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Article

Pre-Exposure Prophylaxis, Anxiety, Depression and Sexual Satisfaction Among Men Who Have Sex With Men

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ABSTRACT

Background: Pre-exposure prophylaxis (PrEP) has been implemented as a prevention against HIV; however, its impact on mental health, sexual and life satisfaction has not been addressed. **Method:** We assessed 114 HIV-negative participants from Spain with ages ranging from 19 to 58 years; 60.5% were PrEP users (n = 69) and 39.5% were non-users (n = 45). They completed five questionnaires about life and sexual satisfaction, depression and anxiety. We performed correlations and multiple regression analyses. **Results:** The PrEP group showed a statistically significant relationship between better sexual satisfaction, and greater life satisfaction. The PrEP group also showed a statistically significant negative relationship with depression and anxiety which was not found in PrEP non-users. Moreover, we found that younger PrEP users had higher scores in anxiety and lower scores in depression than older users. The hierarchical regression analyses also showed that number of sexual partners was a major predictor in the PrEP group for NSSS. **Conclusions:** The indirect correlation between sexual satisfaction, depression, and anxiety in the PrEP group could underly the benefits of PrEP for patients' sex lives such as increased sexual liberties due to lower anxiety and mental comfort when experiencing chemsex.

Profilaxis Pre-Exposición, Ansiedad, Depresión y Satisfacción Sexual en Hombres que Tienen Sexo con Otros Hombres

Palabras clave:
Virus de inmunodeficiencia humana
Profilaxis pre-exposición
Satisfacción sexual
Depresión
Ansiedad

RESUMEN

Antecedentes: El impacto de la profilaxis pre-exposición (PrEP) sobre la salud mental, así como en la satisfacción sexual y con la vida son aún desconocidas. **Método:** Analizamos 114 participantes VIH negativos de España con rango de edad [19-58 años], donde el 60,5% eran usuarios de PrEP (n = 69) y el 39,5% no (n = 45). Completaron cinco tests sobre la satisfacción sexual y con la vida, la depresión y la ansiedad. Realizamos correlaciones y análisis de regresión múltiple. **Resultados:** El uso de PrEP correlacionó con un incremento de la satisfacción sexual y con la vida. Mostraron una correlación negativa en depresión y ansiedad que no se observó en los no consumidores de PrEP. Los usuarios de PrEP más jóvenes mostraban puntuaciones más altas en ansiedad y más bajas en depresión que los de mayor edad. Los análisis de regresión jerárquica mostraron que el número de parejas sexuales fue un predictor importante en el grupo de PrEP para la NSSS. **Conclusión:** La correlación indirecta entre la satisfacción sexual, la depresión y los síntomas de ansiedad en los usuarios de PrEP, podría ser la base de los beneficios que la PrEP puede ofrecer a la vida sexual de los pacientes.

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Pre-exposure prophylaxis (PrEP) is a powerful method of HIV prevention (Underhill et al., 2010; Ware et al., 2012). PrEP is an FDA-approved once-daily pill of emtricitabine-tenofovir that, when taken consistently, lowers the risk of HIV infection by over 98% (Volk et al., 2015). PrEP regimens have been demonstrated to significantly reduce HIV acquisition among high-risk men who have sex with men (MSM), people who use intravenous drugs and heterosexual men and women (Chou et al., 2019).

Despite its advantages, there has been a potential concern that initiating PrEP may be an excuse for individuals to engage in risky behaviors (Calabrese & Underhill, 2015). This is in line with the reported satisfaction goals among men such as self-focus and expressed desire to balance their sexual desires and stay HIV-negative (Cusick & Rhodes 2000; Gamarel & Golub, 2015; Golub et al., 2012). As such, desires for a satisfying and fulfilling sex life may be an important goal for men in adopting PrEP as their prevention strategy. In particular, the MSM population has a 25 times higher risk of HIV infection than the general population (United Nations Program on HIV/AIDS, 2018). In addition, the fact that there is no effective cure for this illness means it is essential to work on control and prevention of HIV (Reis et al., 2011).

In this regard, and due to the potential importance of PrEP as a prevention strategy, the majority of PrEP studies have focused on addressing efficacy, adherence, drug use, consumption pattern or different ways to implement PrEP (Hospital, NGO, GP or Sexual Transmission Infection clinic) (Iniesta et al., 2021). However, the psychological impact of PrEP consumption has hardly been addressed. Various studies have shown that MSM suffered increased fear of HIV infection which was related to high anxiety levels, even when their sexual partner was HIV positive with a suppressed viral load (Mabire et al., 2019), where there is no risk of HIV infection (Rodger et al., 2019). In fact, MSM have been described as being able to feel anxious for months after unprotected sexual intercourse (Godin et al., 2000; Siria et al., 2020), and also as avoiding being tested for HIV due to the fear of a possible positive result (Kellerman et al., 2002; Lorenc et al., 2011). These results revealed that mental health concerns such as depression or anxiety could be associated with PrEP use and they could have an impact on life and sexual satisfaction. Moreover, it should be taken into account that if the HIV infection finally occurs, that will have a deep impact on emotional welfare and personal and social functioning (Castedo & Santos, 2008).

