

# Early Adopters of Event-driven Human Immunodeficiency Virus Pre-exposure Prophylaxis in a Large Healthcare System in San Francisco

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Among 279 patients within a large healthcare system in San Francisco, event-driven HIV pre-exposure prophylaxis using a 2–1–1 regimen was a desirable alternative to daily dosing. Problems with adherence, planning sex in advance, or side effects were infrequent (13.9%). We found no new HIV infections over 136 person-years of follow-up.

**Keywords.** pre-exposure prophylaxis; event-driven PrEP; 2–1–1; implementation.

Estimates indicate that only 1 in 5 individuals with an indication for human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) have been prescribed PrEP [1]. Studies have identified cost, daily adherence, and side effects as barriers to PrEP use [2, 3]. Event-driven PrEP using a “2–1–1” regimen is an alternative dosing strategy that may mitigate some of the challenges of daily dosing. The 2–1–1 regimen is a nondaily dosing regimen where patients use PrEP only around the time of potential HIV exposure: 2 doses 2–24 hours before sex and single doses for 2 days thereafter. Data from the IPERGAY trial demonstrated that 2–1–1 PrEP using emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) was highly efficacious in preventing HIV in men who have sex with men (MSM) [4]. However, data evaluating 2–1–1 from clinical practice settings are limited.

While the Centers for Disease Control and Prevention (CDC) has not issued clinical guidelines supporting the use of 2–1–1, the International Antiviral Society–USA [5] and the World Health Organization [6] have endorsed the use of 2–1–1

in MSM. In February 2019, Kaiser Permanente San Francisco (KPSF) began offering 2–1–1 as an option to new and existing PrEP patients. In this study, we describe the demographic and clinical characteristics of early 2–1–1 adopters at KPSF, as well as characterize patterns of use, motivations for choosing 2–1–1, challenges, adherence, and HIV incidence.

## METHODS

Kaiser Permanente is a not-for-profit integrated healthcare system that provides comprehensive care to over 240 000 residents of San Francisco, California. The KPSF PrEP program is staffed by physicians, medical assistants, and a dedicated nurse practitioner [7]. Patients access the program through self-referral or through a referral from a clinician. As part of 2–1–1 implementation, male patients on daily PrEP with an online patient portal account (98.5% of KPSF PrEP patients) were contacted via secure message between February and March 2019. The message included information about 2–1–1 and how it may be an option for men who have infrequent sex and plan sex in advance. Interested patients who were previously on daily PrEP had a telephone discussion with a clinician prior to starting the 2–1–1 regimen. Beginning February 2019, new patients starting PrEP at KPSF were informed about 2–1–1 at an in-person PrEP intake visit. Patients were educated about dosing instructions, adherence, and side effects.

In this analysis, we included all patients prescribed 2–1–1 PrEP on or before 31 August 2019. Clinicians collected clinical and behavioral data at the time of 2–1–1 initiation and at a 3-month follow-up visit as part of routine care. All follow-up visits were conducted by telephone. Information abstracted from the electronic health record included patient demographics, prior PrEP use, dosing regimen used in the last 3 months (ie, 2–1–1, daily, combination of both, or other), reasons for using 2–1–1, challenges with 2–1–1, number of 2–1–1 courses in the prior month, any missed doses around the last sexual encounter, and use of HIV postexposure prophylaxis (PEP) after missed PrEP doses.

Data were summarized using descriptive statistics. We used Fisher's exact tests to assess differences in dosing regimens used in the last 3 months by age and race/ethnicity. To estimate HIV incidence, we followed patients from their intake visit until the earliest of HIV diagnosis, health plan disenrollment, or 31 January 2020. The Kaiser Permanente institutional review board approved our study with a waiver of informed consent.

## RESULTS

As of 31 August 2019, there were 2338 active PrEP patients in KPSF, including 279 (11.9%) who were prescribed 2–1–1. Of the 279, 56.3% were white, 21.5% Asian, 11.8% Latinx, 3.2%

Received 18 February 2020; editorial decision 7 April 2020; accepted 21 April 2020; published online June 4, 2020.

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Clinical Infectious Diseases® 2020;XX(X):1–3

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African American, and 7.2% other or unknown. Median age was 43 years (interquartile range [IQR], 34–54 years). All were male, 98.6% were MSM, and 76.0% had previously used PrEP, including 11 (5.2%) who used 2–1–1 prior to implementation at KPSF and 6 (2.8%) who used a different nondaily dosing regimen. These nondaily regimens other than 2–1–1 included “Ts & Ss” (ie, taking PrEP on Tuesdays, Thursdays, Saturdays, and Sundays) and “vacation dosing” (ie, taking PrEP only when on vacation). Patients on nondaily regimens other than 2–1–1 were advised to transition to 2–1–1.

Of the 279 prescribed 2–1–1, 273 (97.9%) completed their 3-month follow-up visit (Table 1). Of those, 140 (51.3%) exclusively used 2–1–1 in the prior 3 months, 53 (19.4%) opted to use daily dosing despite their initial interest in 2–1–1, 41 (15.0%) used a combination of 2–1–1 and daily dosing, 11 (4.0%) reported using other nondaily dosing regimens, and 8 (2.9%) never started PrEP. The most common reasons patients reported for using 2–1–1 were infrequent sex (57.9%) followed by concerns around potential side effects from daily dosing (4.0%), cost of daily PrEP (2.6%), and difficulty with daily adherence (2.2%). The 3-month follow-up data showed no differences in dosing regimens used by age ( $P = .91$ ) or race/ethnicity ( $P = .35$ ).

