reduced HIV incidence by 44%[3] and 86%[4] vs placebo.

Adherence is better with daily PrEP than event-driven PrEP

Three prospective cohort trials evaluated PrEP adherence (extent that participants were taking PrEP at the time of sexual encounters) with different dosing regimens and found that event-driven PrEP tended to have lower adherence than daily PrEP. An open-label trial in Bangkok and Harlem (New York City) randomized 357 at-risk patients to 1 of 3 regimens: event-driven (1 tablet before and after sex), time-driven (1 tablet twice weekly with a postsex dose), and daily. Overall, patients with event-driven PrEP had lower adherence than those with daily PrEP (67% event-driven vs 97% daily; $P < 0.0001$).[5]

In an open-label prospective cohort trial in Belgium, at-risk patients chose between using event-driven (N = 44) and daily (N = 135) PrEP. Analysis was conducted for both high-risk HIV exposure days (defined as condomless anal receptive intercourse with a new or HIV-positive steady partner with a detectable viral load) and low-risk HIV exposure days (consistent condom use or condomless anal intercourse with a steady partner who is HIV-negative). Over 18 months, lower adherence was demonstrated with event-driven PrEP than with daily PrEP for high-risk days (88% [95% CI, 86%-90%] vs 97.5% [95% CI, 97%-98%]; $P < .0001$) and also for low-risk days (42% [95% CI, 40%-45%] vs 96% [95% CI, 95%-96%]; $P < .0001$).[6] Researchers diagnosed no new HIV infections in any participant, and the incidence of STIs was the same in both groups.

A third open-label trial evaluated adherence among 178 South African women randomized to event-driven or daily PrEP and found lower sexual event coverage with event-driven PrEP (52% vs 75%; odds ratio = 2.76; 95% CI, 1.68-4.53; $P < 0.0006$). Four women in each group seroconverted to HIV positive.[7]

Drug costs, patient preferences, and STI risk are important considerations

Several of the above trials reported use of fewer pills in the event-driven groups, with lower drug costs.[2,5,7] A large prospective cohort trial of men who have sex with men (N = 1049) with an average of 10 sexual partners found that most (76%) opted for event-driven PrEP.[8] Researchers also reported no difference in STI rates (RR = 1.24 for "at least 1 bacterial STI"; 95% CI, 0.84 to 1.81).[8] However, a smaller, open-label prospective cohort trial (N = 200) found that more participants chose daily PrEP than event-driven PrEP (76.5% vs 23.5%), although almost all said they would change their dosing regimen in the next year.[9]

Recommendations from others

In 2019, the World Health Organization recommended oral PrEP as an additional prevention choice for people at substantial risk for HIV infection and stated that different dosing strategies offer users flexibility, choice, and convenience.[10] Also in 2019, the US Preventive Services Task Force published a recommendation that clinicians offer PrEP with effective antiretroviral therapy to patients at high risk for HIV acquisition. They did not specify which regimen to offer.[11]

Editor's takeaway

While there are theoretical reasons why event-driven PrEP might not work as well as daily PrEP, we have 1 RCT that suggests the real-world outcomes are similar. Given the apparent effectiveness of either option, the best choice is the one the patient will use. **JFP**

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