

Supplementary data

Table S1. Summary of studies reporting data on the prevalence and associated factors of polypharmacy in PLWH taking ART

M	Country	Sample size	Study design and main patients' characteristics	Male, n (%)	Age (years)	Prevalence of polypharmacy in PLWH	Other findings	Factors associated to polypharmacy (Adjusted association measure, p)
Krentz HB, 2015	Canada	1329 (1190 on ART)	Observational Adult patients from Southern Alberta Clinic Cohort	Total sample: 1008 (75.8) ^a Taking ART: 907 (90.0) ^a	≤30: 108 (8.1) ^a 31-40: 342 (25.7) ^a 41-50: 493 (37.1) ^a 51-60: 288 (21.7) ^a ≥60: 98 (7.4) ^a	≥ 5 non-ART (of those taking ART): 32.2%	Higher percentage of patients on polypharmacy in older age groups: ≤30: 6.8% 31-40: 16.1% 41-50: 31.6% 51-60: 38.9% ≥60: 55.1% Higher percentage of male patients on polypharmacy: Male: 34.1% Female: 26.1%	NA
Kim TW, 2017	United States	250	Observational, longitudinal HIV-infected adults and substance dependence and/or injection drug use	157 (62.8) ^a	50 (44-56) ^b	≥ 5 non-ART: 91.0%	NA	NA
Holtzman C, 2013	United Kingdom	3810	Observational, cross-sectional Outpatient adults treated with ART	3001 (79) ^a	Median age: 46 Age groups: ≤ 40: 1189 (31.20) ^a 40-49: 1615 (42.38) ^a ≥ 50: 1006 (26.40) ^a	≥ 5 non-ART: 39%	Higher percentage of patients on polypharmacy in older age groups: ≥ 50: 706/1312 (54%) < 50: 788/2498 (32%)	NA
Moore HN, 2015	United States	7360 000 weighted visits for PLWH 374 626 000 weighted visits for non-PLWH	Observational, retrospective Adult outpatient visits	PLWH 18-29: 50.9% 30-49: 69.2% ≥50: 73.5% Non-PLWH 18-29: 25% 30-49: 33.6% ≥50: 39.5%	PLWH 18-29: 13% 30-49: 55% ≥50: 32% Non-PLWH 18-29: 18% 30-49: 32% ≥50: 50%	PLWH taking ≥ 5 non-ART (end of study period): 35% Non-PLWH taking ≥ 5 non-ART (end of study period): 32%	Older age was associated with ≥ 5 prescription medications after adjusting in both PLWH and non-PLWH Increased throughout the five-year period: ≥ 5 non-ART (PLWH): 16% to 35% ≥ 5 non-ART (non-PLWH): 24% to 32%	Age 30-49 years (OR 2.54, 95% CI: 1.31-4.92, p = 0.0058) Age > 50 years (OR 2.70, 95% CI: 1.68-4.35, p < 0.0001)
Guaraldi G, 2018	Italy	1573 (1258 PLWH)	Observational, cross-sectional Geriatric PLWH treated at 10 clinics and non-PLWH controls attended at a single geriatric clinic	1302 (82.77) ^a	Non-PLWH 65-74: 224 (71.11) ^a ≥ 75: 91 (28.89) ^a PLWH 65-74: 965 (76.71) ^a ≥ 75: 293 (23.29) ^a	≥ 5 non-ART (PLWH): 37% ≥ 5 non-ART (non-PLWH): 24%	Higher percentage of patients on polypharmacy in older age groups: 65-74 Years Old PLWH: 169 (35.28) ^a Non-PLWH: 44 (19.64) ^a ≥ 75 Years Old PLWH: 73 (42.94) ^a Non-PLWH: 32 (35.16) ^a	HIV 0-10 years (OR 1.94, 95% CI: 1.12-3.34, p = 0.02) HIV 10-20 years (OR 2.12, 95% CI: 1.41-3.21, p < 0.01) HIV >20 years (OR 3.25, 95% CI: 2.1-5.07, p < 0.01) Age ≥ 75 years (OR 1.76, 95% CI: 1.25-2.48, p < 0.01)
