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► To cite this version:

C Protiere, L Sagaon-teyssier, C Donadille, A Sow, G Gaubert, et al.. Perception of PrEP-related stigma in PrEP users: Results from the ANRS-PREVENIR cohort. *HIV Medicine*, 2023, 24, pp.938 - 945. 10.1111/hiv.13491 . inserm-04312192

HAL Id: inserm-04312192

<https://inserm.hal.science/inserm-04312192v1>

Submitted on 28 Nov 2023





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SHORT COMMUNICATION**Perception of PrEP-related stigma in PrEP users: Results from the ANRS-PREVENIR cohort**

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Funding information

ANRS | Emerging Infectious Diseases; Gilead; Sidaction

Abstract

Introduction: Since the advent of HIV pre-exposure prophylaxis (PrEP), stigma has been shown to be a major barrier to its uptake and adherence. It is therefore essential to define the proportion of users who consider that PrEP can negatively impact their image and the factors associated with this perception.

Method: We performed a multivariable logistic regression on data from the 2567 participants in the ANRS-PREVENIR study who answered the outcome question.

Results: Almost one-third of the sample (comprising mostly cisgender men who have sex with men [94.3%]) considered that taking PrEP could give others a negative image of them. Younger participants (adjusted odds ratio [aOR] 0.98; 95% confidence interval [CI] 0.97–0.99) and more psychologically vulnerable participants (i.e., lower self-esteem score [aOR 0.98; 95% CI 0.96–0.99] and higher depression score [aOR 1.02; 95% CI 1.00–1.03]) were also more likely to have this perception. In contrast, participants encouraged to take PrEP by their main partner (aOR 0.67; 95% CI 0.51–0.88) and friends (aOR 0.79; 95% CI 0.66–0.95), and those who protected themselves more because they had knowledge of their most recent sexual partner's HIV status (aOR 0.83; 95% CI 0.69–0.99) and systematic use of PrEP and/or condoms during intercourse in the previous 3 months (aOR 0.80; 95% CI 0.67–0.96) were less likely to have this perception.

Discussion: Given the strong interrelation between stigmatization (real or perceived), risky behaviours and adherence, our results emphasize the need for HIV prevention campaigns to promote a positive image of PrEP users. They also show that stigmatization and its effects need to be fully considered to

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improve HIV prevention offers to current and potential PrEP users who are most likely to be psychologically vulnerable.

KEYWORDS

MSM, PrEP, psychological vulnerability, representations, stigma

INTRODUCTION

Although pre-exposure prophylaxis (PrEP) is an effective strategy to reduce HIV transmission [1–4], the proportions of people taking it do not meet expectations in several geographical areas [5–8]. Some documented barriers to expanding PrEP roll-out (e.g., being unaware of PrEP, misinformation among potential users and healthcare providers about its effectiveness and side effects [5, 7, 9]) can be addressed by widespread distribution of more appropriate public information with the involvement of community-based organizations and by providing specific training to healthcare providers. Potential PrEP-related stigmatization is a major barrier that requires more focused, sex-positive, and in-depth educational interventions.

Since the advent of PrEP, the literature has highlighted the negative impact of stigmatization (real or perceived) on uptake and adherence [5, 6, 10–12]. PrEP users and community stakeholders face several forms of shaming and moral judgement that persist over time.

PrEP-related stigmatization is complex and multifaceted [6, 11]. Stigmatization can be perceived from both the general population and – intentionally or otherwise – PrEP users' relatives, partners, friends (including members of their community), and healthcare providers. The qualitative literature details several forms of stigma [5, 11, 13]: perceiving or experiencing rejection from potential or current sexual partners [10, 14], being perceived by others as irresponsible [15], and the perception in social and sexual circles of taking PrEP being equivalent to having anal sex without protection (e.g., barebacking), chemsex [10, 14, 16], or treatment for HIV [6, 11, 16]. PrEP is also considered indicative of existing general stigmatization of homosexuality by the social environment and by physicians [10]. PrEP shaming illustrates the persistence of homonegativity and internalized homophobia in gay communities [17]. All these issues impact PrEP uptake and adherence.

