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TITLE

Awareness of, willingness to take PrEP and its actual use among Belgian MSM at high risk of HIV infection: secondary analysis of the Belgian European MSM Internet Survey

ABSTRACT

We examined PrEP awareness, willingness to take it and early PrEP use among men who have sex with men (MSM) at increased risk of HIV acquisition in Belgium. This analysis of the Belgian EMIS data of 2017-2018 adopts a cascade approach, with the following steps quantified as conditional probabilities: being eligible for, aware of, and willing to take PrEP and PrEP use. One out of three MSM was eligible to use PrEP according to the operationalized Belgian reimbursement criteria. PrEP awareness was lower among socioeconomically vulnerable MSM, MSM living outside large cities, MSM who were less open about their sexuality and who did not identify as gay or homosexual. A lack of PrEP knowledge, a higher level self-efficacy regarding safe sex, having a steady partner and a higher risk of depression were related to unwillingness to use PrEP. Among those willing to take PrEP, less than one third were actually using PrEP. Not using PrEP was associated with living in small cities and experiencing financial problems.

Keywords (4-5): Pre-exposure prophylaxis (PrEP) use, Cascade approach, Men who have Sex with Men (MSM), eligibility criteria, awareness of and willingness to use PrEP

INTRODUCTION

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Oral Pre-Exposure Prophylaxis (PrEP) is the use of antiretrovirals as a HIV prevention method, recommended for HIV negative individuals at substantial risk of HIV infection (3). The World Health Organization recommends PrEP to be provided as part of a comprehensive approach including biomedical, behavioral, and structural interventions designed to meet the HIV prevention needs of specific people and communities (3). Although there is a decreasing trend in new HIV diagnoses among men who have sex with men (MSM) in the European Union (EU), sex between men remains the predominant mode of HIV transmission, accounting for about 39% of all diagnoses in 2019 (1). The uptake of PrEP as novel HIV prevention tool may be crucial to further reduce the number of HIV infections (4, 5). In Belgium, the yearly incidence of HIV diagnoses per 100,000 inhabitants is relatively high (8.1 in 2019) (2) when compared to the EU average (5.4 in 2019) (1). For PrEP to be effective in reducing the number of HIV infections at population level, uptake needs to be ensured among those who are at highest risk of HIV infection (6). Therefore, PrEP guidelines usually include eligibility criteria for PrEP initiation, based on factors that are known to be associated with an increased risk for HIV infection (7,8). These eligibility guidelines are country specific, based on the local context, HIV epidemiology, groups most at risk of HIV acquisition and strategic planning and program focus (8). In Belgium the guidelines for MSM includecondomless anal intercourse with at least two partners in the last 6 months, multiple Post Exposure Prophylaxis (PEP) treatments in the last 12 months and/or episodes of STIs last 12 months (9). PrEP has been made available in Belgium since June 2017 through 12 HIV reference centers (HRC). HRCs are specialized outpatient clinics providing multidisciplinary HIV and PrEP care. PrEP is partially reimbursed for individuals at increased risk for HIV infection, identified through the eligibility criteria (9,10). An online survey conducted from November 2016 to February 2017 demonstrated that the awareness of PrEP among HIV negative Belgian MSM was high (about 92%) and that about 70% of them were willing to take it (11). However, as this survey (11) took place just before the PrEP

reimbursement in Belgium it did not include information about actual PrEP use and we do not know how far this theoretical willingness is translated into a real use of PrEP. By December 2019, HRCs registered approximately about 4,000 PrEP users, 99% men and 98% MSM (2). But it remains unclear to what extent MSM at elevated risk of HIV acquisition are aware of, and willing to take PrEP, and actually taking it. Measuring these gaps and identifying associated factors will help to inform HIV prevention strategies and increase PrEP uptake among those most in need.