In this line of thought, several studies have reported that participants described PrEP as providing 'peace of mind' (Hojilla et al., 2016; Mutchler et al., 2015; Yang et al., 2020). Indeed, in one study, participants identified reduced anxiety as a primary motivator for willingness to take PrEP (Brooks et al., 2012). Moreover, anxiety symptoms in PrEP non-users were positively correlated with the number of condomless anal sex partners, suggesting that PrEP could have an effect on these anxiety symptoms (Fernández-Rodríguez et al., 2022; Moeller et al., 2020). Contrary to these results, two studies found no relationship between anxiety and PrEP awareness as well as willingness to use PrEP (Blackstock et al., 2021; Liu et al., 2021).

Similar to these results, contradictory data have been found when approaching depression in the context of PrEP use. Indeed, in some studies depression was not associated with PrEP awareness or willingness to use it; whereas in others, depressive symptoms were associated with a higher likelihood of being willing to use PrEP to prevent HIV, although depressive symptoms have been identified as barriers to PrEP care (Gámez-Guadix et al., 2022; Laborde et al., 2020; Watson et al., 2020).

Based on the abovementioned impact of PrEP use on mental health conditions, it is also important to note that the use of PrEP could have a positive effect on sexual, and ultimately, life satisfaction. Thus, although Whitfield et al. (2019) have not found any impact of PrEP use on sexual satisfaction (Whitfield et al., 2019), a recent study showed improved sexual satisfaction in PrEP users (Montgomery et al., 2021).

Therefore, in this study we aimed to: (i) determine the relationship between depression, anxiety and PrEP use; (ii) determine the differential associations of these mental health outcomes and sexual and life satisfaction in a group of MSM.

Methods

Participants

Participants´ mean age was 35.30 years (*SD* = 9.28; range [19-58 years]), 60.5% were PrEP users (*n* = 69) and 39.5% were non-users (*n* = 45). Statistical power calculations gave the following values: *n* = 115 with α = .05 and β = .95. All participants were HIV negative and men who have sex with men (MSM). PrEP users reported taking it mostly daily (*n* = 62, 87.3%). In the majority of the cases, participants included in the study defined themselves as homosexual (*n* = 103, 90.4%), a cis gender man (*n* = 111, 97.4%), Spanish (*n* = 104, 91.2%) and having university studies (*n* = 84, 73.7%) (Table 1). No associations between any variables and the use of PrEP were found.

Data were collected using a patient-reported outcome measure (PROMs) through an online questionnaire. Those that completed the questionnaire were identified as potentially eligible in having met the criteria of being aged 18 or older, having an active sex life and presenting a high risk of getting HIV through sex defined as at least one insertive or receptive penetration without a condom in the previous month. All these criteria are consistent with the Spanish government eligibility criteria for PrEP treatment. A total of 114 participants met the inclusion criteria and were included in the study. For the recruitment of the participants five infectious units at different Public Hospitals (three in Seville, and one in Barcelona), and all the 75 associations from CESIDA, the Spanish HIV/AIDS coordinator were invited to participate in the current study.

Instruments

The online questionnaire included instruments according to their psychometric properties, validity and availability of cut-off points. Additionally, we used a Spanish version of an instrument if it was available. When it was not, we made a translation of the instrument. The final questionnaire of this study included the following instruments:

Demographic and Background Characteristics: Participants reported demographic characteristics, including age, gender, sexual orientation, level of education, nationality, as well as relevant information about sexual activity, relationship status, consumption of drugs and PrEP use.

Table 1.
Descriptive statistics of the sociodemographic characteristics of the participants.

Variable		*n*		Mean (SD)	
		PrEP user (*n* = 69)	PrEP non-user (*n* = 45)	PrEP user (*n* = 69)	PrEP non-user (*n* = 45)
Age (years)		-	-	37.1 (8.3)	32.6 (10.1)
PrEP prescription					
	Daily	61	-	-	-
	On demand (2+1+1)	8	-	-	-
Gender					
	CIS gender man	68	43	-	-
	Trans man	0	2	-	-
	Other	1	0	-	-
Sexual Orientation					
	Homosexual	63	40	-	-
	Bisexual	5	5	-	-
	Other (pansexual/ queer)	1	0	-	-
Nationality					
	Spain	62	43	-	-
	Latin America	4	1	-	-
	United Kingdom	2	0	-	-
	France	0	1	-	-
	Portugal	1	0	-	-
Education					
	University studies	55	30	-	-
	Secondary Education	11	14	-	-
	Primary Education	3	1	-	-

Note: n: frequencies or number of participants; PrEP: Pre-Exposure Prophylaxis; SD: Standard Deviation.