However, according to a recent review [16] the proportion of PrEP users who perceive that PrEP-related stigma exists remains unknown. The French ANRS-PREVENIR cohort provided us the opportunity to

evaluate the proportion of PrEP users who perceived that taking PrEP could give others a negative image of them and the factors associated with this perception. This information is crucial to not only improve educational interventions but also better identify PrEP users who need greater support and potential users who fear PrEP-related stigma, with a view to strengthening uptake.

MATERIALS AND METHODS

Survey population

ANRS-PREVENIR is an ongoing biomedical cohort initiated in 2017 in 26 sites in the Île-de-France region of mainland France [4]. It aims to reduce the number of new HIV infections by providing participants with the option to choose event-driven or daily PrEP, early antiretroviral therapy in case of seropositivity at inclusion or during follow-up, community-based support or therapeutic education, and quarterly HIV and sexually transmitted infection (STI) tests (<https://clinicaltrials.gov/ct2/show/NCT03113123>).

Participants are seronegative volunteers – men who have sex with men (MSM), heterosexual men and women, transgender people, and sex workers – at high risk of HIV infection (i.e., self-declared condomless anal sex with at least two partners during the 6 months before cohort enrolment). At enrolment, they receive an information letter and provide written consent. After enrolment, all participants receive quarterly online questionnaires.

Dependent variable

In a dedicated section of the first online self-questionnaire administered at enrolment, participants were asked whether they considered that taking PrEP could give others a negative image of them (possible answers were 'totally disagree', 'mostly disagree', 'mostly agree', and 'totally agree'). Answers were dichotomised as follows to build the dependent variable:

totally disagree and mostly disagree = 0 versus 'mostly agree' and 'totally agree' = 1.

Independent variables

The following characteristics were used as independent variables.

- Socioeconomic characteristics: gender, age, education level, living conditions, employment, and self-perceived financial situation.
- Psychosocial and behavioural characteristics: depression as measured with the Center for Epidemiologic Studies Depression (CES-D) scale (range 0–60), self-esteem as measured with the Rosenberg scale (range 10–40), psychological health history (treatment, hospitalization, follow-up with a professional), self-perception of social support (feeling surrounded or lonely, having moral/emotional support), having a main partner, number of casual partners, drug and alcohol use during sex, systematic prevention during sexual intercourse (PrEP and/or condoms), knowledge of most recent partner's HIV status, level of pleasure (range 1–4) and of excitation (range 1–4) during the most recent sexual intercourse, satisfaction with sexual life, and sexual orientation.
- Clinical characteristics (STI at enrolment).
- PrEP-related characteristics: PrEP user at enrolment, event-driven/daily PrEP use, people who encouraged PrEP initiation (main partner, casual partner(s), friends, family, community actors, physicians).

Statistical analysis

Univariate logistic regressions were performed using all potential covariates as described in Table 1. Variables significant at the 20% level were considered eligible for multivariable logistic regression models. The final parsimonious model was obtained using a backward elimination procedure (using R version 4.1).

Because of the well-known interrelation between depression and self-esteem [18], a correlation would be expected between the CES-D and the Rosenberg scales. We therefore tested four models as follows: one excluding the CES-D and the Rosenberg scales, one including only the CES-D scale, one including only the Rosenberg scale, and one including both scales. The best fit model was chosen using the Akaike information criterion.

RESULTS

Among the 3067 participants included in the ANRS-PREVENIR cohort between May 2017 and May 2019, a total of 2631 (85.8%) completed the enrolment questionnaire. Of these, 2567 (97.6%) answered the outcome question (study sample).

The vast majority of the study sample were men (99.5%), almost three-quarters (73.0%) had at least a 3-year university degree, and 70.6% perceived their financial situation as comfortable. Almost all (93.7%) declared that they were homosexual (including three transgender women), 5.3% bisexual (including one transgender man), and 0.9% heterosexual (including one transgender man). Over half (56.4%) were PrEP users before enrolment (Table 1).