The first aim of this study was to examine PrEP awareness, willingness to use PrEP and actual PrEP use among Belgian MSM who are eligible for PrEP. We used a cascade approach, which is in line with similar research on PrEP uptake and lends itself particularly well to identify critical factors to be addressed in order to improve uptake (12-16). A secondary aim was to explore which sociodemographic, structural, cognitive and psychosocial factors are related to the drops in this cascade: 'being unaware of PrEP', 'being unwilling to use PrEP' and 'not using PrEP'. These insights will be particularly useful to tailor strategies for improving PrEP uptake among those at highest risk.

METHODS

44 Data

We conducted a secondary analysis of the European MSM Internet Survey (EMIS)(17). EMIS is a cross-sectional online survey conducted among gay, bisexual, and other MSM, across 50 European countries to understand their needs and to direct prevention programmes at a country level. The recruitment of respondents occurred through advertising on websites of supportive organizations, general-population social network services and MSM targeted geo-spatial 'dating' smartphone applications and websites. Data were collected between 01/11/2017 and 31/01/2018, which is shortly after roll-out and reimbursement of PrEP in Belgium (1/06/2017). The data included sociodemographic characteristics, morbidities, drug use, sexual risk behaviors and HIV-related prevention needs.

For this analysis we selected the Belgian EMIS data (18). Men were eligible to answer the questionnaire if: they were living in Belgium, they were at or over the age of homosexual consent (16 years old), they were identifying themselves as a man or trans man, and they were sexually attracted to men and/or having sex with men. The total number of respondents in Belgium was 2,746. All respondents provided consent to participate. Detailed study procedures are published elsewhere (17, 19). We excluded persons younger than 18 years (N=12) or HIV positive (N=338; 12.4%) from the sample, since they are not eligible to use PrEP according to Belgian criteria (8,9). This bring us to a sample size of 2,396 respondents.

Measures and definitions

62 Eligibility for PrEP use

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- We considered HIV negative MSM eligible to use PrEP if they were at high risk of HIV infection
- according the Belgian eligibility criteria (9) (Table I). We have operationalized seven eligibility criteria
- based on the available information in the EMIS survey (17)(see more detailed information in Appendix
- 66 A). A participant was considered eligible if at least one of these 7 criteria was met. Participants with
- 67 missing data on more than 3 criteria were defined as 'missing' (N=2).
- 68 [TABLE I]
- 69 Awareness
- 70 Participants were considered to be aware of PrEP if they answered 'yes' to the question 'Have you
- 71 heard about PrEP'
- 72 Willingness
- 73 A participant was considered willing to take PrEP when responding 'likely' or 'very likely' on a 5-
- 74 point Likert scale to the question 'If PrEP was available and affordable to you, how likely would you
- 75 be to use it?'.
- 76 Current PrEP use

Current PrEP use is based on the question 'Have you ever taken PrEP?' and operationalized as a dichotomous variable: (1) 'currently using PrEP on a daily basis or on demand' versus (2) 'never used PrEP or used PrEP on a daily basis or on demand but no longer taking it'. Formal channels for obtaining PrEP included a physical pharmacy, a general practitioner or other physician, a hospital, institute, clinic, community or drop in center, and participation in a study. PrEP pills from an online pharmacy, PEP or ART as PrEP, were considered informal circuits.

Potentially associated factors to PrEP awareness, willingness to take PrEP and PrEP use

Sociodemographic factors included: *age* (less than 30, 31 thru 50, above 51), *years of education* (since age 16: 0 to 4 years, 5 to 6 years, 7 years or more), *relation status* (single, steady partner, not sure/complicated), *sexual orientation* (identify themselves as gay or homosexual, bisexual, other), *migrant status* (no migration background, EU/EFTA migrant, non-EU/EFTA migrant) and *employment situation* (employed, unemployed, student, non-employed [retired or inactive due to disability/sickness]).

