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What are the situational and behavioral factors associated with condomless anal sex without PrEP in men who have sex with men? Results from the ANRS-IPERGAY trial

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Abstract

Objective: This study aimed to identify situational and behavioral factors associated with condomless anal sex without on-demand PrEP in the open-label extension (OLE) study of the ANRS-IPERGAY trial.

Methods: Univariable and multivariable modified Poisson regressions with a generalized estimating equation (GEE) were used. The attributable risk percentage for each explanatory variable and for condomless anal sex without PrEP was calculated.

Results: In the OLE, 19% of anal intercourses were unprotected (i.e., no PrEP or condom). Of these, 85% were attributable to sexual intercourse with main partners and 47% with HIV-negative partners. The following factors were positively associated with condomless anal sex without PrEP: a depressive episode in the previous 12 months (aR [95% CI], p-value: 1.49 [1.02;2.17], 0.039), a higher number of sexual intercourses during the previous 4 weeks (1.01 [1.002;1.02], 0.014), and sexual intercourses under the influence of alcohol (1.45 [1.10;1.92], 0.008). By contrast, condomless anal sex without PrEP was less frequent during sexual intercourses with known casual, unknown casual and multiple partners (0.20 [0.14;0.30], <0.001; 0.10 [0.05;0.20], <0.001; 0.11 [0.05;0.29], <0.001, respectively), as well as with HIV+ partners with an undetectable viral load (VL) and HIV+ partners with a detectable/unknown VL or unknown serology status (0.57 [0.38;0.86], 0.007; 0.52 [0.32;0.87], 0.012, respectively).

Conclusions: Choosing to have condomless anal sex without PrEP depends primarily on the sexual partner's characteristics (level of intimacy, serological status). This reflects a form of rationality in HIV risk management. However, our results raise questions about the true efficacy of managing HIV risk using this approach.

Key words: on-demand PrEP; condom; MSM; ANRS-IPERGAY; unprotected anal intercourse

Introduction

In the context of diversified prevention, pre-exposure prophylaxis (PrEP) and condoms constitute the main HIV prevention tools for men who have sex with men (MSM) (1). Several barriers exist to MSM using them. However these barriers have mostly been studied separately.

The main reported barriers to condom use in MSM are the loss of pleasure (2–4) and the lack of intimacy with the partner (5–7).

With regard to PrEP, studies investigating its efficacy have been implemented in the context of the underuse of condoms and the associated lack of any noticeable decline in the HIV epidemic in specific population such as MSM. Identified barriers to PrEP initiation include cost (8–11), distrust in the medical system (8) and stigma (8,9,12). These factors might explain the gap between the number of people targeted for PrEP and the number that actually initiate it. Barriers identified with poor PrEP adherence are a low perceived HIV risk (13) and logistical factors such as stock-outs, losing pills, missing doses due to travel, forgetting to take the pill, and disruption to daily schedules (14,15). With regard to clinical trials, these barriers may also contribute to explain the 28% and 26% of MSM participants who did not take on-demand PrEP (or placebo) during the double-blind and open-label extension phases (16) of the ANRS-IPERGAY trial(17). Moreover, the iPrEx study also showed that the mean percentage of daily PrEP use detected by clinical indicators was 53% at week 24 for MSM participants enrolled in the active arm (18).

Literature provides explanations for the lack of condom use and PrEP adherence separately. A previous study within the ANRS-IPERGAY trial highlighted that 13% of the MSM enrolled were infrequent (“low-level”) users of PrEP and of condoms during the whole trial (19). That study highlighted that low-level users were more often young, unemployed and perceived a

lower HIV risk than participants who frequently used PrEP. However, it did not provide specific information on unprotected (i.e. no PrEP or condom) anal intercourse, which constitutes the greatest HIV infection risk. The specific context of on-demand PrEP need to be investigated because, unlike daily PrEP, it depends much more on perceived risk in a given sexual situation. With on-demand PrEP therefore, people must make an individual choice before having sexual intercourse. In this context, the factors associated with the lack of on-demand PrEP use may be different from those for daily PrEP.

Given this context, the present study aimed to identify the situational and behavioral factors associated with condomless anal sex without PrEP in the OLE study of the ANRS-IPERGAY trial.

Methods

Study population

ANRS-IPERGAY was a double-blind randomized combined prevention trial, conducted in France and Canada (2012-2016), to evaluate the efficacy and safety of on-demand PrEP in high-risk men who have sex with men (MSM). The main inclusion criteria were as follows: HIV negative man or transgender woman having sex with men, aged 18 years or older, and reporting condomless anal sex with at least two different partners in the previous 6 months. The following dosage schedule was prescribed: 2 pills between 2 and 24 hours preceding a sexual intercourse, followed by 1 pill 24 hours and another pill 48 hours after the first drug intake. A comprehensive description of the trial's methodology and results can be found elsewhere (16). In November 2014, following the discontinuation of the double-blind placebo-controlled randomized phase, all

those still being followed were invited to remain and participate in the OLE study. This consisted in continued access to PrEP until its expected approval in France, which was set to occur before June 30, 2016 (in reality, full approval came in January 2016). MSM who had not participated in the double-blind phase but who met eligibility criteria of the latter could also be included in the OLE. All participants in the OLE study provided oral informed consent, 98% of them also providing written informed consent (17). Only the latter were retained for the present analysis.

