Choosing Between Daily and Event-Driven Pre-exposure Prophylaxis: Results of a Belgian PrEP Demonstration Project

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Background: Daily pre-exposure prophylaxis and event-driven pre-exposure prophylaxis (PrEP) are efficacious in reducing HIV transmission among men who have sex with men (MSM). We analyzed baseline data from a PrEP demonstration project "Be-PrEP-ared" in Antwerp, Belgium, to understand preferences for daily PrEP or event-driven PrEP among MSM at high risk of HIV and factors influencing their initial choice.

Methods: Cross-sectional data from an open-label prospective cohort study, using mixed methods. Participants who preregistered online were screened for eligibility and tested for sexually transmitted infections (STIs). Eligible participants chose between daily PrEP and event-driven PrEP and reported on behavioral data through an electronic questionnaire. In-depth interviews were conducted with a selected subsample. Bivariate associations were examined between preferred PrEP regimens and sociodemographic factors, sexual behavior, and STIs at screening.

Results: In total, 200 participants were enrolled between October 2015 and December 2016. Self-reported levels of sexual risk-taking before enrollment were high. STI screening revealed that 39.5% had at least 1 bacterial STI. At baseline, 76.5% of participants preferred daily PrEP and 23.5% event-driven PrEP. Feeling able to anticipate HIV risk was the most frequent reason for preferring event-driven PrEP. Regimen choice was associated with sexual risk-taking behavior in the past 3 months. Almost all participants (95.7%) considered it likely that they would change their dosing regimen the following year.

Conclusion: Event-driven PrEP was preferred by 23.5% of the participants, which better suits their preventive needs. Event-driven PrEP should be included in PrEP provision as a valuable alternative to daily PrEP for MSM at high risk of HIV.

Key Words: PrEP, MSM, HIV prevention, event-driven PrEP, daily PrEP

(*J Acquir Immune Defic Syndr* 2018;79:186–194)

INTRODUCTION

With 1.8 million new HIV infections in 2016 worldwide, HIV prevention remains a public health challenge.[1] In Europe, condomless anal sex between men is the predominant mode of HIV transmission.[2] Almost 40% of all new HIV cases reported in 2016 in Europe were among men who have sex with men (MSM).[3] In Belgium, new HIV infections among MSM represented 52% of all HIV diagnoses in 2016.[4] Although progress has been made in reducing the number of HIV infections worldwide,[1] additional prevention strategies for key populations such as MSM are clearly needed to further reduce the number of new HIV infections.

Pre-exposure prophylaxis (PrEP), with oral emtricitabine and tenofovir disoproxil fumarate (FTC/TDF), is an efficacious biomedical tool for HIV prevention.[5] Its efficacy has been demonstrated in 12 clinical trials within different populations and geographical areas.[6] In 2015, two European clinical trials confirmed PrEP efficacy in reducing the risk of HIV among MSM at high risk of HIV: the PROUD study in England and IPERGAY in France and Canada.[7,8] Both showed PrEP to be safe and to reduce the risk of HIV by 86% among MSM at high risk. To translate clinical trial efficacy into population-wide effectiveness, research informing an optimal implementation is crucial.[9] In particular, insights are needed on how to achieve correct use among those at highest risk, when they are at risk.

Individual-level risk factors for HIV acquisition among MSM have been well documented, such as having had condomless anal intercourse (CAI) and having a sexually transmitted infection (STI).[10] They have been successfully translated into PrEP eligibility criteria to maximize public health impact.[11] Less scientific attention has been devoted to the use of different PrEP dosing regimens to reflect different patterns in sexual risk-taking. Tailoring PrEP use to users' needs could increase its effectiveness, but requires a better understanding of personal regimen choices. This could further

Received for publication March 16, 2018; accepted June 18, 2018.

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Supported by a grant obtained from the Flemish Agency for Innovation and Entrepreneurship. Gilead Sciences donated the drugs (Truvada) for the study.

The study medication of Be-PrEP-ared was donated by Gilead Sciences.

Members of the Be-PrEP-ared study team are listed in the Appendix 1.

