

Polypharmacy in HIV-infected and HIV-uninfected Individuals in the Region of Madrid (Spain): a Population-based Study

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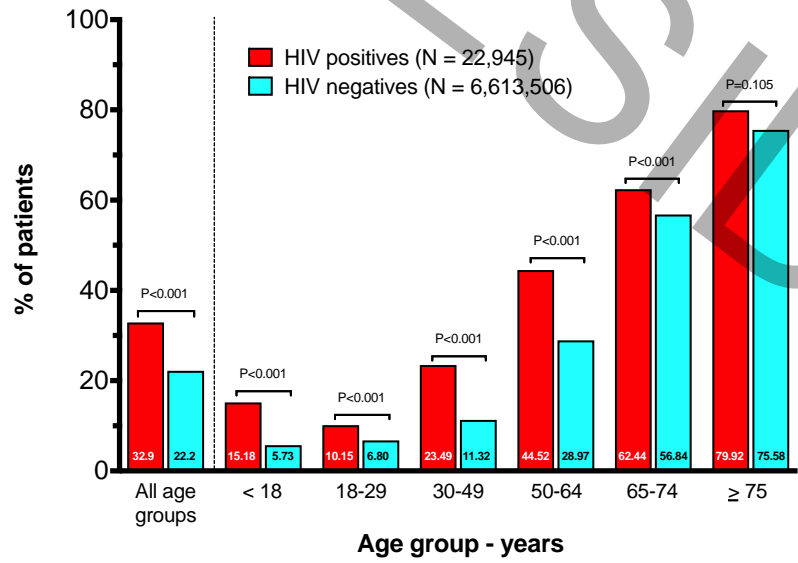
Objective

We assessed polypharmacy in HIV-infected and HIV-uninfected subjects in the region of Madrid and analyzed drug-drug interactions (DDIs) in HIV-infected subjects who received antiretrovirals.

Methods

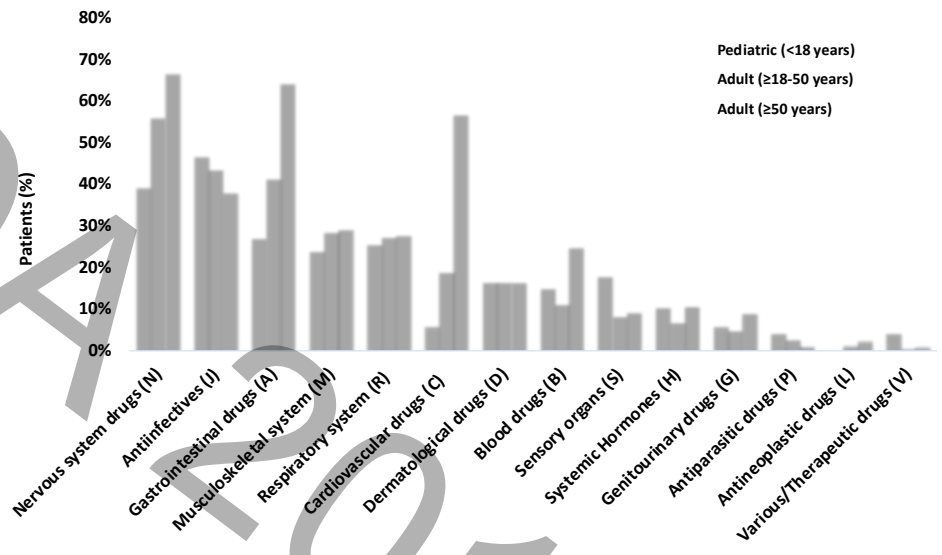
Study Design	Cross-sectional population-based study. Setting: region of Madrid. Study period: January 1 to June 30, 2017
Participants	All HIV-infected and HIV-uninfected individuals who picked-up prescription drugs in hospital and community pharmacies in the region of Madrid. The Madrid Regional Health Service (SERMAS) has a unique regional patient identification code (CIPA), that permits the access to personal information (age, sex, income) and also to all prescription drugs dispensed.
Prescription drugs	ARVs were dispensed in hospital pharmacies and categorized according to class. Non-ARV medications (Co-meds) were dispensed mainly by community pharmacies and classified according to the Anatomical Therapeutic Chemical (ATC) classification system.
Definitions	Polypharmacy was defined as the intake of ≥ 5 Co-meds. Patients were classified as HIV-infected or HIV-uninfected according to whether or not they received ARVs.
Screening for DDIs	Customized Application Programming Interface connecting the SERMAS database and the University of Liverpool (UoL) drug interactions database.
Classification of DDIs	UoL criteria (summarized with a traffic light method).