Questionnaires

Throughout the whole study (i.e., double-blind and OLE phases), a two-yearly questionnaire collected sociodemographic and socioeconomic characteristics of participants, while their psychosocial characteristics as well as data on active involvement in community-based activities on prevention in the previous 12 months were collected annually.

Participants also filled in an anonymous online questionnaire every 2 months, in which a section on "sexuality" recorded information on their sexual behaviors in the previous 2 months and particularly their practices during their most recent sexual intercourse.

Variables

Outcome: No PrEP or condom use during most recent anal intercourse.

A dichotomous outcome of self-reported "condomless sex without PrEP" was constructed according to participants' responses regarding PrEP and condom use during their most recent anal intercourse with the following categories: 0 when participants had used condoms during

anal sex OR when they used PrEP correctly (defined as taking at least one pill within 24 hours before sex and one pill taken within 24 hours after sex), or in a suboptimal fashion (any other pill intake within 48 hours before or 48 hours after the sexual intercourse); and 1 when participants reported condomless anal sex AND did not take any PrEP pill (defined as no pill within 48 hours before or 48 hours after the sexual intercourse).

The decision to categorize suboptimal PrEP use as “0” was based on the fact that we were studying only anal intercourses which were not protected in any way by PrEP, and accordingly suboptimal use could be considered as using PrEP.

Explanatory variables

Sociodemographic, socioeconomic, and psychosocial characteristics of participants, as well as their active involvement in community-based activities on prevention and sexual behaviors, were the variables used to test for an association with condomless sex without PrEP during the most recent anal intercourse. Sociodemographic and socioeconomic characteristics may influence health behaviors (20). Literature also shows a high prevalence of depressive episodes among MSM (21,22). Depressive episodes have been associated with poor adherence to HIV treatment (20,22,23). Therefore, we investigated whether there was an association between sociodemographic, socioeconomic and psychosocial characteristics and condomless sex without PrEP. We also tested for any association between participation in community-based prevention activities and our main outcome, as this could have promoted HIV-transmission prevention behaviors. Finally, we tested for the influence of sexual behaviors on condomless sex without

PrEP in order to evaluate whether prevention strategies differed according to the type of sexual behavior.

Sociodemographic and socioeconomic characteristics included age at enrolment, educational level higher than high-school (yes; no), active employment (yes; no), main partner (yes/no) and comfortable housing (yes; no). Psychosocial characteristics included anxiolytic and antidepressant use in the previous 12 months (yes; no), lifetime experience of depression (no; yes, during the previous 12 months; yes, before (i.e., more than 12 months previously)), and two scales, one for brief sensation seeking (BSSS-4, range: [4;20], a higher score indicating higher levels of sensation seeking) and the other for risk taking (SS2, range: [2;10], a higher score indicating higher levels of risk taking). Both scales were constructed according to Stephenson et al. (24). Participants' sexual behaviors (i.e., number of sexual intercours during the previous 4 weeks, number of sexual partners in the previous 2 months and sexually transmitted infections (detected and/or being treated during the previous 2 months)) were also considered as potential correlates of condomless sex without PrEP, as were sexual behaviors related to their most recent sexual intercourse.

With respect to the most recent sexual intercourse the following three principal variables were included: i) a variable combining the partner's serological status and viral load (VL) using three categories (HIV-; HIV+ with undetectable VL; unknown serology or HIV+ with detectable or unknown VL), ii) the type of intercourse (insertive anal sex and/or oral sex; receptive anal sex and/or insertive anal sex and/or oral sex) and iii) the type of partner(s) (main; casual known; casual unknown; multiple). Other variables also investigated for the most recent sexual intercourse included alcohol consumption (yes/no) and recreational drug use (involving ecstasy,

cocaine, GHB/GBL and ketamine) during sex (yes; no), place of the sexual intercourse (public; private) and perception of risk of HIV infection (on a 10-point scale).

Statistical analyses

To estimate the relationship between the outcome (i.e., condomless anal sex without PrEP) and its potential correlates, univariable and multivariable modified Poisson regressions with a generalized estimating equation (GEE) approach were computed. GEE is a robust methodology that takes into account the intra-individual correlation of observations over time (in the present study, the self-reported absence of PrEP or of condom use during anal sex during a follow-up visits), and therefore leads to increased accuracy of estimates and variances of parameters in regression analyses (25). A modified Poisson regression approach enables robust relative risks to be estimated (26). Variables with a p-value ≤ 0.25 in the univariable analyses were considered eligible for the multivariable model.