Satisfaction with Life Scale (SWLS): The SWLS is a five-item self-report scale designed to measure satisfaction with one's life (Diener et al., 1985). The SWLS is rated on a Likert scale from 1 (strongly disagree) to 7 (strongly agree). The higher scores indicate higher level of life satisfaction. We used a validated Spanish version of this instrument (Vázquez et al., 2013). The estimated reliability of the scale scores in our sample was α = .90.

New Sexual Satisfaction Scale (NSSS): The NSSS consist of a twenty-item self-report scale designed to measure aspect related to sexual satisfaction, like gender, sexual orientation, and neutral relationship status (Stulhofer et al., 2010). The NSSS is rated on a Likert scale from 1 (not at all satisfied) to 5 (extremely satisfied) where the participants are asked to rate their level of satisfaction with their sex life in the preceding six months. The higher scores representing higher levels of sexual satisfaction. We used a validated Spanish version of this instrument (Strizzi et al., 2016). The estimated reliability of the scale scores in our sample was α = .90.

PROMIS V2.0 Satisfaction with Sex Life Scale: The PROMIS V2.0 Satisfaction with Sex Life scale is a five-item self-report scale designed to measure how satisfying and pleasurable the participants regard their sexual activities, with no constraints on how the person defines "sex life" (Weinfurt et al., 2015). The PROMIS V2.0 is rated on a Likert scale from 1 (Not at all, None or Never, depending on the item) to 5 (very, a lot or always, depending on the item) where the participants are asked to rate their level of satisfaction with their sex life in the preceding 30 days. The higher scores indicate more satisfying sexual experiences. The estimated reliability of the scale scores in our sample was α = .88.

PHQ–9: The PHQ–9 is a nine-item self-report scale designed to measure the frequency of symptoms of depression concordant with the DSM–5 over the previous two weeks (Kroenke et al., 2001). The PHQ–9 is rated on a Likert scale from 0 (not at all) to 3 (nearly every day). The higher scores indicate greater depression symptom severity. We used a validated Spanish version of this instrument (Díez-Quevedo et al., 2001). The estimated reliability of the scale scores in our sample was α = .88.

GAD–7: The GAD–7 is a seven-item self-report scale designed to measure symptoms of generalized anxiety disorder (GAD) in the past two weeks as indicated in the DSM–5 (Spitzer et al., 2006). The GAD–7 is rated on a Likert scale from 0 (not at all) to 3 (nearly every day). The higher scores indicate greater anxiety symptom severity. We used a validated Spanish version of this instrument (García-Campayo et al., 2010). The estimated reliability of the scale scores in our sample was α = .90.

Internal Consistency of the Measurement Instruments

For the dimensions of the instruments used in the current study (PROMIS, NSSS, GAD-7), all of them presented an omega index ranging from .894 to .965. Ω coefficient revealed values of .894 in the PROMIS V2, .910 in the PHQ-9, .929 in the SWLS, .965 in the NSSS and .902 in the GAD-7.

Procedure

A retrospective *ex post-facto* research design was implemented considering the use of PrEP before the beginning of the study. A total of 193 homosexual men, or MSM, were recruited using non-probability sampling techniques from May to October 2021. The participants were recruited through the Infectious Unit of different Public Hospitals in Spain, as well as associations for the prevention of HIV infection. All participants` answers were collected via the *Google Forms* web application. All the participants resided in Spain and they were Spanish speakers.

The study was approved by the Ethics Committee of the Antonio de Nebrija University, Spain (code: UNNE-2021-008). All participants signed informed consent forms before data collection began.

Data Analysis

All data were analyzed using IBM SPSS Statistics (Version 22) and expressed as the mean ± standard deviation. The results were considered statistically significant if $p < .05$. The Kolmogorov-Smirnov and Levene tests were performed to verify the normality and homoscedasticity of the sample, respectively. The variables showed a non-normal distribution ($p < .05$), and, in all the cases, equality of variances was assumed ($p > .05$).

To analyze the association of qualitative variables, percentage and frequencies, with drug abuse during sexual intercourse a χ^2 asymptotic test and Cramer's V coefficient were calculated.

To analyze the quantitative variables, we performed a non-parametric Mann-Whitney U test. Also, Rosenthal´s r was obtained to determine the effect size. The interpretation was done according to Rosenthal´s r (Rosenthal, 1991).

Then, we went on to assess whether the different HIV behaviors, particularly stable relationships and STI, (a) were also non-trivial predictors and, if so, (b) whether they had incremental validity, which involves that they add information beyond that provided by PrEP use. In this part of the study, we used the non-parametric Spearman´s rho correlation and hierarchical multiple regression.

We then calculated reliability of the PROMIS V2, PHQ9, SWLS, NSSS and GAD7 including the omega coefficient to assess internal consistency. The omega coefficients were calculated according to Hayes and Coutts (2020) with Jamovi. software.

Results

HIV Risk Behaviors

Most of the participants did not have a stable relationship, as stated in the questionnaire, as a relationship lasting longer than three months (n = 78, 68.4%) and the mean of sexual partners in the previous 6 months was 23.33 (SD = 33.7). Of the participants, 59.6% (n = 68) reported not being diagnosed with a sexually transmitted infection (STI) during the previous 6 months (Table 2).