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optimize prevention behavior, public health impact, and cost-effectiveness of PrEP.[12]

Almost all clinical trials have focused on daily oral PrEP.[6] The IPERGAY study was the first to demonstrate the efficacy of a nondaily regimen among MSM at high risk of HIV, referred to as "event-driven" or "on-demand" PrEP.[8] Event-driven PrEP entails the use of 2 tablets of PrEP between 2 and 24 hours before anticipated sex, continuing with 1 tablet every 24 hours until 2 days after the last sex event. Nondaily regimens have the advantage of requiring fewer tablets, thus reducing potential side-effects and cost, although they are less forgiving of missed doses.[13] We hypothesize that for a subgroup of MSM at high risk of HIV, event-driven PrEP is preferred. However, we do not yet know what proportion of MSM prefers to take event-driven (versus daily) PrEP when given that choice, what their profile is, and what influences their decision.

In this article, we present baseline data from a PrEP demonstration project among MSM in Belgium: the Be-PrEP-ared study. More particularly, we examine the proportion of MSM preferring daily PrEP or event-driven PrEP, the reasons for their initial choice, and associations with sociodemographic and sexual behavior factors.

METHODS

Design

Cross-sectional baseline data were used from the Be-PrEP-ared study: a single-site, open-label prospective cohort study using a mixed-method approach with an embedded qualitative component (EudraCT 2015-000054-37). The study site is the HIV/STI clinic of the Institute of Tropical Medicine in Antwerp, Belgium. The aim of Be-PrEP-ared is to evaluate whether daily PrEP and event-driven PrEP, provided within a comprehensive prevention package, are feasible and acceptable additional prevention tools for MSM at high risk of HIV acquisition in Belgium. Study procedures and details have been described in the published study protocol.[14] A community advisory board was set up to provide advice throughout the entire research process and to act as a link to local MSM communities.

Study Population

To be included in the study, participants had to be: born as male, test HIV-negative, be aged 18 years and older, be able and willing to provide written informed consent and to participate as required by the protocol, have had sex with another man in the past 12 months, be motivated to strengthen own prevention efforts, and to correspond to at least 1 criterion for 'high risk of HIV' (Box 1). Exclusion criteria included the following: symptoms of acute HIV infection, an estimated creatinine clearance of <60 mL/min/1.73 m^2 according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi) formula, an active hepatitis B infection, or taking postexposure prophylaxis or other products containing emtricitabine, tenofovir disoproxil or other cytidine analogues (such as lamivudine), or adefovir dipivoxil.

Box 1. Criteria for 'high risk for HIV'

- Reported condomless anal intercourse in the past 6 months with a casual partner with unknown or HIV positive status;
- Reported (at least) 1 STI episode in the past 6 months;
- Reported having taken postexposure prophylaxis in the past 6 months.

Participant Recruitment

The study was advertised through the community advisory board's social media, national media (eg, newspaper and television), and person-to-person promotion. Potential participants could preregister for participation on the study website (www.be-prep-ared.be) between September 9, 2015, and June 18, 2016. Participants who registered before September 25, 2015, were randomized to a ranking number on the list with the screening appointments. Thereafter, the screening list was completed in chronological order of registration, to allow for continuous preregistration and screening of participants until the sample size of 200 was reached.

Enrollment Study Procedures

At the screening visit, written informed consent was obtained, and potential participants were screened for eligibility. Study procedures also included the collection of basic sociodemographic characteristics and current sexual behavior, a medical examination with special attention to symptoms of an acute HIV infection, and the collection of blood, urine, anal, and pharyngeal samples for kidney, liver, HIV, and STI testing. The screening visit ended with preventive sexual health counseling.

Potential participants were invited to come back to the clinic within 2 weeks to confirm eligibility and enrollment in the study. Symptoms of acute HIV infection were reassessed, and data were collected on relevant medical history, current medication, and recreational drug use. Participants were instructed to complete a baseline questionnaire on an electronic tablet in the waiting room. A counselor thoroughly informed participants about the PrEP dosing regimens, invited them to choose between daily and event-driven regimens, and provided sexual health and adherence counseling. When asked, participants were explained that both regimens were considered equally efficacious, if taken correctly. Participants then received box with 30 PrEP tablets and started with their preferred regimen.