The significance threshold was fixed at 25% to prevent the omission of important predictors given the multiple confounding effects present in the data (27,28). We calculated the main attributable risk percentages for our explanatory variables and for condomless anal sex without on-demand PrEP. Attributable risk is a measure of the proportion of the outcome that can be attributed to a certain risk factor, i.e., the extent to which the incidence of the outcome would be reduced if the risk factor did not exist (29,30). We calculated attributable risk percentages after adjustment for all other correlates by using relative risks from the multivariable GEE model as follows: attributable risk = (relative risk - 1) / relative risk (30).

We computed the variance inflation factor (VIF) to test for multicollinearity in equivalent linear models and interpreted VIF values <5 as presenting no multicollinearity issues (31).

All analyses were based on two-sided p-values, with $p \leq 0.05$ indicating statistical significance. They were conducted using SAS 9.4 software (SAS Institute, Cary, NC).

Results

The present study included all participants in the ANRS-IPERGAY OLE study (M0 to M18) with available data on their use of PrEP and condoms during their most recent anal intercourse (n=319, 1,253 visits).

Description of the study sample

Mean age of the 319 participants was 37 years (sd: ± 10), 76% had a high-school diploma and 84% reported being employed; 94% judged their housing to be comfortable (see Table 1). At baseline, 43% reported a main partner. With regard to their psychological profile, 27% and 16%, respectively, had taken anxiolytics or antidepressants during the previous twelve months, while 56% reported lifetime experience of depression, whether during the previous twelve months (23%) or before (33%). Among the 1253 most recent anal intercourses reported over follow-up in the OLE study, 237 (19%) were condomless and without PrEP.

Factors associated with condomless sex without PrEP during the most recent anal intercourse

Results from the univariable analyses

In the univariable analyses (see Table 2), condomless anal sex without PrEP was more frequent ($p \leq 0.25$) among younger participants, the unemployed, those who reported having a depressive episode before the previous 12 months, those with higher risk-taking scores in the SS2 scale and those having a main partner. With regard to sexual practices, participants with higher numbers of sexual partners during the previous two months were less likely to report condomless anal sex without PrEP, while those reporting a higher number of sexual intercourses during the previous 4 weeks were more likely to do so. With respect to sexual practices during the most recent anal intercourse, condomless sex without PrEP was less frequently reported for the following categories: casual known or unknown partners, multiple partners, HIV+ partners with undetectable VL and partners with unknown serology or HIV+ partners with detectable or unknown VL. This was also true when the most recent anal sexual intercourse happened in a public place, under the influence of drugs, or when participants perceived a higher risk of HIV infection. By contrast, condomless anal sex without PrEP was more frequently reported when the sexual intercourse happened under the influence of alcohol.

Results from the multivariable analysis

Variables from univariable analyses with a p-value ≤ 0.25 were included in the multivariable analysis. The GEE estimates (Table 2) confirmed the impact of mental health in uptake of prevention strategies. Estimates indicated that participants who experienced a depressive episode during the previous 12 months (adjusted risk-ratio [95% confidence interval] (aRR [95% CI]), p-

value: 1.49 [1.02;2.17], 0.039), were more likely to report condomless sex without PrEP during their most recent anal intercourse. However, the results from the univariable analysis indicated a significant relationship between the study outcome and experiencing depression *before* the previous 12 months. This difference between the two models, in terms of the association between depression and the outcome, was due to the stepwise introduction of the following two explanatory variables into the multivariable model: partner's serological status and viral load and main partner.

GEE estimates confirmed that participants reporting a higher number of sexual intercourses during the previous 4 weeks (1.01 [1.002;1.02], 0.014) and those whose most recent sexual intercourse occurred under the influence of alcohol (1.45 [1.10;1.92], 0.008) were also more likely to report condomless sex without PrEP during their most recent anal intercourse. In contrast, condomless anal sex without PrEP was less frequent with casual or multiple partners (known casual, 0.20 [0.14;0.30], <0.001; unknown casual, 0.10 [0.05;0.20], <0.001; multiple, 0.11 [0.05;0.29], <,001) and with non HIV-negative partners (i.e., HIV-positive with undetectable VL, 0.57 [0.38;0.86], 0.007; unknown serological status or HIV-positive with detectable/ unknown VL, 0.52 [0.32;0.87], 0.012).

After adjustment for all potential correlates, 85 % of most recent condomless anal intercourses without PrEP were attributable to sexual intercourse with a main partner, 47 % with an HIV-negative partner, 32 % under the effect of alcohol, 30 % in people who had a depressive episode in the previous 12 months, and 1 % to a high number of sexual intercourses during the previous 4 weeks.

The other explanatory variables significantly associated with our outcome in the univariable analyses were not confirmed in the multivariable analysis. We found no issue of multicollinearity in the model.