Structural barriers such as financial hardship and geographical distance to the PrEP facility may occur and potentially reduce the PrEP accessibility (and thus effective PrEP use). In the analysis we included *struggling with present income* (feelings about present income using a 5-point Likert scale from 'really struggling on present income' to 'living really comfortable on present income'), and *size of the city of residence* (large/medium city, small city/town, and village/countryside) as proxies for the financial and geographical barriers. HRCs in Belgium are geographically distributed across large or medium cities, which may limit the geographical accessibility for people living outside large or medium cities.

We hypothesized cognitive factors to be related to PrEP awareness, PrEP use and in particular willingness to use PrEP (11, 20). Hence, we included in the analysis *self-efficacy regarding safe sex*, and *prior knowledge on PrEP and HIV transmission*, similar to the French study about PrEP using the EMIS data (20). Self-efficacy regarding safe sex was assessed using a 5-point Likert scale from 'strongly disagree' to 'strongly agree' to the statement 'The sex I have, is always as safe as I want it to

be'. Prior PrEP and HIV transmission knowledge were based on previous knowledge of two statements: 'PrEP can be taken as a single daily pill if someone does not know in advance when they will have sex' and 'A person with HIV who is on effective treatment (called 'undetectable viral load') cannot pass their virus to someone else during sex'. The five answers categories were dichotomized: yes ('I knew this already') versus no ('I wasn't sure about this', 'I didn't already know this', 'I don't understand this', 'I do not believe this').

Level of outness, alcohol dependency and depression and anxiety are included as psychosocial factors, as they are known to be negatively related to PrEP use (21). Level of outness is a potential emotional barrier of PrEP use and was based on an item analyzed in previous publications (20, 22-24): 'Thinking about all the people who know you (including family, friends, and work or study colleagues), what proportion knows that you are attracted to men?' Possible options were: 'no one'; 'few'; 'less than half'; 'more than half'; 'all or almost all'. In line with previous research on outness (24), the variable was dichotomized as follows: those out to 'no one,' to 'few' the people they know (defined as 'in the closet' or 'having a low level of outness') versus those out to 'less than half,' 'more than half' or to 'all or almost all' of the people they know (defined as 'out' or 'having a medium to high level of outness'). The CAGE-4 screening measure was used to assess possible alcohol dependency. The CAGE-4 questionnaire for alcohol misuse has been previously validated for use in the general population (25). The relatively low Cronbach's alpha we found among MSM (0.6) is comparable to other studies (26, 27). Depressive and anxiety were measured by the validated Patient Health Questionnaire-4 (PHQ-4), which is a brief and accurate measurement of core symptoms/signs of depression and anxiety (28). The Cronbach alpha is 0.9.

Analyses

We use a cascade approach with the following steps (bars): among the *MSM eligible for PrEP* (Bar 1), we examined the proportions being *aware of PrEP* (Bar 2), *willing to use PrEP* (Bar 3) and actually *using PrEP* (Bar 4). In an unconditional approach, each step is quantified with a fixed denominator, i.e.

all MSM being eligible for PrEP in the sample. In the conditional approach, the denominator of each step is equal to the nominator of the previous step, implying for example that willingness to take PrEP only needs to be examined among those being aware of it, or that PrEP use only needs to be examined among those being willing to take it.

Thereafter, the drops in the cascade were quantified (conditionally) as outcome variables of the bivariate and multivariable logistic regression analyses: unaware vs. aware (among the eligible MSM, Sample 1); unwilling vs. willing (among the eligible and aware, Sample 2); and not using PrEP vs. using (among the eligible, aware and willing, Sample 3). We determined the relationships between the drops and potentially associated factors using bivariate statistics resulting in a contingency table (Table III) and bivariate logistic regressions (Table IV). Wald Chi-square tests were used to determine whether the associations between these variables were significant (with a p value < 0.05) and the strength of the associations were measured by unadjusted (or crude) odds ratio's (OR). Next, we performed multivariable logistic regression analyses to investigate which factors were independently associated with the drops in the cascade, including the factors that were significant in the bivariate analyses. Strengths of associations were measured using adjusted odds ratio's (AOR) (Table IV).