Thirty-eight (13.9%) patients reported challenges with using 2–1–1, including 16 (5.9%) who had issues related to

adherence and/or the dosing pattern, 13 (4.8%) who had difficulty planning sex in advance, and 8 (2.9%) who experienced side effects. Of the 38 who experienced problems with 2–1–1, 22 (57.9%) switched to daily dosing on their own prior to the 3-month follow-up visit. At the 3-month follow-up, 20 (7.3%) had discontinued PrEP, including 14 (5.1%) who lost health insurance coverage, 4 (1.5%) who reported reductions in sexual risk, and 2 (0.7%) because of side effects. Of the 2 who discontinued PrEP due to side effects, one had a decrease in creatinine clearance and the other opted to discontinue because of chronic, intermittent transaminitis despite a recommendation from his PrEP clinician to continue treatment. None of the 273 patients were prescribed PEP.

Among the 181 patients who used 2–1–1 exclusively or a combination of 2–1–1 and daily dosing, we observed a total of 136 person-years of PrEP use. The median number of 2–1–1 courses in the last month was 1 (IQR, 1–2), with 19.9% reporting none. Only 3.9% of patients reported missing a dose at their last sexual encounter. There were no HIV diagnoses during the 136 person-years of follow-up (upper limit of 1-sided 97.5% confidence interval, .03%).

## DISCUSSION

Our clinical experience supports the use of event-driven PrEP using a 2–1–1 regimen as an appealing alternative to daily dosing in men. The majority of patients in our cohort described infrequent sex as their motivation for using 2–1–1. While some reported challenges with the regimen, side effects and missed doses were rare, and were less frequent than those observed in clinical trials [4, 8]. In addition, the majority of individuals who experienced problems with using 2–1–1 transitioned to daily dosing without additional provider interventions. There were no new HIV infections among patients using either 2–1–1 exclusively or a combination of 2–1–1 and daily dosing. Notably, we found that patients opting for 2–1–1 in our cohort reported more infrequent PrEP use than in previous studies [9, 10], with a median of only 4 pills in the prior month.

We observed fluid patterns of PrEP dosing, similar to what others have described in European demonstration projects [11, 12]. Although most chose to exclusively use 2–1–1, others moved between daily dosing and 2–1–1. Fluctuations between dosing regimens reflect variability in sexual behaviors over time and underscore the necessity for patient education so that individuals can adapt their PrEP dosing to meet their HIV-prevention needs. Patients on 2–1–1 will continue to require regular HIV testing and follow-up to assess any potential challenges with adherence and ensure that individuals transition between different dosing regimens safely. Clinicians offering 2–1–1 need to recognize that patients may alternate between dosing regimens and will require additional support and education to ensure effective PrEP use. Further, it is important to

**Table 1. Patients Prescribed 2–1–1 PrEP at Kaiser Permanente San Francisco, Assessed at the 3-Month Follow-up Visit**

	No. (%)
Dosing regimen in the prior 3 months	
Exclusively 2–1–1	140 (51.3)
Daily	53 (19.4)
Combination of 2–1–1 and daily	41 (15.0)
Stopped PrEP	20 (7.3)
Other nondaily dosing	11 (4.0)
Never started PrEP	8 (2.9)
Reasons for selecting 2–1–1	
Infrequent sex	158 (57.9)
Concerns around side effects from daily dosing	11 (4.0)
Cost	7 (2.6)
Difficulty with daily adherence	6 (2.2)
Advice by medical provider	3 (1.1)
Challenges with 2–1–1 PrEP	
Adherence/difficulty with dosing pattern	16 (5.9)
Unable to plan sex in advance	13 (4.8)
Side effects	8 (2.9)
Cost	1 (0.4)
Reasons for stopping PrEP	
Lost health insurance coverage	14 (5.1)
Reduction in sexual risk	4 (1.5)
Side effects	2 (0.7)

N = 273.

Abbreviation: PrEP, pre-exposure prophylaxis.

underscore that data supporting 2–1–1 efficacy are currently only in MSM using FTC/TDF [5, 6].

Our study has several limitations. First, this is an insured cohort of predominantly white male patients with access to care, most of whom had previously used PrEP. Second, our analysis involved early adopters of 2–1–1 who were likely highly motivated individuals. Third, the low number of 2–1–1 courses used in the prior month suggests that our cohort may have a lower risk of HIV acquisition and may not be representative of others using 2–1–1 PrEP. However, our results corroborate findings from IPERGAY that found that 2–1–1 was effective even among individuals who had less frequent sex [9]. Conclusions around uptake are also limited because the proportion of patients contacted who proceeded to initiate 2–1–1 dosing was not systematically collected. Last, further studies with longer follow-up are needed.

Despite these limitations, our findings provide important insights to support the implementation of 2–1–1 among MSM in the United States. We found that 2–1–1 is a desirable alternative for many patients, particularly those who have less frequent sex. Offering 2–1–1 in addition to daily dosing provides flexibility in tailoring PrEP regimens based on individual patient needs and preferences. There were no new HIV infections among patients using 2–1–1, and issues related to adherence, planning sex in advance, and side effects were minimal. Clear guidance from the CDC and other public health agencies are needed so that 2–1–1 can be scaled up effectively alongside daily PrEP.

## Notes

**Financial support.** This work was supported by a Kaiser Permanente Northern California Community Benefit research grant and the National Institutes of Health (grant numbers T32 DA007250, K01 AI122853, K24 AA025703).

**Potential conflicts of interest.** J. L. M. has received research grant support from Merck and has consulted on a research grant to Kaiser Permanente Northern California from Gilead Sciences. C. B. H. and M. J. S. have received research grants from Gilead Sciences. All other authors report

no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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