

# BMJ Open Prevalence and clinical impact of recreational drug consumption in people living with HIV on treatment: a cross-sectional study

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## ABSTRACT

**Objectives:** Drug interactions, poor adherence to medication and high-risk sexual behaviour may occur in individuals with HIV using recreational drugs. Thus, we aimed to assess the prevalence of recreational drugs use and to explore its clinical impact in HIV patients on treatment.

**Methods:** Observational, cross sectional, study conducted in a 700 bed university hospital, Barcelona, Spain. A total of 208 adults living with HIV on treatment were included. A questionnaire was administered by clinical pharmacists, including evaluation of sociodemographic variables, past 12-month drug consumption, adherence to antiretrovirals (Simplified Medication Adherence Questionnaire) and high-risk sexual behaviour (condomless sex/multiple partners). Additional data were obtained from clinical records. Recreational drug-antiretroviral interactions were checked in reference databases. Prevalence was calculated for 5% precision and 95% CI. Crude and adjusted binary logistic regressions were performed to identify associations between recreational drug use and adherence problems, and between recreational drug use and high-risk sexual behaviour.

**Results:** From the overall sample, 92 participants (44.2%) consumed recreational drugs over the past 1 year. Of these, 44 (48.8%) had used different types of recreational drugs in this period. We detected 11 recreational substances, including sildenafil and nitrites. The most consumed drugs were: cannabis (68.5%), cocaine (45.5%), nitrites (31.5%), sildenafil (28.3) and ecstasy (19.6%). Relevant interactions occurred in 46 (50%) of the individuals consuming drugs. Recreational drug consumption was found to be related to adherence problems with antiretrovirals (OR: 2.51 (95% CI 1.32 to 4.77)  $p=0.005$ ) and high-risk sexual behaviour (OR: 2.81 (95% CI 1.47 to 5.39)  $p=0.002$ ).

**Conclusions:** Recreational drugs are frequently used by HIV patients on treatment. Classical drugs and new substances consumed in sexual context are usual. Recreational drug consumption interferes with several clinical outcomes, including potentially relevant interactions between drugs and antiretrovirals,

## Strengths and limitations of this study

- We studied the prevalence of recreational drug consumption in people living with HIV on treatment and its association with relevant clinical outcomes.
- The high prevalence and specific patterns of recreational drug use found in our study may vary across countries according to sociodemographic and lifestyle characteristics.
- Relevant theoretical interactions between recreational and antiretroviral drugs occurred in half of the patients using recreational drugs. To what extent these interaction may lead to clinically relevant interactions is uncertain.
- Adherence problems with the antiretroviral treatment in the individuals consuming recreational drugs may result in treatment failure depending on the recreational drug patterns of use, the degree of non-compliance and the pharmacokinetic profile of antiretrovirals.
- Owing to the cross-sectional nature of the study, causality cannot be totally inferred.

adherence problems and high-risk sexual behaviour. Thus, there is the urgent need of implementing patient-centred care involving recreational drug consumption.

## INTRODUCTION

HIV continues to be a major public health challenge, with two million new infections globally in 2014.<sup>1</sup> In Spain, about 150 000 people were estimated to live with HIV in 2015.<sup>2</sup> The incidence rate was 9.34 cases per 100 000 inhabitants in 2014, higher than the average incidence in the European Union.<sup>3</sup> Among the new cases in Spain, 53.9% were men who have sex with men (MSM), followed by heterosexuals (26.0%) and injecting drug users (3.4%).<sup>3</sup> In contrast with the

spread of HIV transmission, the effectiveness of highly active antiretroviral therapy (HAART) has translated into a decrease in mortality by 42% since 2004 globally.<sup>1</sup> Mortality reduction in people living with HIV (PLWHIV), along with improved tolerability of newer drugs, have led to consider HIV as a chronic condition.<sup>4</sup> Consequently, there is a need for a clinical approach in which care of PLWHIV is tailored to each individual's needs. This implies addressing conventional concerns such as linkage to care, and emerging issues such as recreational drug consumption.