RESULTS

PrEP cascade: Awareness of and willingness to take PrEP and PrEP use

Figure 1 shows the PrEP cascade using a conditional and unconditional approach. The corresponding numbers of the PrEP cascade are presented in Table II. One out of three MSM (33.2%; 795/2,396) in this sample were *eligible for PrEP use* according the Belgian criteria (Bar 1). Around seventy percent of all MSM (70.7%; 1,659/2,346) were *aware of PrEP* (Bar 2). For PrEP eligible MSM, the proportion being aware of PrEP was somewhat higher: 82.1% (641/781). Nearly half of the MSM (43.3%; 1,037/2,396) indicated to be *willing to use PrEP* and among PrEP eligible MSM who were aware about its existence this was more than half (66.1%; 424/641) (Bar 3). About 22.5% of those willing to use PrEP were not eligible.

The proportion of MSM currently using PrEP was 6.9% (164/2,376) in the whole sample, 18.0% (142/791) among MSM eligibly to use PrEP and 30.7% (130/424) among PrEP eligible MSM who are aware of PrEP and willing to use it was actually using PrEP (Bar 4). The majority of them (90%; 117/130) were using PrEP via the formal circuit and 2.1% (6/130) informally. Twenty-two MSM were using PrEP while not eligible according the criteria, representing 0.9% (22/2,376) of all the MSM or 13.4% [22/164] of all PrEP users. Among eligible PrEP users 87.7% (114/130) had received a medical prescription for PrEP, the majority (81.5%) from a HIV reference centers or primary health care center (drop in).

164 [Figure 1]

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165 [Table II]

Factors associated with the drops in the PrEP cascade

- Table III shows the distribution of each factor for every sub-sample. The results of the logistic
- regression analyses with the 'drops in the cascade' as dichotomous outcomes are presented in Table IV.
- 169 [Table III]
- Eligible MSM who were 51 years or older were more *likely to be unaware of PrEP* as compared to
- those below 30 years old, even after controlling for other factors. Being unaware of PrEP was also
- significantly associated with lower education level, unemployment, living in a small city, low level of
- outness, self-identification as bisexual and no prior HIV knowledge on 'undetectable=untransmittable'.
- Among PrEP eligible MSM who were aware about PrEP, the unwillingness to use PrEP was higher
- among those with a migration background (in particular non-EU/EFTA migrants), those who did not
- identify themselves with homosexuals, who were unemployed, who scored higher on anxiety and
- depression scales, who lacked PrEP knowledge and who had higher scores on self-efficacy regarding
- safe sex, when compared with their respective counterparts. After adding the confounding factors, MSM
- with a steady partner were also more likely to be unwilling to use PrEP compared to single MSM.

Among those who were eligible, aware of, and willing to use PrEP, *not using PrEP* was related with struggling with financial resources, being a student, living in a small city/town, and lack of prior knowledge about PrEP and HIV transmission. In the multivariate analysis, struggling with income was no longer significantly related to not using PrEP.

[Table IV]

DISCUSSION

In this study we examined PrEP awareness, willingness to use PrEP and PrEP use among PrEP eligible MSM soon after the roll-out of PrEP implementation in Belgium. First, we found that 82.1% of the eligible MSM was aware of PrEP, 62.6% was willing to take it and 18% was actually using it Second, different sociodemographic, structural, cognitive and psychosocial factors were related to the drops in the cascade (unaware, unwilling and not using PrEP).

The proportion of Belgian MSM in our sample aware of PrEP is 70%, increasing to 82% among MSM eligible to use PrEP. This figure is comparable to other studies performed in Belgium and France around the same period (12, 20). Socioeconomic vulnerability was related to poor awareness of PrEP and PrEP awareness was lower among MSM from outside urbanized areas, among older MSM and MSM who are bisexual or less open about their sexuality. These findings are in line with previous research on PrEP awareness (13, 29-31) and require tailored interventions. Lack of PrEP awareness was shown to be an important barrier to PrEP use, especially among the most vulnerable groups who are also at high risk of HIV (32). There is a need for more inclusive awareness campains that can reach larger groups of MSM, in particular those who are less directly connected to the gay communities, also paying attention to groups with a lower socioeconomic status.