Discussion

This study explored the factors which contribute to explaining condomless anal sex and without on-demand PrEP in MSM. Results showed a type of rationality in HIV risk management. Specifically, condomless anal sex without PrEP was mainly attributable to sexual intercourses with a main partner (attributable risk of 85%) or with an HIV-negative partner (attributable risk of 47%). Moreover, GEE estimates showed that sexual intercourse with casual or multiple partners and with HIV positive (whatever the VL status) or unknown HIV status partners, was associated with a lower probability of reporting condomless anal sex without PrEP. These results highlight the central role of social perception of sexual partners in the implementation of individual prevention strategies, as well as the desire to be protected during a specific sexual intercourse situation which the individual perceives to be riskier than other situations (32).

Other studies have already recommended that the sexual intercourse context (peer norms, representations of sex, recreational drug use, etc.), and more globally, the social and cultural context of sexual health, be taken into account in the implementation of HIV-prevention programs (33,34).

Managing risk by taking into account the type of partner and his/her serology would seem consistent with a rationale based on socially perceived low (e.g., intercourse with a main partner or HIV-negative partner) or high (intercourse with casual or multiple partners, or with partners who are seropositive or whose serology is unknown) risk encounters. However, there are several

associated issues with this strategy. One previous study showed that half of new HIV infections in MSM resulted from sexual intercourses with main partners (35), mainly due to non-exclusive sex (36–38) and to the high prevalence of HIV in MSM (39). Moreover, condomless sex without PrEP with self-reported HIV-negative partners raises the issue of HIV testing in MSM at high risk of HIV infection. Although official French recommendations suggest quarterly HIV testing for this population (41), studies have shown that the majority of MSM report less frequent testing (41,42).

The possibility to use Treatment as Prevention (TasP), which is already included in the combined HIV prevention package, does not explain the lack of combined PrEP and condom uptake in our study (43). Indeed, we found that anal intercourses with HIV-positive partners with undetectable VL were associated with a lower probability of reporting condomless anal sex without PrEP . This result shows the gap between social norms related to HIV risk and scientific advances in HIV prevention. The development of biomedical prevention strategies, such as TasP and PrEP, brings into question the use of serosorting as an effective preventive tool (44,45). Sex with HIV-positive partners with undetectable VL or protected by PrEP, whatever the HIV status of the partner, is less risky than condomless sex without PrEP with HIV-negative partners in MSM community. However, TasP use also requires individuals to be certain that their partner has an undetectable VL.

Our results also showed that three significant factors negatively impacted the use of prevention strategies: a higher number of sexual intercourses in the previous 4 weeks, alcohol consumption during sexual intercourse and experiencing a depressive episode during the previous 12 months. Holistic care, and more specifically, mental health needs must be taken into account in future prevention programs to maximize their efficacy (46–48). Furthermore, our findings suggest that

experiencing depression was closely linked to the participant's conjugal status and to the serological status of their partner (the experience of depression in the previous 12 months became significantly associated with our outcome at $p \leq 0.05$ as soon as these two factors were introduced among the explanatory variables in the multivariable analysis). With regard to a higher number of sexual intercourses in the previous 4 weeks, it is possible that participants were more focused on the benefits linked to their sexual practices than on the related HIV risk. Indeed, studies have shown that the 'distance to the object' (from the homonymous theory) influences perceived risk (49). More specifically, the more frequent a behavior, the less people with that behavior think about its negative consequences (perceived risk, gravity), focusing instead on its benefits. This process enables people to keep the evaluative dimension of their health behaviors at a distance, thereby enabling them to freely negotiate their risk-taking (50). Another possible explanation for a higher number of sexual intercourses in the previous 4 weeks as a factor associated with condomless sex without PrEP, is that participants used non-biomedical strategies as part of their HIV risk management strategy. HIV prevention based on both the level of intimacy with a sexual partner and the partner's serological status was highlighted in our study. Non-behavioral (e.g serosorting, type of partner) HIV prevention strategies were also highlighted in a study conducted in Montreal (40).

Furthermore, the type of practice (i.e., receptive versus insertive) was not associated with our outcome. This was also true for STI. It is possible that these factors separately impact decision-making concerning PrEP and condom use. However, condomless anal sex without PrEP did not seem to be associated with these factors. The socio-cognitive processes (e.g., risk evaluation, strategies of risk management, etc.) involved with this decision may differ than those involved when considering condomless sex and not using PrEP separately.

This study has several limitations. First, the results cannot be generalized due to the joint clinical trial and community-based research context. More specifically, MSM enrolled in ANRS-IPERGAY trial were not representative of the general MSM population, and the follow-up included in the trial differed from that for MSM in real-life situations. Moreover, we have no qualitative data to develop the understanding of our results, especially in terms of the perception of risk in various contexts and social norms related to HIV risk. Other factors which were not explored in this study, such as stigma, could have impacted our results. If, for example, perceived stigma had been found to be associated with not using PrEP, one of the study's recommendations would have been to study whether this impacted sexual intercourse with all type of partners or only some. Similarly, we did not study logistical factors, which may also have led to different recommendations. Had we evaluated their impact we might have been able to identify logistic-based explanations for condomless anal sex without on-demand PrEP, just as has been identified for daily PrEP.