It is estimated that almost a quarter of the adult population in Europe have tried illicit drugs at some point in their lives, being cannabis, cocaine, amphetamines and ecstasy the most consumed in the general population.<sup>5</sup> Some studies have found a great proportion of recreational drug consumption in groups at risk or with great prevalence of HIV infection, especially for MSM, in countries such as the USA.<sup>6 7</sup> In Europe, the EMIS study reported data on recreational drug use in MSM, showing poppers, cannabis and 'sex drugs' as especially prevalent.<sup>8</sup> As for Spain, this relevant study showed cannabis, poppers, sildenafil, cocaine and 3,4-methylenedioxymethamphetamine (ecstasy) as the most consumed substances over the past 12 months.<sup>9</sup> However, only 23% of the individuals in Spain reported being HIV-positive, as this was not the target group of the study.<sup>8 9</sup> Unlike the case of injecting drug users, with clear evidence of poor HIV-related outcomes and specific recommendations,<sup>10</sup> interest in recreational drugs is recent in the HIV field. A previous, systematic review found 12 articles reporting prevalence data on recreational drug use in PLWHIV in Europe.<sup>11</sup> Relevant use of recreational drugs was found in these studies. Moreover, polydrug consumption, defined as the use of various drugs over a period of time, was about 50% in some cases. However, most of the included studies collected data on a limited number of recreational drugs as they primarily focused on other topics and, therefore, methods varied greatly across them. Also, participants were included regardless of receiving HAART in most studies. According to the review results, with the exception of extensive, methodologically sound studies in countries such as the UK,<sup>12</sup> little is known about the use of recreational drugs in many European countries, including Spain.

Consumption of recreational drugs may have relevant clinical consequences for PLWHIV who are on HAART. First, its use has been described as a factor contributing to non-adherence to HAART.<sup>13</sup> Recreational drug use may lead to low disease awareness, temporary cognitive impairment (depending on the substance) and may interfere with daily routine, which would be related to adherence problems.<sup>13</sup> Second, interactions between recreational drugs and HAART may appear and lead to potential toxic effects or insufficient antiretroviral plasma concentrations.<sup>14</sup> Drug efflux transporters and cytochrome P450 (CYP) are the main factors apparently

involved.<sup>15</sup> Additionally, adherence problems are known to appear when individuals prefer not to take their antiretroviral medication in order to prevent these potential interactions.<sup>16</sup> Third, recreational drug consumption could be associated with a high-risk sexual behaviour potentially leading to the acquisition of sexual transmitted diseases (STD) in PLWHIV using drugs. For example, recent results from the ASTRA study showed the independent relationship between increasing polydrug use and increasing prevalence of condomless sex in HIV-diagnosed MSM in London, 85% of whom were under HAART.<sup>12</sup> This potential association should be emphasised since the prevalence of chemsex, a term used to describe sexual relationships under the influence of certain psychoactive substances,<sup>17</sup> has become increasingly popular in certain areas over the past few years.

Despite the potential clinical impact of recreational drug issues, guidelines on HIV antiretroviral therapy have poorly incorporated these elements.<sup>11</sup> Guidelines tend to include general claims but usually lack specific recommendations. This could be explained as many of the efforts in this field have focused on studying the association between recreational drug use and the risk of being infected with HIV<sup>11 18 19</sup> rather than assessing the impact of recreational drugs on people already living with HIV. Clinicians, researchers and policymakers may not be fully aware of the real magnitude of the problem since both the prevalence and the clinical impact of recreational drug use on PLWHIV is unclear, especially referring to those people on treatment. This is especially relevant for countries with very scarce data on this topic; such is the case of Spain.

Thus, the aim of the current study was to examine the prevalence of recreational drug consumption on a representative sample of adult PLWHIV on HAART, and also to explore the clinical impact of these drugs at three levels: adherence to medication, interactions between recreational drugs and HAART and high-risk sexual practices.

## METHODS

### Study design

This hospital-based, observational, cross-sectional study was conducted in a 700 bed University Hospital, between April 2015 and December 2015. This reference hospital services a local population of about 400 000 people in Barcelona (Spain), including 1500 adult PLWHIV on HAART.

### Sample and procedures

The sample included non-institutionalised adults over 18 years old living with HIV and who were on HAART at the time of the interview. Individuals with severe cognitive decline, with language barriers, needing a legal representative, starting their HAART medication since the past 30 days or already enrolled in other studies were

considered not eligible. Participants were recruited on clinical visits to the Hospital Outpatients Pharmacy during the dispensing process (Monday–Friday; 08:00–15:00) to maximise the access and quality of the pharmacist–patient interaction. All interviewers were experienced hospital pharmacists who had participated in the questionnaire design. The final response rate was 89.3% (from a total of 233 individuals invited to participate). The final analysis consisted of 208 participants.