Kong A, 2019	United States	2359 PLWH and 2 010 513 non-PLWH	Observational, cross-sectional Adult ≥ 65 years	1909 (82.92) ^a	71.42 (5.19) ^c	≥ 5 non-ART: > 25%	Higher number of non-ART medications in older age groups: PLWH 65-69 years old: mean: 3.58 (median: 2.92) PLWH 70-74: Mean: 3.88 (median: 3.18) Non-PLWH 70-74 years: mean: 3.62 (median: 3.21) Non-PLWH 80-84 years: Mean: 3.83 (median: 3.48)	NA
Okoli C, 2020	24 countries	2112	Observational, cross-sectional Outpatient adults treated with ART	1487 (70.4) ^a	<50: 1464 (69.32) ^a ≥50: 648 (30.68) ^a	≥ 5 pills/day or taking medicines for ≥ 5 conditions: 42.1%	Significantly higher percentage of patients on polypharmacy in older age groups: ≥ 50 years: 54.6% < 50 years: 36.5% Significantly higher percentage of polypharmacy for those with an earlier HIV-diagnosis year: 50.3% (before 2010) 38.9% (2010-2016) 33.5% (2017-2019)	NA
Loste C, 2020	Spain	91	Observational, cross-sectional ≥ 65 years receiving comprehensive geriatric assessment	74 (81.3) ^a	72.1 (5.6) ^c	≥ 5 non-ART: 59.3%	NA	NA
Livio F, 2021	Switzerland	175 (171 on ART)	Observational, retrospective ≥ 75 years from the Swiss HIV Cohort Study	125 (71) ^a	78 (76-80) ^b	≥ 5 non-ART: 66.0 % 5-10 non-ART: 43.3% ≥ 10 non-ART: 19.5%	Higher risk of female patients to be on polypharmacy: Male: 63.2% Female: 72% Patients with a longer HIV-infection duration tended to take more non-HIV drugs: < 10 years: 4 (2-7) ^b 10-20 years: 5(4-8) ^b > 20 years: 7(4-11) ^b	NA
Ware D, 2018	United States	3160 (1715 PLWH)	Observational, prospective Adult male patients from the Multicenter AIDS Cohort Study from 2004 to 2016	3160 (100) ^a	All participants: 46(39.53) ^b	≥ 5 non-ART at index visit: 24.4%	Higher percentage of patients on polypharmacy in older age groups Evolution of polypharmacy prevalence throughout the twelve-year period: ≥ 50 years: PLWH: 38.4% to 46.8% nonPLWH: 16.7% to 46.0% < 50 years: PLWH: 18.9% to 17.3% nonPLWH: 5.6% to 20.4% PLWH had a higher prevalence of polypharmacy across all visits after adjusting for age, race/ethnicity, medication insurance and enrollment period (25.3% vs. 18.7%, p < 0.0001)	Age ≥ 50 (aPR 1.22, 95% CI: 1.13-1.33, p < 0.005) Medication insurance coverage (aPR 1.14, 95% CI: 1.01-1.27, p < 0.05) Early enrollment period (aPR 1.08, 95% CI: 0.99-1.18, p < 0.05) ART medication use (aPR 1.15, 95% CI: 1.12-1.18, p < 0.05) Non-Hispanic black (aPR 0.83, 95% CI: 0.74-0.92, p < 0.05)
Mazzitelli M, 2019	United Kingdom	790	Observational, prospective ≥ 50 years attended at 50 clinics	733 (92.8) ^a	55.8 (5.6) ^c	≥ 5 non-ART: 44.7% ≥ 10 non-ART: 7.9%	NA	NA
Lopes S, 2019	Germany	2680	Observational, cross-sectional Adult patients from the German Health insurance claims database	2307 (86) ^a	46 ^c	≥ 5 non-ART: 43.5%	Higher percentage of patients on polypharmacy in older age groups: 18-34 years: 25.4% 35-49 years: 37.6% ≥50 years: 60.9% Higher percentage of PLWH on polypharmacy in longer ART duration: ≤ 1 year: 35.8% 1-5 years: 43.1% ≥ 5 years: 48.9%	NA