Almost one-third (32.6%) considered that taking PrEP could give others a negative image of them. Compared with respondents who did not have this perception, these respondents were younger (mean $35.6 \pm$ standard deviation 9.1 vs. 37.4 ± 9.9 ; $p < 0.001$), had a higher depression score (16.9 ± 10.3 vs. 14.2 ± 9.5 ; $p < 0.001$), and had a lower self-esteem score (30.8 ± 5.2 vs. 32.2 ± 5.3 ; $p < 0.001$). In addition, more of these respondents had low self-esteem, defined as a score < 25 (12.8% vs. 8.5%, $p < 0.001$). They were also more likely to be living alone (61.5% vs. 56.8%, $p = 0.026$) and to feel lonely (41.6% vs. 32.8%, $p < 0.001$). In addition, they reported lower levels of excitation (3.8 ± 0.9 vs. 3.9 ± 0.9 , $p = 0.019$) and pleasure (3.7 ± 1.0 vs. 3.8 ± 1.0 , $p = 0.001$) during their most recent sexual intercourse, and were less likely to be satisfied with their sexual life (69.6% vs. 75.5%, $p = 0.002$). Finally, they were less often encouraged to use PrEP by their main partner (12.2% vs. 18.7%, $p < 0.001$) or by friends (44.7% vs. 50.7%, $p = 0.005$), and were less likely to have systematically used protection during sexual intercourse in the previous 3 months (45.5% vs. 51.6%, $p = 0.004$) and to be aware of their most recent sexual partner's HIV status (50.2% vs. 55.2%, $p = 0.020$).

Results from the multivariable model (Table 2) showed that the younger the participant, the lower their self-esteem, and the higher the depression score, the more likely they were to consider that taking PrEP could give others a negative image. Respondents whose main partner and/or friends encouraged them to start PrEP, those who declared systematically using protection in the previous 3 months (PrEP and/or condoms), and those aware of their most recent sexual partner's HIV status were less likely to consider that taking PrEP could give others a negative image of them.

TABLE 1 Sample description according to the perception that PrEP can give others a bad image of them and logistic univariable regression (n = 2567).

| Characteristics | Perceived that PrEP gives a bad image | | | OR | 95% CI | p-value |
|--|---------------------------------------|----------------------|-----------------------------------|------|-----------|---------|
| | No (n = 1731) | Yes (n = 836) | Total (n = 2567) | | | |
| Age | 37.40 ± 9.89 | 35.60 ± 9.14 | 36.82 ± 9.69 ^a | 0.98 | 0.97–0.99 | <0.001 |
| Median age | 36.00 (30.00; 44.00) | 35.00 (28.00; 42.00) | 36.00 (29.00; 43.00) ^a | | | <0.001 |
| Educational level | | | | | | |
| Upper secondary school diploma or lower | 253 (14.62) | 106 (12.68) | 359 (13.99) ^a | Ref. | | |
| Two-year third-level diploma | 233 (13.46) | 101 (12.08) | 334 (13.01) | 1.03 | 0.75–1.43 | 0.838 |
| Three/four-year university degree | 394 (22.76) | 197 (23.56) | 591 (23.02) | 1.19 | 0.90–1.59 | 0.222 |
| Master's university degree or higher | 851 (49.16) | 432 (51.67) | 1283 (49.98) | 1.21 | 0.94–1.57 | 0.139 |
| Employed | 1504 (86.89) | 701 (83.85) | 2205 (85.90) ^a | 0.78 | 0.62–0.99 | 0.039 |
| Living alone | 984 (56.85) | 514 (61.48) | 1498 (58.36) ^a | 1.21 | 1.02–1.44 | 0.026 |
| Self-perceived comfortable financial situation | 1234 (71.29) | 576 (68.90) | 1810 (70.51) ^a | 0.89 | 0.75–1.07 | 0.214 |
| CES-D depression scale | 14.15 ± 9.48 | 16.88 ± 10.31 | 15.04 ± 9.84 ^b | 1.03 | 1.02–1.04 | <0.001 |
| Median (IQR) | 12.00 (7.00; 19.00) | 15.00 (9.00; 22.00) | 13.00 (8.00; 20.00) | | | <0.001 |
| Rosenberg self-esteem scale | 32.23 ± 5.33 | 30.84 ± 5.23 | 31.78 ± 5.34 ^c | 0.95 | 0.94–0.97 | <0.001 |
| Median (IQR) | 33.00 (29.00; 36.50) | 31.00 (27.00; 35.00) | 32.00 (28.00; 36.00) | | | <0.001 |
| Psychological follow-up with a professional | 767 (45.52) | 383 (47.11) | 1150 (46.04) ^d | 1.07 | 0.90–1.26 | 0.455 |
| Treatment for psychological disorder | 457 (27.12) | 236 (29.03) | 693 (27.74) ^d | 1.10 | 0.91–1.32 | 0.319 |
| Hospitalization for psychological disorder | 92 (5.46) | 42 (5.17) | 134 (5.36) ^d | 0.94 | 0.64–1.36 | 0.760 |
| Feeling lonely/not surrounded | 554 (32.82) | 338 (41.57) | 892 (35.67) ^a | 1.46 | 1.23–1.73 | <0.001 |
| Having moral/emotional support | 1587 (94.02) | 751 (92.37) | 2338 (93.48) ^b | 0.77 | 0.56–1.07 | 0.120 |
| Having a main partner | 658 (43.12) | 302 (40.59) | 960 (42.29) ^e | 0.90 | 0.75–1.08 | 0.253 |
| Number of casual partners | 16.53 ± 22.77 | 15.6 ± 21.49 | 16.2 ± 22.36 ^f | 1.00 | 0.99–1.00 | 0.361 |
| Knowledge of most recent sexual partner's HIV status | 897 (55.23) | 398 (50.19) | 1295 (53.58) ⁱ | 0.82 | 0.69–0.97 | 0.020 |
| Sexual intercourse systematically protected during the previous 3 months | 868 (51.61) | 369 (45.50) | 1237 (49.62) ^j | 0.78 | 0.66–0.93 | 0.004 |
| Drug use during most recent intercourse | 253 (14.62) | 111 (13.28) | 364 (14.18) ^a | 0.89 | 0.70–1.13 | 0.363 |