Conclusion:

This study highlights the role of social norms and sexual partners' characteristics in the choice to practice (or not) condomless anal sex without PrEP. This reflects a form of rationality by MSM in self-managing HIV risk. However, it also raises a public health issue about the real efficacy of risk management which is based on assessing a partner's characteristics (e.g., level of intimacy, serological status).

We also found that condomless anal sex without PrEP was linked to mental health disorder, more specifically to having a recent depressive episode, and to alcohol consumption during sexual intercourse. This underlines the need for personalized and holistic care in prevention programs.

References

1. Morlat P. Prise en charge médicale des personnes vivant avec le VIH. Recommandations du groupe d'experts. Paris: CNS et ANRS; 2018 p. 1–46.
2. Calabrese SK, Reisen CA, Zea MC, Poppen PJ, Bianchi FT. The Pleasure Principle: The Effect of Perceived Pleasure Loss Associated with Condoms on Unprotected Anal Intercourse Among Immigrant Latino Men Who Have Sex with Men. *AIDS Patient Care STDs*. 2012 Jun 4;120604112553006.
3. Crosby R, Yarber WL, Sanders SA, Graham CA. Condom Discomfort and Associated Problems With Their Use Among University Students. *J Am Coll Health*. 2005 Nov;54(3):143–7.
4. Sanders SA, Yarber WL, Kaufman EL, Crosby RA, Graham CA, Milhausen RR. Condom use errors and problems: a global view. *Sex Health*. 2012;9(1):81.
5. Golub SA, Starks TJ, Payton G, Parsons JT. The Critical Role of Intimacy in the Sexual Risk Behaviors of Gay and Bisexual Men. *AIDS Behav*. 2012 Apr;16(3):626–32.
6. Mabire X, Puppo C, Morel S, Mora M, Rojas Castro D, Chas J, et al. Pleasure and PrEP: Pleasure-Seeking Plays a Role in Prevention and in Sexual Quality of Life, and Could Lead to PrEP Initiation. *Am J Men's Health*. 2019;In Press:1–14.
7. Greene GJ, Andrews R, Kuper L, Mustanski B. Intimacy, Monogamy, and Condom Problems Drive Unprotected Sex Among Young Men in Serious Relationships with Other Men: A Mixed Methods Dyadic Study. *Arch Sex Behav*. 2014 Jan;43(1):73–87.
8. Auerbach JD, Kinsky S, Brown G, Charles V. Knowledge, Attitudes, and Likelihood of Pre-Exposure Prophylaxis (PrEP) Use Among US Women at Risk of Acquiring HIV. *AIDS Patient Care STDs*. 2015 Feb;29(2):102–10.
9. Eisingerich AB, Wheelock A, Gomez GB, Garnett GP, Dybul MR, Piot PK. Attitudes and Acceptance of Oral and Parenteral HIV Preexposure Prophylaxis among Potential User Groups: A Multinational Study. Tachedjian G, editor. *PLoS ONE*. 2012 Jan 11;7(1):e28238.
10. Holt M, Murphy D, Callander D, Ellard J, Rosengarten M, Kippax S, et al. HIV-Negative and HIV-Positive Gay Men's Attitudes to Medicines, HIV Treatments and Antiretroviral-based Prevention. *AIDS Behav*. 2013 Jul;17(6):2156–61.
11. Wheelock A, Eisingerich AB, Ananworanich J, Gomez GB, Hallett TB, Dybul MR, et al. Are Thai MSM Willing to Take PrEP for HIV Prevention? An Analysis of Attitudes, Preferences and Acceptance. Vermund SH, editor. *PLoS ONE*. 2013 Jan 14;8(1):e54288.
12. Haire B. Preexposure prophylaxis-related stigma: strategies to improve uptake and adherence – a narrative review. *HIVAIDS - Res Palliat Care*. 2015 Oct;241.