### Data collection and variable definitions

Data were obtained from a short survey questionnaire administered to the participants by specialist clinical pharmacists. This questionnaire focused on recreational drug consumption, adherence to medication, sexual behaviour and specific sociodemographic information. Additionally, participants were informed that supplementary information would be collected from electronic clinical records. These supplementary data included variables related to the HIV condition at the time of the interview: HAART, previous viral load, previous CD4 cell count, time on treatment, time from HIV diagnosis, comorbidities and medication other than HAART. Last viral load and last CD4 cell count referred to results from blood tests conducted over the past 4 weeks from the questionnaire response; last viral load category ‘undetectable’ was defined as <20 copies/mL; comorbidities included all chronic conditions obtained from primary care/hospital clinical records; medication included all chronic medication other than HAART obtained from primary care/hospital clinical records. Sociodemographic variables included age, gender, educational level, marital status, country of birth, income, urbanicity (10 000+ inhabitants was considered urban), employment status, HIV transmission route, use of classical IV drugs (heroin, cocaine, morphine) and alcohol consumption. Unhealthy alcohol consumption was assessed through a single screening question ‘How many times in the past year have you had X or more drinks in a day?’ (where X was five for men and four for women, and a response of one or more was considered positive).<sup>20</sup>

As for recreational drug consumption, we used one question assessing the use of certain substances over the past 12 months. There is evidence that the use of a single question for this purpose is valid for screening and preliminary evaluation of the use of substances of abuse compared with long questionnaires.<sup>20</sup> The list of drugs included cannabis, cocaine, amphetamines (including crystal methamphetamine), ecstasy,  $\gamma$ -hydroxybutyric acid (GHB), ketamine, mephedrone, lysergic acid diethylamide (LSD), erection enhancing medication (eg.: sildenafil) and nitrites (poppers). A list of frequently-used synonyms was also used to ensure drugs could easily be identified by patients. Adherence to HAART was assessed by means of the Simplified Medication Adherence Questionnaire (SMAQ), a 6-item, validated tool.<sup>21</sup> High-risk sexual behaviour was

evaluated with two questions according to the previous literature:<sup>12 22 23</sup> a five-categories Likert question relating to the frequency of condom use in sexual intercourse, and a question on the number of sexual partners ( $\geq 10$ ) over the past 12 months. After information was collected, theoretical recreational drug-HAART interactions were checked with daily-practice interaction databases: ‘<http://www.hiv-druginteractions.org>’ by the University of Liverpool<sup>24</sup> and ‘Drug interaction Search’ by Micromedex Solutions, 2015 Truven Health Analytics.

### Statistical analysis

Sample size was calculated with the GRANMO calculator<sup>25</sup> on the basis of determining the recreational drug consumption prevalence in our population group. We considered an approximate number of 1500 PLWHIV on treatment in our hospital, 15% prevalence of drug use in the Spanish general population<sup>26</sup> 5% precision and 95% CI. In order to ensure statistical robustness and facilitate additional statistical data analyses we finally considered an infinite sample for calculation purposes, which resulted in a minimum needed sample size over 200 participants.

Frequencies, proportions, range, mean, SD, CIs and cross tabulations were applied for descriptive analysis.  $\chi^2$  Test, Fisher’s exact test and t-test were used to measure differences in prevalence of sociodemographic and clinical variables across recreational drug consumption.  $\chi^2$  Test was also used to assess differences in adherence to ART medication and measures of sexual risk behaviour across recreational drug consumption. Crude and adjusted binary logistic regressions were used to examine the relationship between recreational drug consumption and the existence of potential problems regarding adherence to HAART. Variables used for bivariate models considered those that are supposed to impact on adherence according to the literature: age, gender, education level, marital status, household income, employment, country, alcohol consumption and pill burden. The multivariate logistic regression model included those variables with an association in the bivariate analyses defined as  $p < 0.1$  (gender, age, country of origin, education level, recreational drug consumption). Results are reported as unadjusted and adjusted ORs with 95% CI. Analogous procedures were used to examine the association between recreational drug consumption and high-risk sexual behaviour, defined as having 10 or more sexual partners over the past 12 months and/or declaring condomless sex during this period. In this case, variables in the bivariate models included age, gender, education level, marital status, household income, employment, country, alcohol consumption and transmission route. In its corresponding multivariate analysis model, apart from the aforementioned statistical procedures (excluding marital status only), we excluded additional variables that measured the same construct as other variables of the model

(gender, alcohol and employment were excluded). Analyses were performed with IBM SPSS statistics V.19.

### Ethics statement

The study was approved by the reference Clinical Research Ethics Committee. Additionally, an independent community representative reviewed the protocol to ensure patient-oriented evaluation and suitability of the study. Written informed consent was obtained from all participants, including the acceptance of data collection from the questionnaire and the revision of clinical records. All investigators worked according to the principles expressed in the Declaration of Helsinki.

### RESULTS

The study population consisted of 208 participants. Participants mean age was 46.8 years (SD: 10.4 years; range: 24–75 years). Practically all individuals lived in urban areas, with 80% of them being men. Regarding their HIV management, 83.2% had undetectable HIV viral load and 35.6% were receiving a single-tablet treatment at the time of the interview. A summary of the full list of sociodemographic and clinical data is available at [table 1](#).