No association was found between the type of relationship or STI and PrEP users/ non-users. Similarly, no differences between groups were found (U = 1242, p = .71) according to the number of sexual partners in the previous six months.

Drug Abuse During Sexual Intercourse

The majority of participants reported not using mephedrone (n = 89, 78.1%), methamphetamine (n = 108, 94.7%), GHB (n = 90, 78.9%), amphetamine (n = 106, 93%) or ketamine (n = 103, 90.4%) during sexual intercourse. In those who reported consuming mephedrone or methamphetamine (n = 26) the drug was sniffed (n = 22, 84.6%). Regarding the consumption of alcohol and popper, 56.7% of the participants (n = 63) reported never or rarely drinking alcohol, 39.5% (n = 45) occasionally and 5.4% (n = 6) usually or always drinking alcohol. Moreover, 66.6% of the participants (n = 74) reported never or rarely taking popper, 24.6% (n = 28) occasionally and 10.8% (n = 12) usually or always taking popper during sexual intercourse.

Moreover, associations between PrEP users and non-users, and the consumption of the majority of the drugs were not found. In this regard, only ketamine showed associations between groups (χ^2 = 12.57, p = .002, V= .33, p = .002); specifically, PrEP non-users were associated with a higher consumption of ketamine compared to PrEP users.

Life and Sexual Satisfaction

Participants showed no differences in the life satisfaction measured by the SWLS (U = 1573.5, p = .12). However, when sexual satisfaction was tested with the NSSS (U = 1203.5, p = .04) and PROMIS, differences were found between groups (U = 1153.5, p = .02) showing a higher sexual satisfaction for PrEP users compare to non-users (Table 3).

Table 2.
Descriptive statistics of the HIV risk behaviors of the participants.

Variable	*n*		Mean (SD)	
	PrEP user (n = 69)	PrEP non-user (n = 45)	PrEP user (n = 69)	PrEP non-user (n = 45)
Stable relationship				
Yes	47	31	-	-
No	22	14	-	-
Number of sexual partners in the last 6 months	-	-	26.7 (38.5)	17.7 (23.7)
STI				
Yes	31	15	-	-
No	38	30	-	-
Kind of STI				
None	38	30	-	-
Gonorrhea	11	7	-	-
Chlamydia	7	1	-	-
Syphilis	5	3	-	-
Genital wart	2	1	-	-
External parasite	1	1	-	-
Mycoplasma	1	0	-	-
Other (anal bacteria, urine bacteria, candida, herpes, scabies)	4	2	-	-
Drug consumption				
Yes	42	20	-	-
No	27	25	-	-
Type of Drug				
Mephedrone	19	7	-	-
Methamphetamine	4	3	-	-
GHB	18	7	-	-
Amphetamine	6	3	-	-
Popper	37	19	-	-
Ketamine	6	6	-	-

Note: GHB: Gamma-hydroxybutyrate; *n*: frequencies or number of participants; PrEP: Pre-Exposure Prophylaxis; *SD*: Standard Deviation; STI: Sexually transmitted infections.

Table 3.
Comparison between PrEP users and non-users in life and sexual satisfaction.

	PrEP	Mean	SD	U	Sig	*dr*
Life satisfaction (SWLS)	Yes	23.8	7.6	1573.5	.903	.15
	No	24.5	6.1			
Sexual satisfaction (NSSS)	Yes	72.9	14.0	1203.5	.043	.38
	No	67.8	12.4			
Sexual satisfaction (PROMIS)	Yes	20.1	3.1	1153.5	.020	.37
	No	18.8	3.4			

Note: n: frequencies or number of participants; NSSS: New Sexual Satisfaction Scale; PrEP: Pre-Exposure Prophylaxis; *SD*: Standard Deviation; SWLS: Satisfaction With Life Scale.
*Range scores for the tests: SWLS (5-35); NSSS (38-100); PROMIS (8-25).

Depression and Anxiety Scales

Depression and anxiety were tested with the PHQ9 and GAD7 respectively, and although differences were not found between PrEP users and non-users in depression ($U = 1719.5$, $p = .97$), participants who take PrEP showed a lower score of anxiety compared to non-users ($U = 1906.5$, $p = .03$) (Table 4).

Table 4.
Comparison between PrEP users and non-users in depression and anxiety scales.