Laboratory Methods

STI testing was performed at the screening visit. Screening for HIV, hepatitis B, hepatitis C, syphilis, and HSV-2 was performed in blood samples. In addition, real-time polymerase chain reaction was used to test for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Mycoplasma genitalium*, and *Trichomonas vaginalis* on urine, pharyngeal, and anorectal samples. Details of laboratory procedures are provided in the protocol.[14]

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Questionnaire

The self-administered baseline questionnaire was developed by an interdisciplinary research team based on surveys used in other studies related to PrEP or HIV prevention among MSM.[7,8,15,16] The questionnaire included questions on sociodemographic information, sexual preferences, the most recent sexual event (eg, last time anal sex occurred), sexual behavior in the past 3 months (eg, number of anonymous contacts), and sexual risk-taking behaviors (eg, last time transactional sex occurred). A list of potential reasons for choosing daily PrEP or event-driven PrEP was provided, adapted to the regimen, including an open-ended "other" option. The questionnaire allowed for multiple answers for this question and asked about the most important reason of choice. The questionnaire was available in 3 languages: Dutch, French, and English. Participants were instructed to complete the questions regarding preferences for daily PrEP or event-driven PrEP after the counselor visit, to ensure that they were properly informed about the regimens.

In-Depth Interviews

The mixed-method design included qualitative research to complement quantitative findings and to get an in-depth understanding of participants' prevention needs, preferences for and attitudes toward PrEP use, user experiences, and perceived impact of PrEP on their sexual life.[14] A preliminary subset of 11 in-depth interviews, conducted by social scientists, was transcribed verbatim and analyzed according to content-analytical principles.

Statistical Analysis

Only participants enrolled in the study were included in the analysis. Participants were considered infected with *N. gonorrhoeae* if they tested positive for *N. gonorrhoeae* in 1 of the 3 biological sites (anorectal, pharynx, or urine), and not infected with *N. gonorrhoeae* if all 3 testing sites were negative. If a test result was invalid or not confirmed at 1 of the 3 sites, the final result was considered invalid. The same was performed for *C. trachomatis*, *M. genitalium*, and *T. vaginalis*. Syphilis was defined as a positive rapid plasma