As for recreational drug consumption, 92 (44.2%) participants declared having consumed drugs over the past 12 months ([table 2](#)). Of them, 44 (47.8%) had taken two or more drugs during that period. As for the drugs consumed, we found 11 recreational drugs, with cannabis (68.5%), cocaine (45.5%), poppers (31.5%) and erection enhancing substances (28.3%) being the most consumed drugs.

Moderate-to-severe, potential and theoretical interactions were found in 46 participants, half of the patients consuming drugs during the past 12 months, as a result of the search in interactions databases with respect to HAART regimens and recreational drugs consumed by these individuals. HAART involved in these interactions were: ritonavir-boosted protease inhibitors, some non-nucleoside reverse transcriptase inhibitors and cobicistat-boosted elvitegravir. All recreational drugs except for LSD and poppers were found to have relevant potential interactions in some individuals. Interactions distribution across recreational drugs is presented at [table 3](#). Problems with adherence were found in 64.1% of the individuals using recreational drugs and in 44.8% of the non-users. Condomless sex and having 10+ different sexual partners during the past year occurred in 49 (53.3%) and 31 (33.7%) individuals using drugs, respectively ([table 4](#)).

[Table 5](#) shows the crude and adjusted logistic regression ORs for the association between recreational drug consumption and the existence of adherence problems with HAART. After adjusting for covariates, recreational drug consumption and educational level were revealed to be associated with adherence problems (OR: 2.51 (95% CI 1.32 to 4.77)  $p=0.005$ ; OR (secondary vs

primary level): 2.56 (95% CI 1.07 to 6.14)  $p=0.035$ , respectively). Also, recreational drug consumption, age and income was associated with sexual risk behaviour after adjusting for covariates (OR: 2.81 (95% CI 1.47 to 5.39)  $p=0.002$ ; OR: 0.96 (95% CI 0.93 to 0.99)  $p=0.032$ ; OR: 0.48 (95% CI 0.25 to 0.91)  $p=0.025$ , respectively). There were no missing data for recreational drug use, clinical variables and most sociodemographic variables. Information on employment status and education level was missing in 3.4% and 6.6% of the participants, respectively. We did not impute these variables as we could not guarantee whether these data were missing at random.

### DISCUSSION

Our study found a relevant prevalence of recreational drug use among PLWHIV on HAART in Spain. A great proportion of the patients consuming recreational drugs had potentially severe interactions between these drugs and their HAART. Moreover, relationships between the use of drugs and other negative clinical outcomes such as problems with adherence to HAART and high-risk sexual behaviour have been detected, which are also essential for better understanding and management of drug consumption in PLWHIV.

Few studies have previously focused on recreational drug use in PLWHIV in Europe, especially in countries such as Spain. The ASTRA study included 2248 MSM living with HIV from eight outpatient clinics in the UK, with 85% on HAART.<sup>12</sup> In that case, they found a prevalence of recreational drug consumption in the past 3 months of about 51%. Our results, although slightly lower than that in the ASTRA Study, confirm the high prevalence of recreational drug consumption in a specific area of Spain. Apart from the prevalence of use, we found certain differences compared with the ASTRA study. For example, in our study cannabis was the most frequent drug, doubling figures of nitrites, the most common drug in the ASTRA study. In fact, cannabis and cocaine, the drugs most frequently used in the general population in Spain, were found to be the most consumed in our study.<sup>5</sup> We also found a high prevalence of sex-related drug use, including nitrites and erection enhancing medication, such as sildenafil. Previous studies in PLWHIV reported high prevalence figures on these drugs in several European countries that confirm the idiosyncrasy of drug consumption in this population.<sup>12 27 28</sup> Coadministration of sildenafil and nitrites is contraindicated because of their increased cardiovascular effects,<sup>29</sup> so that interviewers provided information to individuals who reported using both substances together.

It is worth highlighting the number of different recreational drugs detected in the study, along with the prevalence of individuals who consumed several drugs over the past 12 months. We detected 11 recreational drugs, 9 of them with prevalence over 10% among the