	PrEP	Mean	SD	U	Sig	dr
Depression (PHQ-9)	Yes	6.0	5.5	1719.5	.331	-.16
	No	6.9	5.8			
Anxiety (GAD-7)	Yes	4.9	4.5	1906.5	.039	-.18
	No	6.4	4.7			

Note: GAD-7: Generalised Anxiety Disorder scale seven; PrEP: Pre-Exposure Prophylaxis; PHQ-9: Patient Health Questionnaire; *SD*: Standard Deviation.
*Range scores for the tests: PHQ9 (0-27); GAD7 (0-18)

Correlations

The Spearman's rho pairwise correlations, considering all the participants (Table 5), revealed that participants with a higher rate in sexual satisfaction (NSSS) had also a higher number of sexual partners ($r = .27$, $p = .003$) and better life satisfaction through the SWLS ($r = .40$, $p < .001$). Moreover, drug consumers correlated positively with STI ($r = .22$, $p = .022$), whereas STI correlated with a higher number of sexual partners ($r = .296$, $p < .001$). Similar results have been found in sexual satisfaction measured with the PROMIS and in the satisfaction with life ($r = .39$, $p < .001$) supporting the idea that better sexual satisfaction seems to be related to greater life satisfaction. Also, satisfaction with life positively correlates with sexual satisfaction in both the PROMIS ($r = .39$, $p < .001$) and NSSS ($r = .40$, $p < .001$). Indeed, a positive correlation was found between the NSSS and PROMIS ($r = .69$, $p < .001$) and, also between anxiety and depression ($r = .74$, $p < .001$) as expected. On the other hand, negative correlations have been found between number of sexual partners and the existence of a stable partner ($r = -.22$, $p = .020$), and between satisfaction with life and depression ($r = -.52$, $p < .001$) and anxiety ($r = -.41$, $p < .001$). Negative correlations have also been found between sexual satisfaction and depression ($r = -.31$, $p = .001$) and anxiety ($r = -.23$, $p = .014$) in the NSSS and PROMIS respectively ($r = -.39$, $p < .001$; $r = -.31$, $p = .001$). More-over, negative correlations were found between depression and satisfaction with life ($r = -.52$, $p < .001$), and sexual satisfaction in both tests (NSS: $r = -.31$, $p < .001$; PROMIS: $r = -.39$, $p < .001$). This correlation has also been found with age, in such a way that the younger participants have shown higher scores in anxiety ($r = -.26$, $p = .005$) and depression to a lesser extent ($r = -.20$, $p = .037$) compared to the older ones (Table 5).

Spearman's rho pairwise correlations, when only PrEP users were selected (Table 6), showed that higher life satisfaction correlates positively with a higher sexual satisfaction in both the NSSS ($r = .39$, $p = .001$) and PROMIS ($r = .45$, $p < .001$), and negatively with depression measured by the PHQ9 ($r = -.68$, $p < .001$) and anxiety through the GAD7 ($r = -.58$, $p < .001$). Likewise, sexual satisfaction, measured with both the NSSS and PROMIS, showed a negative relationship with depression ($r = -.43$, $p = .001$, $r = -.37$, $p < .001$) and anxiety ($r = -.56$, $p = .001$, $r = -.47$, $p < .001$). The relationship between sexual satisfaction, depression and anxiety seems to disappear when non-PrEP users were selected, as can be seen in Table 7.

Hierarchical Regressions

As this is a cross-sectional study, the hierarchical regressions and SEM analyses explained below cannot test antecedent-consequent relationships. These analyses only show that the variables are related, but not what the direction of the relationships is. For this reason, the directions of the relationships explained below are based on the literature or on the hypothesis proposed in this study. As expected from the correlational analysis, only stable relationship and number of sexual partners were considered to be relevant depression and anxiety predictors in the first step.

Table 5.
Correlation matrix between variables

	1	2	3	4	5	6	7	8	9
1. Stable relationship									
2. Number of sexual partners	-.22*								
3. Drug consumption	.02	.10							
4. STI	.06	.30**	.22*						
5. Age	.18	.06	-.05	.11					
6. Life satisfaction (SWLS)	.01	.08	.02	.04	-.05				
7. Sexual satisfaction (NSSS)	.06	.27**	.12	.10	-.08	.40**			
8. Sexual satisfaction (PROMIS)	.20*	.18	.16	.16	.02	.39**	.69**		
9. Depression (PHQ-9)	-.01	-.02	.09	-.08	-.20*	-.52**	-.31**	-.39**	
10. Anxiety (GAD7)	-.02	.05	.05	-.08	-.26**	-.41**	-.23*	-.31**	.74**

Note: GAD-7: Generalised Anxiety Disorder scale seven; NSSS: New Sexual Satisfaction Scale; PHQ-9: Patient Health Questionnaire; STI: Sexually transmitted infections; SWLS: Satisfaction With Life Scale; ** Correlation is significant at the .01 level (2-tailed); * Correlation is significant at the .05 level (2-tailed).

Table 6.
Spearman's rho pairwise correlations in PrEP users.

	1	2	3	4	5	6
1. Age	1					
2. Nº of sexual partners	,05	1				
3. Life satisfaction (SWLS)	-.14	.01	1			
4. Sexual satisfaction (NSSS)	.30*	-.07	.39**	1		
5. Sexual satisfaction (PROMIS)	.14	.06	.45**	.70**	1	
6. Depression (PHQ-9)	.04	-.10	-.68**	-.43**	-.56**	1
7. Anxiety (GAD-7)	.17	-.06	-.58**	-.37**	-.47**	.83**

Note: GAD-7: Generalized Anxiety Disorder scale seven; NSSS: New Sexual Satisfaction Scale; PHQ-9: Patient Health Questionnaire; SWLS: Satisfaction With Life Scale;
** Correlation is significant at the .01 level (2-tailed); * Correlation is significant at the .05 level (2-tailed).