Lopez-Centeno B, 2020	Spain	1292	Observational, cross-sectional ≥ 65 years from the dispensation registry of community and hospital pharmacies from the Madrid Regional Health Service	1027 (79.5) ^a	69 (67.73) ^b	≥ 5 non-ART: 65.9%	NA	NA

Lopez-Centeno B, 2020	Spain	22 945	Observational, cross-sectional Dispensation registry of community and hospital pharmacies from the Madrid Regional Health Service including paediatric patients	78.3%	48(39-54) ^c	≥ 5 non-ART: 32.94% ≥ 10 non-ART: 8.85%	Significantly higher percentage of patients on polypharmacy in PLWH (p < 0.001) (except in the sub-group of patients aged ≥ 75 years): <u>PLWH</u> : 32.94% <u>Non-PLWH</u> : 22.16% Higher percentage of female patients on polypharmacy Higher percentage of patients on polypharmacy in older age groups (2016): <u>≥ 50 years</u> : 47.26% <u>≥ 18-50 years</u> : 21.78%	NA
El Moussaoui M, 2020	Belgium	1038 (2016) 911 (2012)	Observational, retrospective Outpatient adults treated with ART	2016: 574 (55.3) ^a 2012: 493 (54.1) ^a 2012: ≤ 50: 647 (71.0) ^a 50-64: 225 (24.7) ^a ≥ 65: 39 (4.3) ^a	2016: ≤ 50: 650 (62.62) ^a 50-64: 320 (30.83) ^a ≥ 65: 68 (6.55) ^a 2012: ≤ 50: 647 (71.0) ^a 50-64: 225 (24.7) ^a ≥ 65: 39 (4.3) ^a	≥ 5 non-ART: 2016: 20.13% 2012: 17.01%	Higher percentage of patients on polypharmacy in older age groups (2016): <u>≤ 50 years</u> : 12.31% <u>50-64 years</u> : 30.62% <u>≥ 65 years</u> : 45.59%	NA
Calcagno A, 2021	Italy	2432 (1158 PLWH)	Observational, retrospective Adult patients from the Therapeutic Drug Monitoring service of the University of Torino	PLWH: 808 (69.8) ^a	PLWH: 51.6 (9.9) ^c	≥ 5 non-ART/non-antitubercular: 21.8% ≥ 10 non-ART/non-antitubercular: 2.6%	Lower percentage of patients on polypharmacy and severe polypharmacy in PLWH: <u>≥ 5 non-ART/ non-antitubercular</u> : PLWH: 21.8% Non-PLWH: 26.1% <u>≥ 10 non-ART/ non-antitubercular</u> : PLWH: 2.6% Non-PLWH: 3.1% Multivariate binary logistic analysis found HIV-positive serostatus, female gender and older age as independent predictors for polypharmacy	More advanced age (aOR for 10 years increase 1.365, 95% CI: 1.272-1.465, p < 0.001) HIV-positive serostatus (aOR 0.759, 95% CI: 0.621-0.928, p = 0.007) Age (aOR 1.303, 95% CI: 1.129-1.505, p < 0.001) Female gender (aOR 1.683, 95% CI: 1.240-2.283, p = 0.001)
Justice A, 2018	United States	49 285 (9473 on ART) US Veterans Affairs Healthcare System PLWH with suppressed HIV-1 RNA Non-PLWH receiving at least one medication	Observational, prospective PLWH on ART with suppressed HIV-1 RNA and non-PLWH receiving at least one medication	All participants: 48 036 (97.5%)	All participants: ≤ 50: 21.2% 50-64: 44.4% ≥ 65: 14.3%	≥ 5 non-ART: 34.1%	Lower percentage of patients on polypharmacy in PLWH: <u>PLWH</u> : 34.1% <u>Non-PLWH</u> : 39.3% Higher percentage of patients on polypharmacy in older age groups of PLWH: <u>PLWH</u> : ≤ 50: 22.3% 50-64: 36.7% ≥ 65: 43.3% <u>Non-PLWH</u> : ≤ 50: 27.1% 50-64: 41.8% ≥ 65: 45.2% HIV + men as likely as HIV + women, uninfected men more likely than uninfected women: <u>PLWH</u> : Male: 34.1% Female: 35.7% <u>Non-PLWH</u> : Male: 39.4% Female: 35.5%	NA