**Table 1** Description of the sample

	Total sample (n=208)	Non-recreational drug users (n=116)	Recreational drug users (n=92)	p Value
<i>Sociodemographic variables</i>				
Age (mean, SD) (years)	46.8 (10.4)	48.6 (10.8)	44.5 (9.5)	0.004
Gender (n, %)				0.001
Male	167 (80.3%)	84 (72.4%)	83 (90.2%)	
Female	41 (19.7%)	32 (27.6%)	9 (9.8%)	
Education (n, %)				0.042
≤Primary	51 (26.3%)	36 (33.0%)	15 (17.6%)	
Secondary	92 (47.4%)	49 (45.0%)	43 (50.6%)	
≥Tertiary	51 (26.3%)	24 (22.0%)	27 (31.8%)	
Country of origin (n, %)				0.045
Spain	129 (62.0%)	79 (68.1%)	50 (54.3%)	
Other	79 (38.0%)	37 (31.9%)	42 (68.1%)	
Location (n, %)				1.000
Rural	5 (2.4%)	3 (2.6%)	2 (2.2%)	
Urban	203 (97.6%)	113 (97.4%)	90 (97.8%)	
Employment (n, %)				0.758
Working	140 (69.7%)	78 (70.9%)	62 (68.1%)	
Unemployed	61 (30.3%)	32 (29.1%)	29 (31.9%)	
Marital status (n, %)				0.050
Married/cohabiting	96 (46.2%)	61 (52.6%)	35 (38.0%)	
Single	112 (53.8%)	55 (47.4%)	57 (62.0%)	
Household income (n, %)				0.071
≤Median	105 (50.5%)	52 (44.8%)	53 (57.6%)	
>Median	103 (49.5%)	64 (55.2%)	39 (42.4%)	
Alcohol consumption (n, %)				0.001
Non-consumer	120 (57.7%)	79 (68.1%)	41 (44.6%)	
Consumer	88 (42.3%)	37 (31.9%)	51 (55.4%)	
Classical IV drugs (n, %)				-
Non-user	206 (99.0%)	116 (100%)	90 (97.8%)	
User	2 (1.0%)	-	2 (2.2%)	
Transmission route (n, %)				0.001
Heterosexual/IV drugs use/transfusion	87 (41.8%)	61 (52.6%)	26 (28.3%)	
MSM	121 (58.2%)	55 (47.4%)	66 (71.7%)	
<i>Clinical variables</i>				
ART pill burden (n, %)				0.383
1 pills/day	74 (35.6%)	39 (33.6%)	35 (38.0%)	
2 pills/day	67 (32.2%)	42 (36.2%)	25 (27.2%)	
≥3 pills/day	67 (32.2%)	35 (30.2%)	32 (34.8%)	
Viral load (n, %)				0.358
Undetectable	173 (83.2%)	99 (85.3%)	74 (80.4%)	
Detectable	35 (16.8%)	17 (14.7%)	18 (19.6%)	
CD4 cell count (n, %)				0.054
<500 cells/μL	53 (25.5%)	36 (31.0%)	17 (18.5%)	
≥500 cells/μL	155 (74.5%)	80 (69.0%)	75 (81.5%)	
Time on treatment (mean, SD)	10.4 (7.1)	12.0 (7.2)	8.3 (6.4)	0.001
Time diagnosed (mean, SD)	12.8 (8.2)	14.5 (8.1)	10.7 (7.8)	0.001
Other comorbidity (n, %)				0.854
No	36 (17.3%)	21 (18.1%)	15 (16.3%)	
Yes	172 (82.7%)	95 (81.9%)	77 (83.7%)	
Other medication (n, %)				0.381
No	72 (34.6%)	37 (31.9%)	35 (38.0%)	
Yes	136 (65.4%)	79 (68.1%)	57 (62.0%)	

Frequencies, proportions, means and SDs are displayed.  $\chi^2$  Test (for 2xN tables) and t-test (for continuous variables) were performed to compare across recreational drug consumption (also, Fisher's exact test was used for variables 'location' and 'classical IV drugs'). Variables: age, time on treatment and time diagnosed are expressed in years. Employment category 'unemployed' included unemployed and inactive population such as homemakers and retired; Marital status category 'single' included: single, separated, divorced and widowed; Household income 'median' was €16 000/year; Classical IV drugs included heroin, cocaine, morphine; Viral load category 'undetectable' was defined as <20 copies/mL.

ART, antiretroviral therapy.

individuals taking drugs. Some of these drugs can be considered club drugs, such as ecstasy, GHB, amphetamines, speed and ketamine. Moreover, we found a relevant proportion of participants reporting drugs included in the definition of 'chemsex': GHB, metamphetamines

or mephedrone.<sup>17</sup> Apart from interactions, chemsex has been associated with high-risk sexual practices, including condomless sex or slamming, which involves injecting drugs such as mephedrone or GHB.<sup>11 14 17</sup> To what extent these drugs can lead to addiction and abuse needs further study, which should take into account some related sociocultural issues such as the widespread use of geo-sexual networking apps.