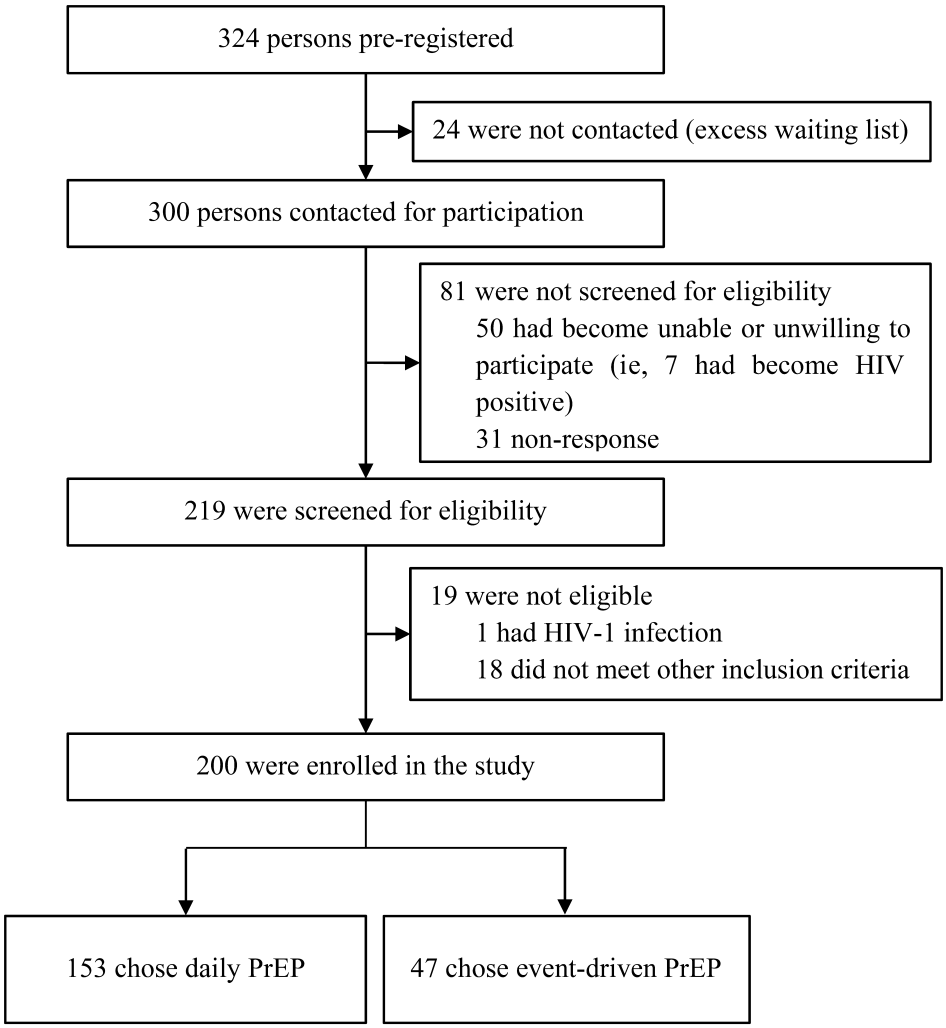

FIGURE 1. Screening and enrollment of participants.

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reagin with a titer of at least 4 and a positive *Treponema pallidum* assay or *Treponema pallidum* particle agglutination test. A gray zone result for HSV-2 was coded as invalid.

We examined associations between factors related to sociodemographic background, sexual behavior factors, and STIs at screening with the preferred PrEP regimen using χ^2 or Fisher exact test. If an association was found in an ordinal variable with more than 2 categories, '*P* value for trend' was calculated using the Mantel–Haenszel linear-by-linear association χ^2 test. IBM SPSS Statistics 24.0 or SAS 9.4 was used for all computations.

Ethics and Quality Assurance

Ethical approval was provided by the institutional review board of the Institute of Tropical Medicine Antwerp and the ethics committee of the Antwerp University Hospital. The protocol and all relevant information were submitted to the Competent Authority of Belgium. The study is monitored in accordance with regulations applicable to clinical trials, including Good Clinical Practice guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use and Good Clinical

TABLE 1. Sociodemographic Characteristics of Study Participants, Total and Per Preferred PrEP Regimen

	Total	Daily	Event-Driven	
	N = 200, n (%)*	n = 153, %†	n = 47, %‡	*P*§
Age				0.716
18–30	42 (21.0)	22.2	17.0	
31–40	76 (38.0)	37.9	38.3	
41+	82 (41.0)	39.9	44.7	
Sex				0.554
Man	197 (98.5)	98.7	97.7	
Transwoman	3 (1.5)	1.3	2.1	
Racial-ethnic background				0.533
White	178 (89.0)	88.2	91.5	
Other	22 (11.0)	11.8	8.5	
Education				0.644
Primary school	5 (2.5)	2.0	4.3	
Secondary school	40 (20.0)	19.6	21.3	
Higher education	155 (77.5)	78.4	74.5	
Occupation				0.001
Full-time, part-time, or self-employed	157 (78.5)	88.9	68.1	
Not employed‖	43 (21.5)	11.1	31.9	
Average monthly net income (€)¶				0.002#
0–1700	70 (37.4)	30.6	60.5	
1700–2950	79 (42.2)	47.2	25.6	
2950+	38 (20.3)	22.2	14.0	
Health insurance**				0.483
Yes	187 (93.5)	94.7	91.5	
Living situation				0.868
Alone	100 (50.0)	49.7	51.1	
With others††	100 (50.0)	50.3	48.9	
Partner status				0.164
Steady partner	90 (45.0)	47.7	36.2	
No steady partner	110 (55.0)	52.3	63.8	
HIV status steady partner‡‡				0.325
HIV-negative	61 (69.3)	67.1	80.0	
HIV-positive	27 (30.7)	32.9	20.0	
Circumcision				0.815
Yes	36 (18.0)	17.6	19.1	

*Frequency and percentage within total.
†Percentage within daily PrEP.
‡Percentage within event-driven PrEP.
§*P* value of the χ^2 or Fisher exact test for associations between chosen regimen and variables.
‖Category includes the following: "unemployed," "student," "retired," or "disabled or long-term sick leave."
¶"Rather not say" (n = 13) was excluded from the analysis.
#*P* value for trend is 0.003.
**"Rather not say" (n = 1) was excluded from the analysis.
††Category includes the following: "with parents," "with partner," and "with others."
‡‡HIV status only for "steady partner" (n = 90) and "not sure" or "don't know" (n = 2) was excluded from the analysis.

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Laboratory Practice requirements, institutional-specific monitoring, and source data verification standard operating procedures.