Table 7.
Spearman's rho pairwise correlations in PrEP non-users.

	1	2	3	4	5	6
1. Age	1					
2. Nº of sexual partners	.06	1				
3. Life satisfaction (SWLS)	-.07	-.04	1			
4. Sexual satisfaction (NSSS)	-.21	.19	.31*	1		
5. Sexual satisfaction (PROMIS)	-.19	.22	.24	.62**	1	
6. Depression (PHQ-9)	-.30*	-.07	-.34*	-.18	-.20	1
7. Anxiety (GAD-7)	-.42**	-.10	-.27	-.06	-.09	.76**

Note: GAD-7: Generalized Anxiety Disorder scale seven; NSSS: New Sexual Satisfaction Scale; PHQ-9: Patient Health Questionnaire; SWLS: Satisfaction With Life Scale.
** Correlation is significant at the .01 level (2-tailed); * Correlation is significant at the .05 level (2-tailed).

Hierarchical regression was performed by fitting one block of variables in each step (e.g., Hunsley & Meyer, 2003). Each block included the criteria variable such as the PHQ-9 and GAD-7. Incremental validity was operationalized as the increase in squared multiple correlation when the second block of variables was entered. In the NSSS, multiple R for the first block was .04, $F(1, 113) = .18$, $p = .676$ When the second block of variables was added, multiple R increased to .28, $F(1, 113) = 4.85$, $p = .01$. The increase in R^2 was .08, $F(1, 111) = 9.51$, $p = .003$. The same procedure was carried out separately for PrEP and non- PrEP users. For PrEP consumers in the NSSS, multiple R for the first block was .73, $F(1, 68) = 0.36$, $p = .549$. When the second block of variables was added, multiple R increased to .34, $F(2, 68) = 4.31$, $p = .017$. The increase in R^2 was .115, $F(1, 66) = 8.21$, $p = .006$. For non-PrEP users in the NSSS, multiple R for the first block was .022, $F(1, 44) = .02$, $p = .886$. When the second block of variables was added, multiple R was .09, $F(2, 44) = .19$, $p = .826$. The increase in R^2 was .01, $F(1, 42) = .36$, $p = .549$.

In the PROMIS, multiple R for the first block was .207, $F(1, 113) = 5.01$, $p = .027$. When the second block of variables was added, multiple R increased to .293, $F(2, 113) = 5.21$, $p = .007$. The increase in R^2 was .09, $F(1, 111) = 5.23$, $p = .024$. For PrEP consumers in the PROMIS, multiple R for the first block was .18, $F(1, 68) = 2.32$, $p = .132$. When the second block of variables was added, multiple R increased to .27, $F(2, 68) = 2.49$, $p = .091$. The increase in R^2 was .07, $F(1, 66) = 2.60$, $p = .112$. For non-PrEP users in the PROMIS, multiple R for the first block was .25, $F(1, 44) = 2.87$, $p = .097$. When the second block of variables was added, multiple R was .32, $F(2, 44) = 2.31$, $p = .112$. The increase in R^2 was .10, $F(1, 42) = 1.71$, $p = .199$.

In the SWLS, multiple R for the first block was .04, $F(1, 113) = .17$, $p = .680$. When the second block of variables was added, multiple R increased to .11, $F(2, 113) = .70$, $p = .498$. The increase in R^2 was .01, $F(1, 111) = 1.23$, $p = .269$. For PrEP consumers, multiple R for the first block was .10, $F(1, 68) = .67$, $p = .417$. When the second block of variables was added, multiple R increased to .20, $F(2, 68) = 1.32$, $p = .274$. The increase in R^2 was .04, $F(1, 66) = 1.96$, $p = .166$. For non-PrEP users, multiple R for the first block was .08, $F(1, 44) = .25$, $p = .619$. When the second block of variables was added, multiple R was .09, $F(2, 44) = .17$, $p = .846$. The increase in R^2 was .01, $F(1, 42) = .09$, $p = .767$.

In the GAD-7, multiple R for the first block was .09, $F(1, 113) = .79$, $p = .378$. When the second block of variables was added, multiple R increased to .13, $F(2, 113) = .99$, $p = .372$. The increase in R^2 was .02, $F(1, 111) = 1.21$, $p = .274$. For PrEP consumers, multiple R for the first block was .10, $F(1, 68) = .71$, $p = .401$. When the second block of variables was added, multiple R increased to .19, $F(2, 68) = 1.17$, $p = .318$. The increase in R^2 was .03, $F(1, 66) = 1.61$, $p = .209$. For non-PrEP users, multiple R for the first block was .05, $F(1, 44) = .1$, $p = .724$. When the second block of variables was added, multiple R was .09, $F(2, 44) = .18$, $p = .837$. The increase in R^2 was .01, $F(1, 42) = .23$, $p = .632$.