The prevalence of relevant potential interactions between recreational drugs and HAART in Spain is unclear to date. The results of our study revealed a great proportion of relevant potential interactions in PLWHIV on treatment. These interactions involved 10 different recreational drugs and 3 antiretroviral groups (ritonavir-boosted PIs, non-nucleoside reverse transcriptase inhibitors and cobicistat-boosted integrase inhibitors). Although several mechanisms have been described in the literature, most of the relevant interactions between recreational drugs and HAART are known to occur through the CYP metabolic pathway.<sup>14 30</sup> Moreover, most interactions described in the literature result in accumulation of recreational drugs or their toxic metabolites, leading to potential risk of adverse effects by these substances. As expected, that was the case in our study. However, we also found six individuals with an interaction between cannabis and atazanavir, which is known to decrease blood levels of atazanavir below its therapeutic range in 50% of the individuals on treatment with atazanavir using cannabis.<sup>24</sup>

In contrast with issues such as poor tolerability or poor adherence to medication, it may seem that potential severe interactions between recreational drugs and HAART need to be reconsidered in future clinical approaches. We hypothesise two main reasons leading to this situation: unawareness of the relevance of these interactions by clinicians and, especially, the fact that drug use can be an undisclosed issue by patients. In fact,

**Table 2** Prevalence of past 12-month recreational drug consumption among individuals consuming recreational drugs (n=92)

Type of drug	Number of individuals (%)	Mean (min–max; days)
Cannabis	63 (68.5)	164.5 (1–365)
Cocaine	40 (45.5)	14.9 (1–156)
Poppers	29 (31.5)	14.7 (1–52)
Sildenafil	26 (28.3)	12.6 (1–104)
Ecstasy	18 (19.6)	5.9 (1–24)
GHB	14 (15.2)	12.7 (1–100)
Amphetamines	11 (12.0)	5.6 (1–20)
Speed	11 (12.0)	13.45 (2–52)
Ketamine	9 (9.8)	6.1 (1–24)
Mephedrone	4 (4.3)	16.3 (1–50)
LSD	1 (1.1)	1 (1–1)
Number of drugs		
1	48 (52.2)	–
2	14 (15.2)	–
3	10 (10.9)	–
4	6 (6.5)	–
5	5 (5.4)	–
6+	9 (9.8)	–

Values calculated for the group of individuals taking recreational drugs. Frequencies, proportions, means and ranges are displayed. 'Mean' refers to the average consumption of each drug over the past 12 months.

Amphetamines, include crystal meth; GHB,  $\gamma$ -hydroxybutyric acid; LSD, lysergic acid diethylamide; MDMA, 3,4-methylenedioxymethamphetamine (commonly known as ecstasy).

**Table 3** Past 12-month, potential, relevant interactions between recreational drugs and antiretrovirals (n=46)

	Ritonavir boosted PI			NNRTI				Cobicistat boosted INSTIs
	Atazanavir/r	Darunavir/r	Lopinavir/r	Efavirenz	Etravirine	Nevirapine	Rilpivirine	
Amphetamines	–	–	–	–	–	–	–	3
Cannabis	6	–	–	–	–	–	–	–
Cocaine	4	8	2	2	3	1	12	7
Ecstasy	–	4	–	–	–	–	–	–
GHB	1	2	–	–	–	–	–	–
Ketamine	–	2	1	1	1	–	–	1
Mephedrone	–	1	–	–	–	–	–	–
Speed	1	1	–	2	–	–	–	3
Sildenafil	1	4	–	2	5	1	–	2

Potential, relevant interactions between HAART regimens and recreational drugs used over the past 12 months were assessed according to reference databases (frequencies are displayed). The table shows interactions in 46 individuals from the 92 recreational drug users. Results in the table refer to the number of participants with each interaction. No interactions were found in consumers of poppers and LSD. GHB,  $\gamma$ -hydroxybutyric acid; HAART, highly active antiretroviral therapy; INSTIs, integrase strand transfer inhibitor; LSD, lysergic acid diethylamide; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitors.

**Table 4** Outcomes on adherence to ART medication and measures of sexual risk behaviour over the past 12 months

	Total sample (n=208)	Non-recreational drug users (n=116)	Recreational drug users (n=92)	p Value
Adherence to ART				0.004
Good adherence	97 (46.6%)	64 (55.2%)	33 (35.9%)	
Poor adherence	111 (53.4%)	52 (44.8%)	59 (64.1%)	
Sexual intercourse				0.001
Condom-protected sex	129 (62.0%)	86 (74.1%)	43 (46.7%)	
Condomless sex	79 (38.0%)	30 (25.9%)	49 (53.3.0%)	
Sexual partners				0.001
<10	164 (78.8%)	103 (88.8%)	61 (66.3%)	
≥10	44 (21.2%)	13 (11.2%)	31 (33.7%)	