(Continues)

TABLE 1 (Continued)

| Characteristics | Perceived that PrEP gives a bad image | | | OR | 95% CI | p-value |
|--|---------------------------------------|---------------|---------------------------|------|-----------|---------|
| | No (n = 1731) | Yes (n = 836) | Total (n = 2567) | | | |
| Cannabis use during most recent intercourse | 127 (7.49) | 69 (8.42) | 196 (7.80) ^g | 1.14 | 0.83–1.54 | 0.414 |
| Alcohol use during most recent intercourse | 356 (21.00) | 170 (20.76) | 526 (20.92) ^g | 0.99 | 0.80–1.21 | 0.887 |
| Level of pleasure during most recent intercourse | 3.82 ± 0.98 | 3.68 ± 1.02 | 3.78 ± 1.00 ^g | 0.87 | 0.80–0.95 | 0.001 |
| Level of excitation during most recent intercourse | 3.93 ± 0.92 | 3.84 ± 0.90 | 3.90 ± 0.91 ^g | 0.90 | 0.82–0.98 | 0.019 |
| Satisfying sex life | 1278 (75.49) | 568 (69.61) | 1846 (73.58) ^h | 0.74 | 0.62–0.90 | 0.002 |
| At least one STI at enrolment | 419 (24.21) | 228 (27.27) | 647 (25.20) ^a | 1.17 | 0.97–1.42 | 0.094 |
| Being PrEP user before enrolment | 964 (55.72) | 482 (57.66) | 1446 (56.35) ^k | 1.08 | 0.92–1.28 | 0.355 |
| Daily PrEP regimen use | 865 (50.09) | 397 (47.54) | 1262 (49.26) ^l | 0.90 | 0.77–1.07 | 0.228 |
| Encouraged to take PrEP by the main partner | 306 (18.70) | 99 (12.21) | 405 (16.55) ^m | 0.60 | 0.47–0.77 | <0.001 |
| Encouraged to take PrEP by a casual partner | 674 (40.95) | 326 (40.20) | 1000 (40.70) ⁿ | 0.97 | 0.82–1.15 | 0.722 |
| Encouraged to take PrEP by friends | 842 (50.72) | 364 (44.66) | 1206 (48.73) ^o | 0.78 | 0.66–0.93 | 0.005 |
| Encouraged to take PrEP by family | 26 (1.59) | 12 (1.48) | 38 (1.55) ^p | 0.93 | 0.45–1.81 | 0.835 |
| Encouraged to take PrEP by a community actor | 436 (26.85) | 213 (26.39) | 649 (26.85) ^q | 0.98 | 0.81–1.18 | 0.812 |
| Encouraged to take PrEP by a physician | 687 (41.74) | 352 (43.40) | 1039 (42.29) ⁿ | 1.07 | 0.90–1.27 | 0.432 |

Note: Missing values: a = 0, b = 66, c = 67, d = 69, e = 297, f = 109, g = 53, h = 150, j = 74, k = 1, l = 5, m = 120, n = 110, o = 92, p = 121, q = 136.