Forty-three % of MSM in our total sample were *willing to use PrEP*. This proportion is similar to the willingness to use PrEP in other studies conducted in high income countries (between 40% and 60%) (11, 20, 31, 33-35). Among MSM eligible for PrEP use, we found that more than one third was not (very) likely to use PrEP. Especially among these MSM at increased risk for HIV acquisition, such low levels of willingness to use PrEP are problematic from a public health point-of-view, as the benefits of PrEP cannot be fully exploited. Similar to other research (35), we observed that unwillingness to use PrEP is higher among MSM who did not identify themselves as gay or homosexual and among those with a migration background. This is possibly because the initial PrEP studies and campaigns in Europe were focusing on white homosexual men (36). Furthermore, perceived social stigma associated with same-sex attraction, HIV and PrEP use may present a strong barrier for PrEP uptake, especially among

MSM with a migration background (37). There is a need to further study potential uptake of PrEP and its barriers among migrant communities (36). We also found that a lack of PrEP knowledge, suffering from depression and anxiety, a belief that the sex they have is always as safe as they wanted and having a steady partner, were all related to unwillingness to use PrEP. From other studies (30, 35), we know that a lack of PrEP knowledge is one of the most frequently reported barriers of PrEP use. One of the other main reasons of this drop in the cascade indicated in previous research (13) is a poorer risk assessment of HIV. MSM with depressive symptoms may have a poorer risk assessment and engagement in self-care and preventive health (38, 39). This may contribute to their lower willingness to use PrEP, despite their higher risk of HIV infection.

The largest drop in the cascade was found between willingness to use PrEP and actual PrEP use, with less than one third of the MSM being aware and willing to use PrEP (30.7%) actually using PrEP. This was expected as the gap between people who are likely to use PrEP but not using it, was also highlighted in previous European (40) and American research (41). Interventions for the improvement of the level of awareness and willingness to use PrEP alone are thus not enough to improve PrEP uptake. It confirms that the theoretical willingness to use PrEP strongly differs from actual PrEP use (31). As a result, action has to be taken to improve this last step of the PrEP cascade, by motivating people to take concrete steps towards using it (e.g. making an appointment, getting a prescription, etc.), and overcoming the last barriers to facilitate the uptake of PrEP. In previous research (20, 30), poor knowledge about PrEP, PrEP stigma, the related costs, and the poor accessibility of medical facilities where PrEP can be prescribed and followed up, were reported as potential barriers of PrEP use. The latter barrier may explain our finding that MSM living in small cities use PrEP less than MSM living in larger cities, where HRC are located. Our findings also suggest that financial barriers restrain MSM from using PrEP. Indeed: MSM at increased risk of HIV acquisition and willing to use PrEP, but who struggled with their income were less likely to using PrEP in our study.

Limitations

The EMIS uses convenience sampling, so our data may not be representative for all MSM in Belgium. As frequently seen in MSM surveys using the internet, the EMIS dataset is likely to be biased towards more highly educated MSM and fewer older MSM, migrant MSM and those more distant from the gay community (20, 42, 43). Furthermore, recruitment strategies may have had a substantial impact on our findings (44). The use of sexual networking applications for recruiting participants may have led to a selection bias, i.e., participants with high levels of sexual activity, seeking sex partners on the internet, or with a particular interest in PrEP (7). However, whilst the findings are not generalizable to the wider MSM population, respondents do represent the target group of highly sexually active and therefore most at-risk men.