Frequencies and proportions are displayed.  $\chi^2$  Tests for 2x2 tables were performed to compare across recreational drug consumption. Adherence to ART was measured with the SMAQ questionnaire; Sexual intercourse category 'condomless sex' refers to having any/all sexual intercourse without condom over the last 12 months; Sexual partners refers to the count of different sexual partners over the past 12 months. ART, antiretroviral therapy; SMAQ, Simplified Medication Adherence Questionnaire.

a recent analysis by Daskalopoulou *et al*<sup>31</sup> of participants on HAART from the ASTRA study found very similar prevalence of recreational drug consumption across different HAART regimens, suggesting that clinicians do not consider drug use as a relevant issue in HAART selection. The authors also claim for the need of non-judgmental attitudes by healthcare providers when discussing drug use along with the benefits of community peer-led initiatives.<sup>31</sup>

Adherence to HAART is essential for controlling HIV infection. The prevalence of individuals with adherence problems in our study was 64.1% in those people using recreational drugs and 44.8% in non-users. The results of the multivariate logistic regression showed a statistically significant relationship between recreational drug use and lower adherence rates. Our results agree with the ones of the ASTRA study, in which recreational drug use was associated with lower adherence rates.<sup>12</sup> Also, as in the ASTRA study, prevalence of undetectable viral load in the group consuming recreational drugs on HAART was above 80%, which highlights that consuming recreational drugs is not necessarily related to adherence problems leading to clinical complications.<sup>12</sup> It is estimated that a minimum adherence rate of about 85% is needed to suppress RNA in about 80% of patients on HAART treatment.<sup>32</sup> As a consequence, the number of missed doses along with the pharmacokinetic profile of antiretrovirals may modulate the final impact of treatment efficacy.

From a behavioural perspective, several aspects should be considered when interpreting the association between recreational drug consumption and adherence problems. Individuals consuming recreational drugs may be concerned by severe potential intoxications or adverse effects due to interactions between recreational drugs and medicines. This concept is known as 'interactive toxicity belief'.<sup>16</sup> Thus, some people may anticipate, delay or miss their HAART medication, which may partly explain the results found in our study. For example, Kalichman *et al*<sup>16</sup> found that 35% of PLWHIV

on treatment intentionally miss doses when they are using drugs, being those individuals with interactive toxicity belief at greater risk. Apart from intentional non-adherence, temporary cognitive impairment due to the use of recreational drugs may interfere with memory or routine activities and eventually impact negatively on adherence to HAART.<sup>13</sup> To what extent each component, intentional versus non-intentional non-adherence, affects our results is unknown and should be subject of further investigations.

Finally, our results showed a clear association between the past 12-month recreational drug consumption and high-risk sexual behaviour, including condomless-sex and multiple sexual partners. Caution should be exercised in the interpretation of this result. High-risk sexual behaviour may lead to a greater risk of acquiring sexually transmitted infections by individuals consuming recreational drugs. Our results expand and complement the evidence found in previous studies which found a clear association between the use of recreational drugs and several measures of high-risk sexual practices, such as unprotected anal intercourse, group sex or multiple sexual partners.<sup>12 33</sup> Moreover, risk of HIV transmission to other sexual partners would be low as most individuals in the study had suppressed HIV viral load, which relates to a minimal transmission risk according to the results found in the PARTNER study.<sup>34</sup> There is however, the risk of HIV transmission in the case of individuals with detectable HIV viral load. Since alcohol and drug use can be relatively common during unprotected sexual relationships in specific population groups, interventions would also be justified to prevent HIV transmission.<sup>27</sup> Thus, our results underline the need of comprehensive interventions aiming to prevent new HIV transmissions in specific population groups and also to reduce sexually transmitted infections in PLWHIV using recreational drugs. As aforementioned, further studies should continue exploring the risks of chemsex, as this may involve polydrug use and particularly high-risk sexual behaviour along with possible addictive-related concerns.<sup>12 14 17</sup>