Data are presented as n (%), mean ± standard deviation or median (interquartile range).

Abbreviations: CES-D = Center for Epidemiologic Studies Depression scale; CI = confidence interval; OR = odds ratio; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infection.

TABLE 2 Factors associated with PrEP users' perception that taking PrEP can give others a negative image of them – results from the multivariable logistic regression (n = 2248).

| Characteristic | aOR | 95% confidence interval | | p-value |
|--|------|-------------------------|------|---------|
| Age | 0.98 | 0.97 | 0.99 | 0.002 |
| Encouraged to take PrEP by main partner | 0.67 | 0.51 | 0.88 | 0.004 |
| Encouraged to take PrEP by friends | 0.79 | 0.66 | 0.95 | 0.011 |
| Knowing most recent sexual partner's HIV status | 0.83 | 0.69 | 0.99 | 0.042 |
| Sexual intercourse systematically protected during the previous 3 months | 0.80 | 0.67 | 0.96 | 0.016 |
| Center for Epidemiologic Studies Depression scale | 1.02 | 1.004 | 1.03 | 0.009 |
| Rosenberg self-esteem scale | 0.98 | 0.96 | 0.99 | 0.045 |
| Akaike information criterion | 2791 | | | |

Abbreviations: aOR = adjusted odds ratio; PrEP = pre-exposure prophylaxis.

DISCUSSION

PrEP effectiveness directly depends on adherence. Consequently, non-optimal adherence represents a major challenge to successful PrEP global implementation [19]. The willingness of people at risk of HIV to initiate and adhere to PrEP depends on internal (e.g., individual representations of PrEP, homonegativity) and external (e.g., stigmatization, PrEP shaming) psychosocial factors. Our study brings new insights to the stigmatization debate. First, it provides a measure of the proportion of respondents in the ANRS-PREVENIR who considered that taking PrEP can give others a negative image of them. In our sample, which included PrEP users and non-users at enrolment, almost one-third of participants had this perception. This result is important given that a large proportion of our sample were highly educated people with a comfortable financial situation.

Second, it identifies the factors associated with this perception. In our survey, only psycho-socio-behavioural factors were associated with the perception that taking PrEP gives a negative image. Neither having at least one STI before enrolment nor PrEP uptake status (i.e., naive or not) at enrolment was associated with this perception.

Younger participants, those with low self-esteem, and those with a high depression score were more likely to perceive that taking PrEP could give others a negative image of them. As some respondents were PrEP-naive at the time of the survey, this result suggests that this perception may, at least in part, be related to pre-existing psychological vulnerabilities. Of course, we cannot exclude the possibility that psychological vulnerability may increase the perception of stigma. Irrespective of the direction of causality, given that psychological vulnerability has been associated with low PrEP adherence [20],

particular attention should be given to young and psychologically vulnerable PrEP users to increase their uptake and reduce the likelihood of discontinuation.

Respondents whose main partner and/or friends had encouraged them to take PrEP were less likely to perceive that PrEP could give others a bad image of them. This highlights the strong impact of a person's immediate social and normative environment. Therefore, the positive aspects of PrEP [10], such as increased pleasure during intercourse [21], perceived self-control, and assuming responsibility for protecting oneself and others [5, 6, 11], must be regularly emphasized in communications addressed to healthcare providers, the general population, and (potential) PrEP users. This is especially true given that strategies that mainly focus on highlighting sexual risks have proven to be counterproductive [15].