In the PHQ-9, multiple R for the first block was .07, $F(1, 113) = .53$, $p = .468$. When the second block of variables was added, multiple R increased to .07, $F(2, 113) = .26$, $p = .769$. The increase in R^2 was .01, $F(1, 111) = .00$, $p = .979$. For PrEP consumers, multiple R for the first block was .13, $F(1, 68) = 1.11$, $p = .297$. When the second block of variables was added, multiple R increased to .13, $F(2, 68) = .56$, $p = .575$. The increase in R^2 was .02, $F(1, 66) = .02$, $p = .876$. For non-PrEP users, multiple R for the first block was .19, $F(1, 44) = .02$, $p = .902$. When the second block of variables was added, multiple R was .04, $F(2, 44) = .03$, $p = .972$. The increase in R^2 was .00, $F(1, 42) = .04$, $p = .840$. These results suggest that the number of sexual relationships, even in a stable relationship can explain sexual satisfaction in both the NSSS and PROMIS beyond what can be explained by the other relevant variables but only in PrEP users for the NSSS.

Discussion

HIV pre-exposure prophylaxis (PrEP) was established as a once daily chemoprophylaxis to reduce the likelihood of HIV acquisition among persons at elevated risk of infection (Grant et al., 2010). PrEP is an antiretroviral medication that can be used for HIV prevention (Parsons et al., 2013). When taken daily as prescribed, PrEP has been shown to reduce the likelihood of HIV seroconversion by up to, and possibly in excess of, 99% (Grant et al., 2010). Despite the known efficacy of PrEP, its impact on psychological variables has been scarcely explored. Indeed, there is a need to explore the psychological implications related to PrEP use due to its potential impact on personal confidence, increased sexual liberties, enhancement of pleasure due to reduced anxiety, and heightened sensation. Also, PrEP could provide greater comfort to experiment with a variety of sexual practices which is not only

related to sexual satisfaction, but also could have an impact on life satisfaction. So, in this study, we have analyzed the relationship between the consumption of the PrEP drug with life and sexual satisfaction, in addition to the presence of depressive and anxious symptoms, in MSM.

A high prevalence of depression and anxiety among the populations at high risk for HIV has been reported (Nunn et al., 2017); however, the potential bidirectional relationships between the PrEP care continuum, and depression and anxiety are unclear. Indeed, differences in depressive symptoms between PrEP users and non-users in cross-sectional analyses have shown inconsistent findings. Three studies with MSM found no association between depression and PrEP use (Friedman et al., 2019; Krakower et al., 2012; Liu et al, 2021). Similarly, in another two cross-sectional studies with cisgender males and individuals dependent on opioids, no relationship between depressive symptoms and self-reported PrEP use was found (Ni et al., 2021; Wood et al., 2021). Moreover, in a study by Moeller et al. (2020) the use of PrEP did not predict depression in a sample of gay, bisexual and other MSM (Moeller et al., 2020). However, opposite results were found in a sample of MSM in the United States, where PrEP users reported lower levels of depression than non-PrEP users (Chandler et al., 2020). In this line of thought, higher depressive symptoms were associated with black MSM who were PrEP users compared with non-PrEP users (Eaton et al., 2017; 2018).

Our data revealed no differences in the analysis of depressive symptomatology measured by the PHQ9 questionnaire between PrEP users and non-users. However, our correlation analyses have shown that higher depression scores have been related to lower sexual and life satisfaction scores, but only in PrEP users. These results could be underlying the fact that depressive symptoms alone do not stymie PrEP uptake (Okafor et al., 2020; Wood et al., 2021). Indeed, cross-sectional analyses have found depressive symptoms to be positively associated with PrEP use (Eaton et al., 2017; 2018; Moeller et al., 2020).

Regarding anxiety, a national cohort study in the United States enrolling cisgender men and transgender individuals who have sex with men revealed no linked between anxiety and self-reported PrEP use current or past (Carneiro et al., 2021). Furthermore, Young et al. (2020) demonstrated that poorer PrEP adherence was associated with greater anxiety symptoms (Young et al., 2020). These findings could be highlighting that positive perceptions of PrEP may be associated with reduced anxiety. In this same vein, our results have shown that PrEP users have lower scores on the GAD7 questionnaire compared to non-users. Moreover, our correlation analyses have shown a negative relationship between the presence of anxiety symptoms and life and sexual satisfaction in PrEP users, but, surprisingly, this relationship seems to disappear in non-users. Our results are in line with the description of PrEP by participants in several studies as providing "peace of mind" (Hojilla et al., 2016; Mutchler et al., 2015; Yang et al., 2020). Participants also identified PrEP as a possible component of a couple's sexual agreements, in order to reduce sexual anxiety (Mitchell et al., 2016).