RESULTS

Screening and Enrollment

We enrolled 200 participants in the study between October 2015 and December 2016 (Fig. 1). In total, 324 persons preregistered for participation, and 300 potential participants were contacted. Of them, 31 could not be reached; 7 reported having become HIV-positive between time of registration and time of contact; and 43 had become unable or unwilling to participate because of changes in occupation, place of residence, or relationship. On screening, 1 person was found HIV-positive, and 18 did not meet other inclusion criteria.

Among the 200 participants enrolled, 47 (23.5%) chose event-driven PrEP, and 153 (76.5%) preferred the daily PrEP regimen.

Profile of Study Participants

The median age of the study participants was 38 years, with a minimum of 22 years and a maximum of 70 years. Three participants were transgender women. Participants were predominantly white (89.0%), highly educated (77.5%), and employed fulltime, part-time, or were self-employed (78.5%; Table 1).

Participants who were not employed and those with a lower average net income were significantly more likely to prefer event-driven PrEP over daily PrEP.

Reasons for PrEP Regimen Choice

Table 2 shows the most common reported reasons for PrEP regimen choices. The most important reasons for choosing event-driven PrEP were as follows: feeling able to anticipate the risk of HIV (41.3%), perceiving it as less burdensome for the body (23.9%), assessing one's own risk of HIV to be low (13.0%), or being afraid of adverse events (13.0%). Triangulation with qualitative findings from the in-depth interviews corroborated these preferences as illustrated by the quotes (Boxes 2 and 3).

Box 2. Participant preferring event-driven PrEP, 38 years old

> "Mostly when I have sex, then I do know it beforehand, or I know there will be a chance.[…] It's not that frequent and mostly it's in the weekend that I have sexual intercourses, so then I only [take tablets] in the weekend, and perhaps the days thereafter when sex has occurred"

Box 3. Participant preferring event-driven PrEP, 23 years old

> "Yeah, but I have to think about my body […], that it does not get damaged. So I was thinking like, […] I'm going to choose so that there is no harm, that I have to take as little [tablets] as possible, that I'm only going to take it when I'm going to have sex."

By contrast, the most important reasons for choosing daily PrEP were as follows: safety (31.5%), ease of daily pill-taking (20.8%), and difficulties with anticipating HIV risk (20.8%), as illustrated in Box 4: the participant would not be able to take PrEP in advance or to plan it as such, which rendered event-driven PrEP less safe according to him.

Box 4. Participant preferring daily PrEP, 30 years old

> "I have a lot of routine in my life, but I have a hard, stressful and irregular job. […] I think that daily [PrEP] is most safe, and that's it. If you take the other [regimen] then you really have to have it planned to [take it] in advance, and that's just really something I cannot do."

Almost all participants anticipated that the odds were high that they would switch PrEP regimen in the following year: 45 (95.7%) in the event-driven group, and 145 in the daily group (95.4%).

Sexual Behavior

The median reported total number of sexual partners in the past 3 months before enrollment was 12. Half of the participants reported 4 or more occasional sex partners in the past 3 months, and 64.5% reported 4 or more anonymous sex partners (Table 3). Sexual risk-taking in the past 3 months was high, with 70.5% of the participants reporting CAI with at least 1 occasional partner and 60.0% with at least 1 anonymous partner. Sixty-four percent had participated in group sex, and 61.5% had sex while using recreational drugs.

Preferring daily PrEP was associated with more recent anal sex before enrollment and higher reported number of occasional and anonymous partners in the past 3 months. Participants who preferred daily PrEP were more likely to have had CAI with at least 1 occasional partner, to have participated in group sex, and to have had sex while being drunk in the past 3 months, as compared with event-driven users.