**Table 5** Multivariable logistic regression results

	Adherence model				Sexual risk model			
	OR crude (95% CI)	p Value	AOR (95% CI)	p Value	OR crude (95% CI)	p Value	AOR (95% CI)	p Value
Gender								
Male	1.00		1.00		1.00		–	–
Female	1.91 (0.93 to 3.89)	0.076	1.91 (0.85 to 4.30)	0.117	0.35 (0.16 to 0.73)	0.006	–	–
Age	0.97 (0.94 to 0.99)	0.036	0.97 (0.95 to 1.01)	0.157	0.94 (0.92 to 0.97)	0.000	0.96 (0.93 to 0.99)	0.032
Country of origin								
Spain	1.00		1.00		1.00		1.00	
Other	1.62 (0.92 to 2.86)	0.095	1.37 (0.72 to 2.63)	0.340	1.66 (0.94 to 2.92)	0.079	1.17 (0.61 to 2.28)	0.636
Education level								
≤Primary	1.00		1.00		1.00		1.00	
Secondary	2.25 (1.01 to 5.01)	0.047	2.56 (1.07 to 6.14)	0.035	0.45 (0.21 to 0.99)	0.049	0.81 (0.31 to 2.11)	0.810
≥Tertiary	0.99 (0.50 to 1.96)	0.971	0.97 (0.47 to 2.00)	0.936	0.56 (0.28 to 1.13)	0.104	0.66 (0.31 to 1.41)	0.288
Employment								
Working	1.00		–	–	1.00		–	–
Unemployed	0.74 (0.40 to 1.36)	0.331	–	–	0.57 (0.31 to 1.06)	0.075	–	–
Marital status								
Single	1.00		–	–	1.00		–	–
Married/cohabiting	1.06 (0.62 to 1.83)	0.830	–	–	1.10 (0.64 to 1.90)	0.732	–	–
Household income								
>Median	1.00		–	–	1.00		1.00	
≤Median	1.36 (0.79 to 2.35)	0.271	–	–	0.58 (0.34 to 1.01)	0.054	0.48 (0.25 to 0.91)	0.025
Alcohol consumption								
Non-consumer	1.00		–	–	1.00		–	–
Consumer	1.49 (0.86 to 2.60)	0.157	–	–	1.74 (0.99 to 3.03)	0.051	–	–
Transmission route								
Heterosexual/IV drug use/transfusion	–	–	–	–	1.00		1.00	
MSM	–	–	–	–	2.57 (1.45 to 4.55)	0.001	1.46 (0.71 to 3.02)	0.301
Pill burden								
1 ART	1.00		–	–	–		–	–
2+ ART	1.13 (0.64 to 2.00)	0.665	–	–	–		–	–
Recreational drugs								
Non-consumer	1.00		1.00		1.00		1.00	
Consumer	2.20 (1.26 to 6.86)	0.006	2.51 (1.32 to 4.77)	0.005	3.09 (1.75 to 5.47)	0.000	2.81 (1.47 to 5.39)	0.002

Results refer to univariate and multivariable logistic regression for the total sample.

Results with 95% CI. Age was included as a continuous variable. In the variable 'transmission route' heterosexual, IV drug use and transfusion was grouped together due to the small number of individuals.

AOR, adjusted OR; ART, antiretroviral therapy; MSM, men who have sex with men.



Our study has certain limitations. First, its cross-sectional nature identifies associations but does not allow causal relationships to be determined. Second, we used a self-reported, interviewer-administered, data collection method that could bias the results. Some individuals may be reluctant to report drug use as it is not socially accepted and they may fear being judged by health professionals. Thus, there is the possibility that the prevalence/frequency of recreational drug use is underestimated. For the same reason, it could be the case that some of the PLWHIVs not accepting to participate in the study had some issues with accepting recreational drug use publicly. Third, our results may only apply to our geographical area or to very similar ones (urban areas with same socioeconomic level) in Spain. Extrapolation of the results to other contexts is not straightforward as recreational drug patterns are heterogeneous across countries in Europe, while differing recall periods may also make difficult comparisons of prevalence estimates with other studies. Also, since consumption patterns change with time, results on prevalence of use and their impact could differ with ours in the long term. Another limitation may be the choice of 10 different sexual partners in the past year, which could lead to potential overestimation of sexual risk behaviour, especially for MSMs who may have high partner turnover. Finally, most drug-recreational drug interaction databases base their information on theoretically expected interactions according to metabolic pathways. Lack of clinical studies on real-life interactions leads to a useful but imprecise picture on this outcome, potentially omitting certain interactions not yet described.

In conclusion, prevalence of recreational drug consumption is particularly high in PLWHIV on treatment, the use of different drugs being relatively frequent. Furthermore, the results of our study contribute to a deeper understanding of the impact of recreational drugs at various levels. First, theoretically relevant interactions occurred in half of the individuals using drugs. Clinicians should be aware of the most relevant interactions and may adapt antiretroviral therapy in certain cases according to the pharmacokinetics of the antiretrovirals and recreational drug patterns of use. Second, recreational drug use was associated with lower adherence to antiretrovirals and high-risk sexual behaviour, which may lead to a higher risk of therapy failure and STD acquisition, respectively. Recreational drug consumption should be discussed openly between health professionals and PLWHIV on treatment seeking to clarify both general and individual recreational drug-related concerns. Further exploration on possible interventions aiming to decrease negative clinical outcomes related to recreational drugs are needed to minimise their risks in PLWHIV on treatment.

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