13. Corneli A, Wang M, Agot K, Ahmed K, Lombaard J, Van Damme L. Perception of HIV Risk and Adherence to a Daily, Investigational Pill for HIV Prevention in FEM-PrEP: JAIDS J Acquir Immune Defic Syndr. 2014 Dec;67(5):555–63.
14. Kebaabetswe PM, Stirratt MJ, McLellan-Lemal E, Henderson FL, Gray SC, Rose CE, et al. Factors Associated with Adherence and Concordance Between Measurement Strategies in an HIV Daily Oral Tenofovir/Emtricitibine as Pre-exposure Prophylaxis (Prep) Clinical Trial, Botswana, 2007–2010. AIDS Behav. 2015 May;19(5):758–69.
15. Agot K, Taylor D, Corneli AL, Wang M, Ambia J, Kashuba ADM, et al. Accuracy of Self-Report and Pill-Count Measures of Adherence in the FEM-PrEP Clinical Trial: Implications for Future HIV-Prevention Trials. AIDS Behav. 2015 May;19(5):743–51.
16. Molina J-M, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. N Engl J Med. 2015 Dec 3;373(23):2237–46.
17. Molina J-M, Charreau I, Spire B, Cotte L, Chas J, Capitant C, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. Lancet HIV. 2017 Sep 1;4(9):e402–10.
18. Amico KR, Marcus JL, McMahan V, Liu A, Koester KA, Goicochea P, et al. Study Product Adherence Measurement in the iPrEx Placebo-Controlled Trial: Concordance With Drug Detection. JAIDS J Acquir Immune Defic Syndr. 2014 Aug;66(5):530–7.
19. Sagaon-Teyssier L, Mabire X, Laguette V, Fressard L, Suzan-Monti M, Rojas Castro D, et al. A Group-Based Trajectory Model for Changes in Pre-Exposure Prophylaxis and Condom Use Among Men Who Have Sex with Men Participating in the ANRS IPERGAY Trial. AIDS Patient Care STDs. 2018 Dec;32(12):495–510.
20. Gordillo V, del Amo J, Soriano V, Gonzalez-Lahoz J. Sociodemographic and psychological variables influencing adherence to antiretroviral therapy. AIDS. 1999;(13):1763–9.
21. Cochran SD, Sullivan JG, Mays VM. Prevalence of mental disorders, psychological distress, and mental health services use among lesbian, gay, and bisexual adults in the United States. J Consult Clin Psychol. 2003;71(1):53–61.
22. O’Cleirigh C, Skeer M, Mayer KH, Safren SA. Functional impairment and health care utilization among HIV-infected men who have sex with men: the relationship with depression and post-traumatic stress. J Behav Med. 2009 Oct;32(5):466–77.
23. Mays VM, Cochran SD. Mental Health Correlates of Perceived Discrimination Among Lesbian, Gay, and Bisexual Adults in the United States. Am J Public Health. 2001 Nov;91(11):1869–76.
24. Stephenson MT, Hoyle RH, Palmgreen P, Slater MD. Brief measures of sensation seeking for screening and large-scale surveys. Drug Alcohol Depend. 2003 Dec;72(3):279–86.

25. Liang K-Y, Zeger SL. Longitudinal Data Analysis Using Generalized Linear Models. *Biometrika*. 1986;73(1):13–22.
26. Zou G. A Modified Poisson Regression Approach to Prospective Studies with Binary Data. *Am J Epidemiol*. 2004 Apr 1;159(7):702–6.
27. Maldonado G, Greenland S. Simulation Study of Confounder-Selection Strategies. *Am J Epidemiol*. 1993 Dec 1;138(11):923–36.
28. Mickey RM, Greenland S. THE IMPACT OF CONFOUNDER SELECTION CRITERIA ON EFFECT ESTIMATION. *Am J Epidemiol*. 1989 Jan;129(1):125–37.
29. Saville WJ, Wittum TE. Veterinary Epidemiology. In: *Equine Internal Medicine* [Internet]. Elsevier; 2004 [cited 2020 Jan 27]. p. 1513–28. Available from: <https://linkinghub.elsevier.com/retrieve/pii/B0721697771500238>
30. Thelle DS, Laake P. Epidemiology. In: *Research in Medical and Biological Sciences* [Internet]. Elsevier; 2015 [cited 2020 Jan 27]. p. 275–320. Available from: <https://linkinghub.elsevier.com/retrieve/pii/B9780127999432000094>
31. Rogerson P. *Statistical Methods for Geography*. SAGE; 2001. 249 p.
32. Morin M, Apostolidis T. Contexte social et santé. In: *Traité de psychologie de la santé*. Dunod. Paris: Gustave-Nicolas Fisher; 2002.
33. Campbell C, Foulis CA, Maimane S, Sibiya Z. The impact of social environments on the effectiveness of youth HIV prevention: A South African case study. *AIDS Care*. 2005 May;17(4):471–8.
34. Roberts AB, Oyun C, Batnasan E, Laing L. Exploring the social and cultural context of sexual health for young people in Mongolia: implications for health promotion. *Soc Sci Med*. 2005 Apr;60(7):1487–98.
35. Sullivan PS, Salazar L, Buchbinder S, Sanchez TH. Estimating the proportion of HIV transmissions from main sex partners among men who have sex with men in five US cities: *AIDS*. 2009 Jun;23(9):1153–62.
36. Hoff CC, Campbell CK, Chakravarty D, Darbes LA. Relationship-Based Predictors of Sexual Risk for HIV Among MSM Couples: A Systematic Review of the Literature. *AIDS Behav*. 2016 Dec;20(12):2873–92.
37. Mitchell JW, Lee J-Y, Woodyatt C, Bauermeister J, Sullivan P, Stephenson R. HIV-negative male couples' attitudes about pre-exposure prophylaxis (PrEP) and using PrEP with a sexual agreement. *AIDS Care*. 2016 Aug 2;28(8):994–9.
38. Shernoff M. Negotiated Nonmonogamy and Male Couples. *Fam Process*. 2006 Dec;45(4):407–18.