STI Prevalence

In 39.5% of participants at least 1 bacterial STI was detected at screening, 15 (7.5%) had syphilis, and 3 participants were diagnosed with hepatitis C (Table 4). Among the 24

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TABLE 2. Reasons for PrEP Regimen Preferences

Daily PrEP (n = 149)*	n (%)†	Event-Driven PrEP (n = 46)‡	n (%)†
Daily PrEP seems to be safer	47 (31.5)	I can anticipate very well when I will be at risk of HIV	19 (41.3)
I think it is easier to take 1 pill a day	31 (20.8)	Event-driven PrEP seems less burdensome for my body	11 (23.9)
I find it difficult to anticipate when I will be at risk of getting HIV	31 (20.8)	I have little risk in acquiring HIV	6 (13.0)
I have a lot of risk of getting HIV	14 (9.4)	I am afraid of adverse events (on long term) when I would take PrEP daily	6 (13.0)
I want to be able to have sex at any given moment without having the risk of getting HIV	11 (7.4)	Event-driven PrEP seems easier to adhere to	2 (4.3)
My steady partner has HIV	8 (5.4)	It is difficult for me to remember to take 1 pill a day	1 (2.2)
I want to have sex without a condom more often	7 (4.7)	I do not like to take pills daily	1 (2.2)

*"Missing" (n = 2) and "other" (n = 2) were excluded from the analysis.
†n: frequency; %: percentage within the chosen PrEP dosing regimen.
‡"Other" (n = 1) was excluded from the analysis.

participants with gonorrhoea, 2 cases were detected in urine, 14 in anorectum, and 1 in the pharynx (data not in table). Among the 23 participants (11.7%) with chlamydia infection, 5 cases were detected in urine, 20 in anorectum, and 2 in the pharynx (data not in table). One case of lymphogranuloma venereum was detected in the anorectum, all other chlamydia infections were non–lymphogranuloma venereum strains. Among the 34 participants (17.2%) with mycoplasma infection, no cases were detected in urine, 17 in anorectum, and 17 in the pharynx. There was no statistically significant difference in prevalence of STIs between participants choosing daily PrEP or event-driven PrEP.

DISCUSSION

We showed that MSM coming forward and screened for PrEP in Belgium were at high risk of HIV acquisition, and among those about 1 in 4 preferred event-driven PrEP over daily PrEP. The choice of event-driven PrEP was related to a 'lower risk-profile' and is motivated by feeling able to anticipate the risk of HIV and concerns about side-effects.

The Be-PrEP-ared study is one of the first European PrEP demonstration projects among MSM at high risk of HIV in which participants were able to self-select between daily PrEP or event-driven PrEP. In our study, 23.5% of the MSM preferred event-driven PrEP over daily PrEP. An ongoing Dutch PrEP demonstration project (ie, AmPrEP) also invited participants to choose between these 2 options and found similar results (ie, 27.4% preferred event-driven).[16,17] The Australian demonstration project PRELUDE found that 20% of MSM would prefer event-driven PrEP (ie, dosing around specific risk events) and 14% periodic PrEP (ie, daily dosing during periods of increased risk). However, in PRELUDE, the choice was hypothetical, ie, participants had to take PrEP daily.[18] In the United Kingdom, 1 study found that among 293 MSM who purchased PrEP on the internet, 16% was following the event-driven regimen.[19] In France, where both daily PrEP and event-driven PrEP are provided since 2015, about 6 out of 10 PrEP users have been prescribed event-driven PrEP.[20] However, it could be questioned whether this high proportion in France is due to the IPERGAY study, in the sense that MSM in France would have been more familiar with this dosing regimen. Taking into account these findings, there is now evidence that at least 1 in 4 of MSM at high risk of HIV acquisition would prefer event-driven PrEP in high-income countries, such as Belgium.

Our study results made it possible to outline a profile of MSM who prefer event-driven PrEP: they had less frequently anal sex, had fewer sex partners, and were less likely to engage in specific sexual risk-taking activities such as group sex in the 3 months preceding study participation. Although MSM preferring event-driven PrEP are at sufficient risk of HIV acquisition, considering the PrEP eligibility criteria, they report relatively less risk behaviors than those opting for daily PrEP. They also consider themselves to be able to anticipate when they will be at risk, thus preferring event-driven PrEP. Hence, it is clear that daily PrEP may not be suitable for all MSM at high risk of HIV, and that event-driven regimens could better suit the prevention needs of a specific group of MSM with less frequent sexual risk-taking.