Using an existing database comes also with inherent limitations: we were unable to directly measure each criterion of the Belgian PrEP eligibility criteria (e.g., PEP use last 12 months). Lack of these data might have resulted in an underestimation or overestimation of the percentage of MSM eligible to use PrEP. In addition, no information was available about some frequent reported barriers of willingness and use of PrEP (28), such as attitudes towards PrEP, worries about PrEP stigma and side effects, a poor risk perception, and not having a doctor to prescribe it, or being ashamed to ask a medical professional about PrEP etc. Self-reported and retrospective data may also lead to underreporting of sensitive subjects (e.g., condomless sex or PrEP-use via informal channels) and be subject to recall bias.

Recommendations and conclusions

Based on our findings we can draw a number of relevant recommendations for clinical practice and public health policy. Our study highlights that although there is a high number of MSM who may benefit from PrEP use, only a small number was actual using PrEP in Belgium at the time of the study. However, we need to be aware of the timing of the EMIS, as the data is collected just after the roll out of PrEP in Belgium. More recent numbers of the HIV Reference centers have pointed to an increase in PrEP use among MSM (2). We expect a further increase in PrEP awareness and willingness to take PrEP, as observed in Australia (12) and the US (41) after making PrEP available in these countries. It should be noted that PrEP users themselves may be drivers of further uptake, by providing information

and disclosing positive experiences to like-minded friends or sexual partners (45). This may partially explain why PrEP mostly remains an MSM-specific HIV prevention tool in countries such as Belgium. While the data of this study pertain to the period 2017-2018, it remains unclear to what extent the associated factors have determined actual uptake in the period thereafter. Therefore, we suggest continuous and further research to assess whether MSM at high risk for HIV acquisition are better reached to improve the roll-out of PrEP.

Across all steps in the PrEP cascade large drops are detected and each drop was associated with different factors, which asks a diversification of policy answers and interventions on the different step in the cascade for different subgroups.

The findings show that more investments are required in improving the awareness of PrEP among high risk MSM. PrEP awareness campaigns need to be up-scaled and reaching all, also the different hard-to-reach groups among the MSM such as the socioeconomic vulnerable groups and MSM who do not identify themselves as homosexual or are less open about their sexuality. Promoting PrEP via primary care services may be a good alternative for improving PrEP awareness and willingness to take it. The long-term and holistic patient-doctor relationship provided by primary care services lends itself to the provision of personalized sexual health information and opportunities. It may help reframe PrEP as sexual health promotion tool, irrespective of gender, sexual orientation, relationship status or ethnicity (46). In addition, information on PrEP could be further and continuously distributed via social and community-based organizations, who are in close contact with the target group.

To increase willingness to use among high risk MSM who are aware of PrEP, it is important to invest in improving PrEP knowledge and MSM's self-perception of their risk of HIV. Effective interventions to help at-risk individuals better understand and act on their HIV risk are required especially among MSM with a non-EU/EFTA migration background, MSM who do not identify themselves as homosexual and those who are convinced that their PrEP and HIV transmission knowledge is sufficient and believe they have safe sex.

To ensure that MSM who are 'aware of PrEP' and 'willing to use PrEP' also actually use PrEP, further investments in the accessibility and availability (proximity) of PrEP are recommended. Although PrEP is reimbursed in Belgium, there is still a relatively high out-of-pocket payment, i.e. approximately 11.90 euros for 30 pills (47). Also indirect costs such as transport costs and the costs of follow-up consultations may add to expenses for PrEP. Especially for people who already struggle with their available resources or who live at a distance from the HIV reference center these may be barriers for using PrEP. Moreover, MSM at high risk with anxiety and depression related symptoms, should be proactively approached and motivated to use PrEP by for example health professionals and social workers, as they may less accurately perceive their need for PrEP, have a poorer PrEP adherence and are probably less concerned about HIV prevention. Future implementation research should explore how these services can be optimized to respond to key populations with unmet HIV prevention needs in different contextual settings (48).

Further research on PrEP, PrEP stigma and self-perceived HIV risk among MSM is needed in Belgium. Future studies should use a more representative sampling method such as a web-based respondent driven sampling technique, which combines 'snowball sampling' with a mathematical model that

weights the sample to compensate for the fact that the sample was collected in a non-random way (49).

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