Polypharmacy among the study population (N = 6,636,451)



P values refer to comparisons of proportions of patients with polypharmacy (≥ 5 Co-meds) between groups

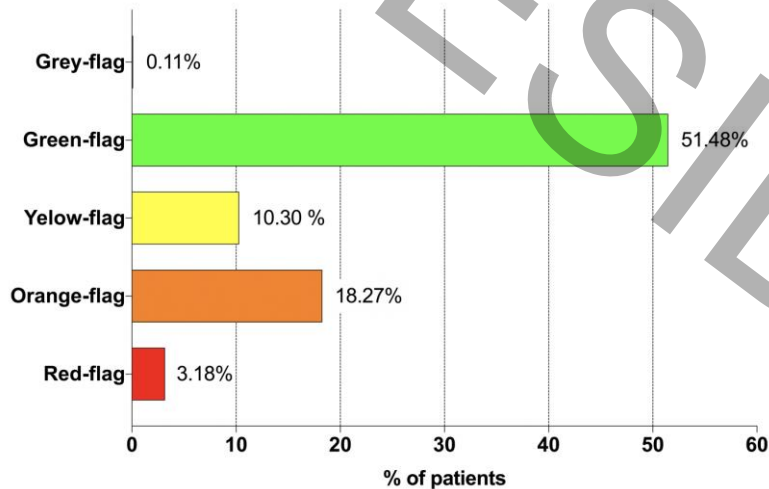
Co-meds in HIV-infected individuals according to ATC code



DDIs in HIV-infected individuals (N=22,945) according to ARVs

ARV class	Red-flag		Orange-flag		Yellow-flag		Green-flag		Grey-flag	
	N°	%	N°	%	N°	%	N°	%	N°	%
Boosted PIs	616	2.68	1,950	8.50	1,263	5.50	2,707	11.80	21	0.09
nnRTIs	89	0.39	1,911	8.33	789	3.44	4,478	19.52	6	0.03
Boosted INSTIs	46	0.20	204	0.89	75	0.33	197	0.86	1	0.00
Non-boosted INSTIs	1	0.00	368	1.60	185	0.81	5,912	25.77	0	0.00
nRTIs	0	0.00	127	0.55	265	1.15	6,083	26.51	0	0.00
CCR5 antagonist	0	0.00	8	0.03	8	0.03	126	0.55	0	0.00

Prevalence of DDIs in HIV-infected individuals (N = 22,945)



DDIs in HIV-infected individuals (N=22,945) according to Co-meds

Co-meds (ATC Code)	Red-flag		Orange-flag		Yellow-flag		Green-flag		Grey-flag	
	N°	%	N°	%	N°	%	N°	%	N°	%
Nervous system drugs (N)	115	0.50	1,833	7.99	1,163	5.07	5,686	5.07	25	0.11
Cardiovascular drugs (C)	97	0.42	674	2.94	730	3.18	3,512	3.18	0	0.00
Musculoskeletal system (M)	1	0.00	575	2.51	16	0.07	3,208	0.07	0	0.00
Antiinfectives (J)	7	0.03	353	1.54	128	0.56	3,179	0.56	0	0.00
Respiratory system (R)	314	1.37	324	1.41	386	1.68	2,248	1.68	0	0.00
Blood drugs (B)	61	0.27	368	1.60	0	0.00	1,998	0.00	0	0.00
Gastrointestinal drugs (A)	62	0.27	273	1.19	9	0.04	1,841	0.04	1	0.00
Dermatological drugs (D)	117	0.51	394	1.72	90	0.39	953	0.39	0	0.00
Systemic Hormones (H)	5	0.02	466	2.03	0	0.00	905	0.00	0	0.00
Genitourinary drugs (G)	11	0.05	342	1.49	20	0.09	674	0.09	0	0.00
Antineoplastic drugs (L)	0	0.00	15	0.07	0	0.00	230	0.00	0	0.00
Sensory organs (S)	0	0.00	23	0.10	31	0.14	179	0.14	0	0.00
Antiparasitic drugs (P)	0	0.00	42	0.18	84	0.37	134	0.37	0	0.00
Various/Therapeutic drugs (V)	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00

Red-flag = contraindicated.