We ensured that participants were well informed about different regimens before choosing. However, it cannot be excluded that the information and counseling provided has influenced participants' preferences in either way. Another limitation is that the enrollment procedure was slow, which may mean that participants enrolled at the beginning of the study (October 2015) may not be entirely comparable with those enrolled later (December 2016). An additional analysis to control for this potential bias did not show any association between time of enrollment and preferred PrEP regimen (not shown in results). The slow enrollment may also have led to the relative large number of persons (n = 81) who had become unreachable, unable, or unwilling to participate. Given the lack of data of people who preregistered but were not screened, we were unable to detect a selection bias in this regard. Different eligibility criteria could have resulted in a different study population. Informing potential participants about the eligibility criteria before preregistration may have reduced the number of those not meeting inclusion criteria. Preventive counseling at the screening visit may have influenced sexual behavior in the week before enrollment.

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TABLE 3. Sexual Behavior Characteristics of Study Participants, Total and Per Preferred PrEP Regimen

	Total	Daily	Event-Driven	
	N = 200, n (%)*	n = 153, %†	n = 47, %‡	*P*§
Sexual attraction to sex				0.045
Only to men	164 (82.0)	85.0	72.3	
Men, sometimes women	35 (17.5)	15.0	25.5	
Men and women	1 (0.5)	0.0	2.1	
Last time anal intercourse				0.039
Within a week	90 (45.0)	49.0	31.9	
More than a week ago	110 (55.0)	51.0	68.1	
No. of steady partners in the past 3 mo				0.273
None	85 (42.5)	41.2	46.8	
One	63 (31.5)	30.1	36.2	
More than 1	52 (26.0)	28.8	17.0	
Number occasional partners in the past 3 mo				0.014‖
None	17 (8.5)	7.2	12.8	
1–3	83 (41.5)	36.6	57.4	
4–10	67 (33.5)	38.6	17.0	
11 or more	33 (16.5)	17.6	12.8	
No. of anonymous partners in the last 3 mo				0.031¶
None	25 (12.5)	9.8	21.3	
1–3	46 (23.0)	20.3	31.9	
4–10	69 (34.5)	37.3	25.5	
11 or more	60 (30.0)	32.7	21.3	
Sexual risk-taking in the past 3 mo				
CAI with at least 1 occasional sex partner	141 (70.5)	81.0	63.4	0.018
CAI with at least 1 anonymous partner	120 (60.0)	69.6	64.9	0.584
Participated in group sex	129 (64.5)	68.6	51.1	0.028
Had sex while used recreational drugs	123 (61.5)	63.4	55.3	0.319
Had sex while used enough alcohol to feel drunk	85 (42.5)	51.0	14.9	<0.001
Paid a man for sex	12 (6.0)	7.2	2.1	0.301
Received money, drugs, or something else for sex	21 (11.0)	12.4	4.3	0.171

*Frequency and percentage within total.
†Percentage within daily PrEP.
‡Percentage within event-driven PrEP.
§*P* value of the χ^2 or Fisher exact test for associations between chosen regimen and variables.
‖*P* value for trend is 0.011.
¶*P* value for trend is 0.006.

Since June 2017, PrEP is reimbursed in Belgium for persons at increased risk of HIV and can be obtained through AIDS Reference Clinics (ie, specialized public HIV treatment centers). In case of eligibility, physicians fill out a reimbursement request, to be submitted to the social health insurance of the future user.[21] The approval is attributed for 1 year, renewable and ensures that users pay €11, 9 maximum as copayment per bottle (ie, 30 pills). After 9 months, approximately 1350 requests were approved, almost exclusively MSM.[21] This number is high when compared with the early uptake in other countries such as France (since 2015) and the United States (since 2012), relative to the number of inhabitants.[22,23] It confirms the high demand and acceptance of this prevention method within this at-risk population. The eligibility criteria for PrEP among MSM and screening procedures used in our study, which are now mostly used in Belgium, have been effective in selecting a subgroup of MSM at substantial risk of HIV. This is corroborated by the self-reported sexual risk behaviors that correspond well to known HIV sexual risk factors (eg, high number of sexual partners),[10] and by the high prevalence of STIs at screening (eg, 39.5% had at least 1 bacterial STI). These results also provide further evidence that routine screening for STIs among MSM when initiating PrEP is important.[11] Preferably, this includes testing in 3 different sites (ie, rectal, urethral, and pharynx), and testing for hepatitis C virus.[17,24]

