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Background: HIV infection has evolved into a chronic condition requiring life-long antiretroviral treatment (ART), exposing people living with HIV (PLWH) to potential drug-drug interactions (pDDIs) with co-administered substances. Chemsex users prescribed with ART are at risk of pDDIs due to intake of recreational drugs. This study aims to characterize potential ART and chemsex drugs pDDIs and evaluate their association with unscheduled relevant medical and psychiatric hospital consultations and admissions.

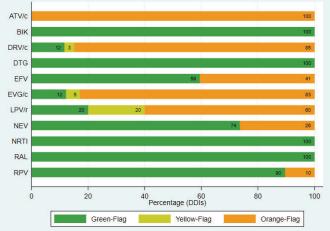
Methods: Single-centre, retrospective, observational study of pDDIs between ART and recreational drugs in a series of gay, bisexual and other men who have sex with men (gbMSM) PLWH who practice chemsex attending a tertiary hospital from February 2018 through August 2019. In order to study associations between all recorded pDDIs and relevant clinical events detected in unscheduled medical visits, we estimated the incidence rate (IR) per 100 persons-year of those events and compared it between patients with green (absence of pDDI) and orange-flag (moderate severity pDDI) or red-flag (high severity pDDI) using the Incidence Rate Ratio (IRR).

Results: A total of PLWH engaged in chemsex were included, as summarized on table 1. ART regimens were prescribed: 44% based on integrase inhibitors, 30% on boosted-ART, and 26% based on non-nucleoside reverse transcriptase inhibitors. The most frequently substances and recreational drugs used were erectile dysfunction agents (83%), methamphetamine (79%), GHB (77%) and alkyl nitrites (71%). Polydrug use was reported in 52%. We observed 2048 pDDIs. Of these, 23% were orange-flag pDDIs; 88% related to boosted ARTs. The IR of the 285 unscheduled relevant episodes in patients with orange-flag pDDIs was 64.67 (95% CI, 40.07–89.28). The IRR of green flag pDDIs was 1.05 (95% CI, 0.60–1.8; p = 0.876).

Figure 1 illustrates the percentage of flags by ART and figure 2 the distribution of ARTs, chems and DDIs.

Table 1. Baseline demogr	aphics and HIV related o	haracteristics
Demographic characteris	tics	
		Mean (SD
Age (years)		39 (9)
		n (%
Region of origin (N=171)	Spain	56 (33%
	Europe (w/o Spain)	29 (17%
	Latin America	82 (48%
	Australia/Oceania	1 (1%
	Asia	1 (1%
	Africa	2 (1%
Clinical characteristics		
		Median (IQR
CD4 (N=171)		677 (523 ; 854
CD8 (N=170)		811 (617 ; 1010
CD4/CD8 (N=170)		0.8 (0.6 ; 1.1
		n (%
Plasma HIV RNA-VL	Detectable	24 (14%
	Undetectable ¹	147 (86%
		Median (IQR
Plasma HIV RNA-VL (copies/ml) (N=24)		4950 (109 ; 88750
ART characteristics		
ART (N=249) ²		n (%
InSTI/b or PI/b		75 (30%
InSTI		109 (44%
NNRTI		65 (26%
SD, standard deviation. IQR		
Integrase Strand Transfer Ir		
Protease Inhibitors boosted		
Transfer Inhibitors. NNRTI,		
¹ Undetectable VL: <50copie		mens (in 172 patients),
one year before and one year	ar after the baseline visit.	

Figure 1. Percentage of flags by ART.



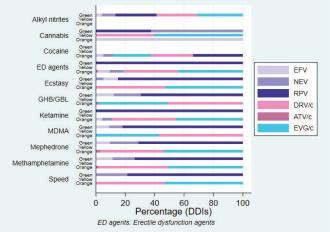
Potential DDIs between ART and *chems* are represented with different colours according to the severity of potential DDIs: orange flag (potential clinical rele yellow flag (weak clinical relevance) and green flag (absence of potential DDIs).

	n (%)
Chemsex-drugs	
Cocaine (N=172)	96 (56%)
Ketamine (N=172)	74 (43%)
GHB/GBL (N=172)	132 (77%)
Methamphetamine (N=172)	136 (79%)
Mephedrone (N=172)	85 (49%)
Speed (N=172)	60 (35%)
Ecstasy (N=172)	76 (44%)
MDMA (N=172)	62 (36%)
Alkyl nitrites (poppers) (N=172)	122 (71%)
Erectile dysfunction agents (N=172)	143 (83%)
Cannabis (N=172)	51 (30%)
Number of drugs used (before or during chemsex)	
1 drug (N=167)	16 (9%)
2 drugs (N=167)	65 (38%)
Polydrug use* (N=167)	88 (52%)
Route of drug administration	
Oral (N=170)	128 (75%)
Inhaled (N=171)	135 (79%)
Sniffed (N=172)	113 (66%)
Sublingual (N=171)	18 (11%)
Rectal (N=172)	29 (17%)
Intravenous (slamming) (N=170)	26 (15%)
Frequency of use	
Every day (N=167)	11 (7%)
Every week (N=169)	76 (45%)
Every month (N=168)	65 (39%
< 1 time per month (N=165)	29 (18%

drugs". MDMA, 3,4-methylenedioxymethamphetamine. Erectile dysfunction agents

Figure 2. Distribution of ARTs, chems and DDIs

include Sildenafil, Tadalafil, Vardenafil



Chemsex-drugs are displayed on the ordinate axis. They are subdivided in bars corresponding to green, yellow and orange flags. These bars are illustrated by colours, representing the proportion of ART corresponding to each flag. On every bar appearing from left to right, the proportion of flags is ranged from lowest to highest. Lilac colours represent NNRTI, rose colours belong to boosted PI and turquoise to boosted InSTI.

Conclusions: One in four pDDIs are of moderate severity predominantly related to boosted ARTs. However, no significant increase in the incidence of unscheduled relevant consultations has been found under these pDDIs We observed a high number of unscheduled consultations, predominantly for psychiatric events and intoxication. Beyond using non-boosted ART to minimize pDDIs, other factors related to the practice of chemsex must be addressed, in order to offer a better approach.





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