Orange-flag = potential interaction: require dosage modification or close monitoring.

Yellow-flag = weak potential interaction: no require additional monitoring or dosage adjustment.

Green-flag = non clinically significant interaction.

Grey-flag = no data to indicate interaction.

Red-flag DDIs (N=729) among HIV-infected individuals

ARVs Class	ARVs	Co-meds (ATC Code)	Chemical substance	Nº (%)
Boosted PIs (RTV or COBI)	bATV bDRV LPV/r FPV/r, SQV/r TPV/r IDV/r	Corticosteroids (R01AD, R03BA, R03AK, H02AB, D07AC)	Budesonide, Mometasone, Fluticasone, Triamcinolone	375 (51.4)
		Antipsychotic drugs (N05AH)	Quetiapine, Clozapine	103 (14.1)
		Antithrombotic agents (B01AC)	Clopidogrel, Ticargelol	61 (12.2)
		Propulsives (A03FA)	Domperidone	50 (6.9)
		Statins (C10AA)	Simvastatin	46 (6.3)
		Diuretic drugs (C03DA)	Eplerenone	21 (2.9)
		Cardiac therapy (C01BD, C01EB)	Amiodarone, Ivabradine, Ranolazine	16 (2.2)
		Calcium channel blockers (C08CA)	Lecarnidipine	9 (1.2)
		Other Co-meds (N03/N05/N06, J04)	Phenytoin, Ziprasidone, Triazolam, Amitriptyline, Rifampicin	11 (1.5)
	Proton pump inhibitors (A02BC)	Lansoprazol, Esomeprazole, Rabeprazole	5 (0.7)	
Boosted INSTIs	EVG/COBI	Corticosteroids (R01AD, R03BA, H02AB, D07AC)	Budesonide, Mometasone, Fluticasone, Triamcinolone	38 (5.2)
		Other Co-meds (A03, B01, C01/C10, N03/N05)	Domperidone, Clopidogrel, Ivabradine, Simvastatin, Phenobarbital, Carbamazepine, Quetiapine	11 (1,5)
nnRTIs	EFV NVP RPV	Imidazole and triazole derivatives (D01AC, J02AC)	Ketoconazole, Itraconazole	61 (8.4)
		Sex hormones and modulators of the genital system (G03AC, G03DC)	Norethisterone [Norethindrone] (POP), Desogestrel (POP)	11 (1.5)
		Proton pump inhibitors (A02BC)	Lansoprazol, Esomeprazole, Rabeprazole	9 (1.2)
		Other Co-meds (N03/N05, J04)	Oxcarbazepine, Carbamazepine, Phenytoin, Ziprasidone, Triazolam, Rifampicin	9 (1.2)
Non boosted INSTIs	DTG	Antiepileptic drugs (N03AF)	Oxcarbazepine	1 (0.1)

Conclusions

- Polypharmacy was significantly more frequent among HIV-infected individuals in comparison with HIV-noninfected individuals across all age strata, except for those aged ≥ 75 years.
- Nervous system drugs followed by gastrointestinal drugs and anti-infectives were the most frequently prescribed Co-meds among HIV-infected subjects.
- The prevalence of red-flag DDIs among HIV-infected individuals was 3.2%.
- The most frequent involved ARVs in red-flag DDIs were boosted PIs, followed by nnRTIs, and boosted INSTIs.
- The most frequently involved Co-meds in red-flag DDIs were corticosteroids (51.4%), followed by antipsychotic drugs, statins, and imidazole and triazole derivatives.