The World Health Organization currently recommends a daily regimen only.[11] However, the World Health Organization also acknowledges that good practices for implementing PrEP should be people-centered, organized around users' needs and preferences.[11] The efficacy of event-driven PrEP has been demonstrated in the IPERGAY trial,[8] and in the open-label phase efficacy increased to 97% compared with the placebo group.[25] It could be argued that the high efficacy found in IPERGAY may be due to the high number of tablets used. However, in a subanalysis focusing on IPERGAY participants with infrequent sexual intercourse and, hence, nondaily pill intake (ie, less than 15 tablets per month), efficacy increased to 100%.[26] Two European demonstration projects, ie, the

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TABLE 4. Sexually Transmitted Infections Found at Screening Among Participants, Total and Per Preferred PrEP Regimen

	Total		Daily		Event-Driven	
	n/N	%*	n/N	%†	n/N	%‡
Syphilis§	15/200	7.5	14/153	9.2	1/47	2.1
Neisseria gonorrhoeae	24/196	12.2	18/150	12.0	6/46	13.0
Chlamydia trachomatis	23/196	11.7	14/151	9.3	9/45	20.0
Mycoplasma genitalium	34/198	17.2	27/151	17.9	7/47	14.9
Any bacterial STI‖	77/195	39.5	58/150	38.7	19/45	42.2
Trichomonas vaginalis	0/197	0.0	0/151	0.0	0/46	0.0
Hepatitis C	3/200	1.5	1/153	0.7	2/47	4.3
HSV-2	68/194	35.1	51/149	34.2	17/45	37.8

*Percentage within total.
†Percentage within daily PrEP.
‡Percentage within event-driven PrEP.
§Positive = rapid plasma reagin < 1/4 and *Treponema pallidum* assay "positive."
‖Positive for Syphilis, *N. gonorrhoeae*, *C. trachomatis*, or *M. genitalium*.

Be-PrEP-ared and AmPrEP now also show that there is a real demand for event-driven PrEP.[16,17] Therefore, we strongly recommend that event-driven PrEP be considered as a valuable alternative regimen in guidelines for the provision of PrEP among MSM. Integrating event-driven PrEP into clinical practice could lead to reduced numbers of pills used and reduced public healthcare expenditure.[27]

Concerns have been raised that event-driven PrEP is less forgiving of missed doses, which may compromise adherence, thus leading to higher chances of seroconverting and developing resistance.[13,28,29] In HIV Pevention Trials Network (HPTN) 067, participants were randomized to take either daily or nondaily regimens (ie, time-driven and event-driven).[30–32] Although adherence levels (ie, coverage of sex acts) for daily PrEP were significantly better among young women in Cape Town and MSM in Harlem than for nondaily regimens, they were comparable among MSM in Bangkok. Whether adherence to event-driven PrEP would be better when MSM can self-select their preferred regimen under real-life conditions remains to be studied. It could be hypothesized that tailoring PrEP use to users' preferences and prevention needs leads to better adherence through improved motivation.

In our study, MSM coming forward for PrEP seemed to be well aware of their risk of HIV, reflected by their PrEP regimen choice. However, it should be noted that almost all participants considered it likely that they would change their dosing regimen the following year. It could mean that participants are aware that their risk of HIV may vary over time, and that PrEP use may be adapted accordingly.[33] The prospective data from Be-PrEP-ared will be important to shed more light on the dynamics of how, when, and why MSM at high risk of HIV switch regimen, maintain adherence, or discontinue PrEP use. It was surprising that employment status and average net income were associated with PrEP regimen choice, given that PrEP in Be-PrEP-ared was provided for free. Potential explanations are that participants choosing event-driven PrEP anticipated they would have to pay for the high costs of the medication after the study because PrEP was not yet reimbursed at the time of data collection. Alternatively, it may reflect socioeconomic disparities in health behavior.[34] This second explanation may be particularly plausible when taken into account that PrEP knowledge and acceptability have also been shown to differ along the traditional lines of health inequality.[35,36] Further studies are needed to better understand intraindividual and interindividual variation in PrEP use and how this may relate to different dynamics in sexual risk behaviors or potential disparities in PrEP use.

CONCLUSION

Event-driven PrEP was preferred by about 1 of 4 PrEP users at high risk of HIV infection in our study, which may better suit their prevention needs. Implementing and including both regimens in PrEP provision for MSM could lead to better tailored HIV prevention approaches.

ACKNOWLEDGMENTS

The authors thank all members of the community advisory board for their continuous support in the Be-PrEP-ared study. They thank Be-PrEP-ared participants for their participation.

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