Gimeno-Gracia M, 2020	Spain	74	Observational, cross-sectional Adult ≥ 65 years treated with ART	64(86.5) ^a	69 (66.7-72.0) ^b	Prescription of at least 6 active ingredients including ART: 71.6% Concomitant use of 11 active ingredients or more: 25.7%	NA	NA
Siefried KJ, 2018	Australia	522	Observational, cross-sectional PLWH on ART and undetectable HIV RNA plasma viral load	494 (94.6) ^a	50.8 (12.3) ^c	≥ 5 non-ART: 23%	NA	Diagnosed comorbidity (OR 4.2, 95% CI: 2.0-8.6, p < 0.001) Estimated glomerular filtration rate < 60 ml/min per 1.73 m ² (OR 3.8, 95% CI: 1.5-10.1, p = 0.006) HIV managed by a hospital-based clinic (OR 2.0, 95% CI: 1.0-3.6, p = 0.030) HIV managed in a general practice (OR 1.9, 95% CI: 1.0-3.7, p = 0.038) Enrolled in a randomized clinical trial (OR 3.5, 95% CI: 1.3-9.0, p = 0.011)
Blanco JR, 2019	Spain	248	Observational, cross-sectional Adult patients on stable ART ≥ 1 year	158 (63.7) ^a	Mean age: 49	≥ 5 non-ART: 13.3%	NA	NA
Courlet P, 2019	Switzerland	996	Observational, prospective Patients from 2 centers within the Swiss HIV Cohort Study	< 65 years: 580 (66.4) ^a ≥ 65 years: 105 (86.8) ^a	< 65 years: 48.8(40.4-55.5) ^b ≥ 65 years: 71 (67.3-74) ^b	≥ 5 non-ART: ≤ 65 years: 12.1% ≥ 65 years: 42.6%	Higher percentage of patients on polypharmacy in older age groups of PLWH	NA
Fernández Cañabate S, 2019	Spain	154	Observational, cross-sectional Outpatient adults ≥ 50 years treated with ART (collecting ART for at least 1 year)	123 (79.9) ^a	56.3 (50-73) ^d	≥ 5 drugs including ART: 40.3%	NA	NA
Khawcharoe nporn T, 2020	Thailand	248	Observational, prospective Adult patients at a tertiary care clinic of an academic care center	177 (71) ^a	37 (28-47) ^b	≥ 5 non-ART: 9%	PLWH with polypharmacy were older (median age: 45 years and 36 years, PLWH and non-PLWH respectively, p = 0.014)	NA
Vinuesa-Hernando JM, 2021	Spain	30	Observational, retrospective ≥ 65 years treated with ART from university/tertiary level hospital	22 (73) ^a	71 (67-76) ^b	> 5 medications: 70% > 10 medications: 30%	NA	NA
Kunimoto Y, 2021	Japan	71	Observational, cross-sectional Outpatient adults treated with ART for at least 48 weeks	67 (94.4) ^a	45 (21-79) ^b	≥ 5 non-ART: 35.2%	NA	NA
Pontelo BM, 2020	Brazil	304	Observational, retrospective Outpatient adults	202 (66.4) ^a	< 50: 228(75) ^a ≥ 50: 72(23.7) ^a	≥ 5 medications: 23.3%	NA	NA