39. UNAIDS. MILES TO GO CLOSING GAPS BREAKING BARRIERS RIGHTING INJUSTICES. Suisse: UNAIDS; 2018 p. 1–268.
40. The Spot Study Group, Otis J, McFadyen A, Haig T, Blais M, Cox J, et al. Beyond Condoms: Risk Reduction Strategies Among Gay, Bisexual, and Other Men Who Have Sex With Men Receiving Rapid HIV Testing in Montreal, Canada. *AIDS Behav.* 2016 Dec;20(12):2812–26.
41. Haute Autorité de Santé. Réévaluation de la stratégie de dépistage de l'infection à VIH en France. Paris: Haute Autorité de Santé; 2017 p. 1–3.
42. Marty L, Cazein F, Panjo H, Pillonel J, Costagliola D, Supervie V, et al. Revealing geographical and population heterogeneity in HIV incidence, undiagnosed HIV prevalence and time to diagnosis to improve prevention and care: estimates for France. *J Int AIDS Soc.* 2018 Mar;21(3):e25100.
43. UNAIDS. PREVENTION GAP REPORT. Geneva: UNAIDS; 2016 p. 1–286.
44. Jin F, Prestage GP, Mao L, Poynten IM, Templeton DJ, Grulich AE, et al. "Any Condomless Anal Intercourse" is No Longer an Accurate Measure of HIV Sexual Risk Behavior in Gay and Other Men Who have Sex with Men. *Front Immunol* [Internet]. 2015 Feb 27 [cited 2019 Jun 5];6. Available from: <http://journal.frontiersin.org/Article/10.3389/fimmu.2015.00086/abstract>
45. Newcomb ME, Mongrella MC, Weis B, McMillen SJ, Mustanski B. Partner Disclosure of PrEP Use and Undetectable Viral Load on Geosocial Networking Apps: Frequency of Disclosure and Decisions About Condomless Sex. *JAIDS J Acquir Immune Defic Syndr.* 2016 Feb;71(2):200–6.
46. Safren SA, Reisner SL, Herrick A, Mimiaga MJ, Stall RD. Mental Health and HIV Risk in Men Who Have Sex With Men: *JAIDS J Acquir Immune Defic Syndr.* 2010 Dec;55:S74–7.
47. Safren SA, Blashill AJ, O'Cleirigh CM. Promoting the Sexual Health of MSM in the Context of Comorbid Mental Health Problems. *AIDS Behav.* 2011 Apr;15(S1):30–4.
48. Stall R, Mills TC, Williamson J, Hart T, Greenwood G, Paul J, et al. Association of Co-Occurring Psychosocial Health Problems and Increased Vulnerability to HIV/AIDS Among Urban Men Who Have Sex With Men. *Am J Public Health.* 2003 Jun;93(6):939–42.
49. Dany L, Abric J-C. Distance à l'objet et représentations du cannabis. *Press Univ Grenoble.* 2007;20(3):77–104.
50. Peretti-Watel P. *Sociologie du risque.* Paris: Armand Colin; 2000.

Table 1. Characteristics of study population at inclusion (ANRS-IPERGAY OLE study, n=319 participants)

	Freq. (N = 316 ^a)	%
<i>Sociodemographic characteristics</i>		
Age, range: [19;61] – mean (SD)	316	36,7 (9,5)
Educational level higher than high-school	239	75,6 3
Active employment	267	84,4 9
Comfortable housing	296	93,6 7
Main partner	136	43,0 4
<i>Psychological profile</i>		
Anxiolytic consumption during the previous 12 months ^b	84	26,9 2
Antidepressant consumption during the previous 12 months ^c	49	15,7 6
Experience of depression ^d		
Yes, during the previous 12 months	74	23,4 9
Yes, before the previous 12 months	104	33,0 2
No, never	137	43,4

		9	
			12,4
BSSS-4 score at most recent assessment; range: [4;20] ^{e,f} – mean (SD)	313	(3,7)
			4,7
SS2-score at the recent assessment; range: [2;10] ^{d,f} – mean (SD)	315	(1,8)
			24,4
Detection or treatment of at least one sexually transmitted infection during the previous 2 months	78	5	
			13,7
Number of sexual partners during the previous 2 months, range: [1;580] – mean (SD)	316	(16,	4)
			13,1
Number of sexual intercours during the previous 4 weeks, range: [0;200] b – mean (SD)	312	(11,	6)
<i>During most recent anal intercourse:</i>			
Type of partner			
Main partner	69	21,8	4
Known casual partner	99	31,3	3
Unknown casual partner	112	35,4	4
Multiple partners	36	11,3	9
Partner serology and viral load			
HIV-	128	40,5	1
HIV+, undetectable viral load	39	12,3	4
Unknown serology or HIV+, detectable or unknown viral load	149	47,1	5
Type of sexual practice ^g			
Oral sex	42	13,5	0

Insertive anal sex and/or oral sex	103	33,1 2
Receptive anal sex and/or insertive anal sex and/or oral sex	166	53,3 8
Sexual intercourse in a public place	60	18,9 9
Under the influence of drugs (ecstasy, cocaine, GHB/GBL or ketamine)	30	9,49
Under the influence of alcohol	39	12,3 4
Perception of HIV-risk of transmission, range: [1;10] – mean (SD)	316	3,6 (2,6)

^a 3 participants did not fill in the inclusion questionnaire.