Finally, respondents with more efficient preventive behaviours (i.e., systematic protection using PrEP and/or condoms, knowledge of their most recent sexual partner's HIV status) were also less likely to perceive that PrEP gave others a negative image of them. One possible reason is that they had enough confidence in their own HIV prevention strategy that they were indifferent to others' perceptions. As previously mentioned, because of the cross-sectional aspect of the analysis, we cannot be certain of the sequence effect: does better protection lead to less perceived stigma or is the opposite true? Whatever the answer, this result reinforces the need to make PrEP uptake and actions in the fight against stigmatization commonplace. This finding is also in line with the results of a qualitative survey showing that some PrEP users reconsidered their negative perception of people living with HIV after they started taking PrEP [10]. The French National AIDS Council recommends that PrEP be routinely proposed to all interested people, irrespective of their level of risk of HIV acquisition. This action might

have the complementary benefit of decreasing the risk of PrEP stigma.

Some study limitations related to the specificity of our sample must be acknowledged. First, we chose the geographical area with the highest prevalence of HIV diagnosis in France. However, people living in this area are more likely to belong to high socio-professional categories, as was the case with the majority of our sample. This selection bias may have led to an underestimation of the proportion of respondents who perceived that PrEP use gave others a bad image of them. Moreover, the fact that our analysis was conducted on a sample of respondents favourable to PrEP (otherwise, they would not have joined the ANRS-PREVENIR cohort) would also suggest this proportion was underestimated. Finally, because the majority of the sample were highly educated cisgender MSM, studies including transgender people, cisgender women, migrants, and people with a lower socioeconomic status are needed. Moreover, qualitative studies may help to disentangle the sequence effect between stigma (real or perceived), psychological vulnerabilities, and prevention behaviours.

In conclusion, our results emphasize the need – at the public health level – for HIV prevention campaigns to promote a positive image of PrEP users, and – at the individual level – the need to propose psychological support to younger and more vulnerable (potential) PrEP users. They also show the importance of studying users' perceptions that PrEP can give others a negative image of them, a phenomenon related to both normative and relational contexts and to individual internal factors. Further studies are needed to explore the evolution over time of this perception of PrEP-related stigma.

AUTHOR CONTRIBUTIONS

CP, LST, GGa, and BS implemented this work. CD led the analysis under the supervision of LST and CP. The manuscript was written collaboratively between CP and GGi with input from DRC, BS, DM, JG, DC and JMM. MM, LA, LB provided ongoing support to design and data collection. AS performed the data management. All authors have critically read and approved the final manuscript.

ACKNOWLEDGEMENTS

The authors thank all the study participants for dedicating their time to this research, as well as the site investigators, the cohort's scientific committee, the community advisory board, and the ANRS | MIE staff. Finally, our thanks to Jude Sweeney for editing the manuscript.

FUNDING INFORMATION

This work was supported by ANRS | MIE, Sidaction, and Gilead.

CONFLICT OF INTEREST STATEMENT

DC reports personal fees from Gilead (2020) and Pfizer (2022) for lectures outside the submitted work. JG reports receiving supports as an advisor for Gilead Sciences, Merck, Janssen, Roche, AstraZeneca, Theratechnologies, and ViiV, and grants from Gilead Sciences and ViiV. JMM reports receiving support as an advisor for Gilead Sciences, Merck, Janssen, and ViiV, and research grants from Gilead Sciences. All others authors declared no conflict of interest.

DATA AVAILABILITY STATEMENT

French law requires that everyone who wishes to access cohort data or clinical study data on humans must ask the French data protection authority (the CNIL) for permission by completing a form that can be provided by Lambert Assoumou (lambert.assoumou@iplesp.upmc.fr). For further information, please see <https://www.cnil.fr/>.

ETHICS STATEMENT

The survey received ethical approval from the Committee for the Protection of Persons (CPP Ile de France IV – 2016-AO1577) and from the National Commission on Informatics and Liberty (CNIL – DR-2017-118). The study is registered with ClinicalTrials.gov, NCT03113123, and EudraCT, 2016A0157744.

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How to cite this article: Protiere C, Sagaon-Teyssier L, Donadille C, et al. Perception of PrEP-related stigma in PrEP users: Results from the ANRS-PREVENIR cohort. *HIV Med*. 2023; 24(8):938-945. doi:10.1111/hiv.13491