Indeed, in one study, participants identified reduced anxiety as a primary motivator for willingness to take PrEP (Brooks et al., 2012). These results are supported by a large longitudinal analysis where sexual anxiety in cisgender MSM showed reduced sexual anxiety after initiating PrEP (Whitfield et al., 2019).

Moreover, a novel finding was related to younger participants showing higher scores in anxiety and lower in depression compared to the older ones. These findings indicate that depression and anxiety have distinct relationships with the PrEP care continuum across time.

Furthermore, although no differences were found between groups in life satisfaction, differences were found between groups in sexual satisfaction for both the PROMIS and NSSS questionnaires with higher scores in PrEP users. These results could be explained by the reduction in anxiety previously reported in this group which could be linked to increased feelings of control (Quinn et al., 2020), responsibility (Zapata et al., 2022), and enhanced sexual well-being (Hammack et al., 2019; Hojilla et al., 2016; Storholm et al., 2017). Moreover, while a greater number of condomless anal sex partners was associated with heightened anxiety symptoms in those not on PrEP, this relationship was not present for those on PrEP, suggesting that PrEP use buffers the effect of number of condomless anal sex partners on anxiety symptoms (Moeller et al., 2020) which could impact on sexual satisfaction. These results were supported by our regression analyses. Finally, PrEP can increase sexual liberties, enhance pleasure (due to reduced anxiety and heightened sensation) and provide greater comfort to experiment with a variety of sexual practices which could increase the scores in the PROMIS and NSSS.

Another important point to assess when exploring the risk of HIV transmission posed to MSM, is the combination of illicit drugs and sex (Maxwell et al., 2019). Chemsex is the planned use of psychoactive drugs before or during sex to initiate, enhance or facilitate the sexual event (Bourne et al., 2014). The drugs associated with chemsex are crystal methamphetamine (crystal meth), mephedrone, gamma-hydroxybutyrate/gamma-butyrolactone (GHB/GBL), ketamine and cocaine (Bourne et al., 2014; 2015). A minority of MSM engage in chemsex but it can involve behaviors, which place this group at high risk of HIV acquisition (Tomkins et al., 2019). The behaviors at one sexual encounter (chemsex event) can include multiple sex partners, high rates of condomless anal intercourse, injecting of drugs and sharing of injecting equipment (Bourne et al., 2015). In this line of research, a UK based study on daily PrEP use reported that 44% of the sample had used chemsex-related drugs prior to study enrolment (Dolling et al., 2016). In addition, a study based in France on episodic PrEP use highlighted that 30% of the sample had been under the influence of psychoactive substances during sex (Roux et al., 2018). This study also reported that the correct use of PrEP was associated with periods when sample members were under the influence of psychoactive drugs during sex (Roux et al., 2018).

In our study, the analysis of drug use showed no differences between groups of PrEP users and non-users. Nevertheless, an association was found in ketamine consumption in the non-users, which was higher compared to PrEP users. These results are in line with recent findings where people who used illicit drugs continue to have low rates of PrEP use and awareness (Maxwell et al., 2020). These results could support the need for implementation of HIV self-testing programs as a viable strategy to increase uptake of PrEP and other HIV prevention strategies among people who used illicit drugs (Biello, et al., 2021; Escudero et al., 2014).

This study has some limitations. Firstly, the scope of the study was limited to Spain-based research and involved a sample consisting of mostly white MSM. Although this was purposeful due to the varying nature of the HIV epidemics and presentation of depression and anxiety across cultural and geographic settings, this limits the generalizability of the summarized findings; also, these results could have differed if the study sample had included greater ethnic and gender diversity. Secondly, despite the non-probabilistic incidental sampling, the analysis has shown that both groups were balanced at the time of registration. Thirdly, cross-sectional studies do not allow establishing causality between variables, so further studies should be performed in this line. Finally, the impact of the extent and number of individuals using on-demand PrEP in our variables is difficult to estimate based on the disproportionately low number of participants using on-demand PrEP in our data. However, this bias is commonly shared by PrEP studies, partly due to the participation biases that could also affect the proportions of consumers of on-demand PrEP use reported, and differ between regions with high satisfied demand and easy access to PrEP, and regions with higher access barriers.

The indirect correlation between sexual satisfaction and depression and anxiety symptoms in PrEP users could be linked to the benefits PrEP can provide for patients' sex lives such as increasing sexual liberties, enhancing pleasure due to decreased anxiety and providing mental comfort when experiencing chemsex.

Moreover, we have observed that younger MSM showed higher scores in anxiety and lower in depression compared to the older ones. These findings do not only indicate that depression and anxiety have distinct relationships with the PrEP care continuum, but it could also explain the greater likelihood of switching between regimens and differences in adherence to PrEP in this population.

Finally, given the importance of anxiety and depression in the PrEP users and their impact on sexual satisfaction, healthcare providers prescribing PrEP should be aware of mental health considerations and be ready to implement screening protocols and provide referrals for mental health services for those with symptoms of anxiety and depression (Golub et al., 2013). Alternatively, self-screening could be implemented for depression and substance use.

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