^b 4 missing values

^c 5 missing values

^d 1 missing value

^e 3 missing values

^f BSSS-4 = brief sensation-seeking scale; SS2=risk-taking scale. Scales constructed according to Stephenson et al., 2003. The higher the scores, the higher the levels of sensation seeking or risk taking, respectively.

Table 2 – Factors associated with condomless sex without PrEP at most recent anal intercourse: results from generalized estimating equations of modified Poisson regressions (ANRS-IPERGAY OLE study, n=319 participants, 1253 questionnaires)

	Condomless sex without PrEP (ref. No)			
	Univariable (n=1253)		Multivariable (n=1223)	
	RR [95% CI]	p	aRR [95% CI]	p
Age at inclusion, range: [19;61] ^a	0.97 [0.94;0.99]	0,01	0.99 [0.97;1.00]	0,14
Educational level higher than high-school (ref. No) ^a	1.09 [0.71;1.68]	0,70		
Active employment (ref. No) ^a	0.71 [0.47;1.09]	0,11	0.87 [0.61;1.26]	0,47
Comfortable housing (ref. No) ^a	0.78 [0.40;1.52]	0,47		
Anxiolytic consumption during the previous 12 months (ref. No) ^b	0.94 [0.59;1.49]	0,78		
Antidepressant consumption during the previous 12 months (ref. No) ^c	1.28 [0.83;1.99]	0,27		
Experienced of depression (ref. No, never) ^d			1.49	
Yes, during the previous 12 months	1.21 [0.76;1.90]	0,42	[1.02;2.17]	0,04
Yes, before the previous 12 months	1.33 [0.85;2.07]	0,21	1.09 [0.80;1.47]	0,58
BSSS-4 score at most recent assessment, range : [4;20] ^{e,f}	1.00 [0.96;1.05]	0,91		

SS2 score at most recent assessment, range: [2;10] ^{f,g}	1.08 [0.97;1.20]	0,15	1.03 [0.96;1.11]	0,39
Active involvement in community-based activities on prevention during the previous 12 months (ref. No)	1.03 [0.74;1.43]	0,87		
Main partner (ref. No) ^d	2.66 [1.88;3.77]	<,00 01	1.27 [0.95;1.71]	0,11
Detection or treatment of at least one sexually transmitted infection during the previous 2 months (ref.No)	0.86 [0.57;1.30]	0,48		
Number of sexual partners during the previous 2 months, range: [1;580] ^h	0.96 [0.90;1.02]	0,17	1.00 [0.98;1.02]	0,69
Number of sexual intercours during the previous 4 weeks, range: [0;200] ^h	1.01 [1.00;1.01]	0,00 1	1.01 [1.00;1.02]	0,01
At most recent anal intercourse:				
Type of partner (ref. Main partner)				
Known casual partner	0.16 [0.11;0.25]	<,00 01	0.20 [0.14;0.30]	<,00 01
Unknown casual partner	0.07 [0.04;0.13]	<,00 01	0.10 [0.05;0.20]	<,00 01
Multiple partners)	0.08 [0.03;0.20]	<,00 01	0.11 [0.05;0.29]	<,00 01
Partner serology and viral load (ref. HIV-)				
HIV+, undetectable viral load	0.50 [0.32;0.79]	0,00 3	0.57 [0.38;0.	0,01

				86]
Unknown serology or HIV+, detectable or unknown viral load	0.18 [0.11;0.29]	<,00 01	0.52 [0.32;0.87]	0,01
Type of practice (ref. Insertive anal sex and/or oral sex)				
Receptive anal sex (and/or insertive anal sex and/or oral sex)	1.14 [0.81;1.60]	0,46		
Sexual intercourse in a public place (ref. No)	0.19 [0.09;0.41]	<,00 01	0.94 [0.39;2.27]	0,90
Under the influence of drugs (ecstasy, cocaine, GHB/GBL or ketamine) (ref. No)	0.33 [0.16;0.66]	0,00 2	0.62 [0.34;1.13]	0,12
Under the influence of alcohol (ref. No)	1.25 [0.87;1.79]	0,24	1.45 [1.10;1.92]	0,01
Perception of risk of HIV infection, range: [1;10]	0.83 [0.77;0.91]	<,00 01	1.04 [0.98;1.12]	0,22

Abbreviations: RR [95% CI] = risk-ratio [95% confidence interval]; aRR = adjusted risk-ratio

^a 17 missing values in questionnaires due to 3 participants who did not fill in the inclusion questionnaire

^b 20 missing values

^c 14 missing values

^d 11 missing values

^e 36 missing values

^f BSSS-4 = brief sensation-seeking scale; SS2=risk-taking scale. Scales constructed according to Stephenson et al., 2003. The higher the scores, the higher the levels of sensation seeking or risk taking, respectively.

^g 21 missing values

^h 3 missing values