Morillo-Verdugo R, 2022	Spain	1225	Observational, cross-sectional Outpatient adults treated with ART visited at the pharmacy department of 81 hospitals	79%	49 (40-54) ^b	≥ 6 drugs including ART: 32.4% ≥ 11 drugs including ART: 5.5%	NA	Complexity index total score (aOR 2.399, 95% CI: 2.041-3.311, p = 0.000) Number of comorbidities (aOR 1.511, 95% CI: 1.014-2.193, p = 0.030) Presence of potential interactions (aOR 6.974, 95% CI: 3.035-16.029, p = 0.000) Antilulcer drugs (aOR 8.815, 95% CI: 2.474-31.402, p = 0.001) Psychotropics drugs (aOR 5.639, 95% CI: 2.276-13.975, p = 0.000) Cardiovascular (including antihypertensive) treatment (aOR 10.276, 95% CI: 1.743-60.580, p = 0.010) Number of polypharmacy patterns (aOR 9.895, 95% CI: 2.346-41.738, p = 0.002)
Ware D, 2019	United States	3160 (1715 PLWH)	Observational, prospective Adult male patients from the Multicenter AIDS Cohort Study from 2004 to 2016	3160 (100) ^a	All participants: 53 (46-60) ^b	≥ 5 non-ART across all study visits: 36.2%	The overall prevalence of polypharmacy across all study visits was 33.1% and was more common in PLWH compared with non-PLWH (36.2% and 30.0%, respectively, p < 0.001)	Sustained polypharmacy: Reporting public insurance (aOR 2.39, 95% CI: 1.71-3.34, p < 0.05) Being enrolled in the earlier enrollment period (compared with later recruitment) (aOR 2.58, 95% CI: 1.68-3.96, p < 0.05) Having a college degree or higher (aOR 1.99, 95% CI: 1.30-3.06, p < 0.05)

								Health care use (aOR 1.11, 95% CI: 1.08–1.14, p < 0.05) Age ≥ 50 years (aOR 2.23, 95% CI: 1.65–3.01, p < 0.05) Rapidly increasing polypharmacy: Age ≥ 50 (aOR 2.42, 95% CI: 1.74–3.39, p < 0.05) Health care use (aOR 1.10, 95% CI: 1.07–1.13, p < 0.05) ART medication use (aOR 1.87, 95% CI: 1.11–3.12, p < 0.05) Death (aOR 3.47, 95% CI: 1.24–9.76, p < 0.05) Slowly increasing polypharmacy: Age ≥ 50 (aOR 1.45, 95% CI: 1.12–1.86, p < 0.05) Public insurance (aOR 1.62, 95% CI: 1.21–2.15, p < 0.05) Health care use (aOR 1.08, 95% CI: 1.05–1.11, p < 0.05)
Ssonko M, 2018	Uganda	411	Observational, cross-sectional Outpatient adults ≥ 50 years	172 (41.8) ^a	50-54 years: 170 (41.4) ^a 55-59 years: 128 (31.1) ^a 60-64 years: 60 (14.6) ^a ≥ 65 years: 53 (12.9) ^a	≥ 4 non-ART: 15.3%	Higher percentage of female patients on polypharmacy: Male: 10.0% Female: 19.0% Participants aged ≥ 65 years were more likely to have polypharmacy than those aged 50 to 54 years (34% and 13%, respectively)	One or more hospitalisations in the previous year (PR 1.8, 95% CI: 1.1–3.1, p = 0.029) Had an internist's prescription (PR 3.6, 95% CI: 1.3–10.5, p = 0.02) Frailty score 5–6 (PR 10.6, 95% CI: 1.4–78, p = 0.02) Frailty score ≥ 7 (PR 17.4, 95% CI: 2.4–126.5, p = 0.005)
Zheng C, 2022	China	185	Observational, cross-sectional ≥ 50 years	137 (73.5) ^a	58.8 (50-84) ^b	≥ 5 medications: 40%	NA	NA
Funke B, 2021	Germany	453	Observational, cross-sectional Adult PLWH treated with ART	355(78.4) ^a	46 (18-86) ^c	≥ 4 medications: 21.2%	NA	NA
Ruelian AL, 2021	France	239	Observational, cross-sectional ≥ 65 years treated with ART receiving at least one comedication	187(78.2) ^a	69 (67-73) ^c	≥ 5 non-ART: 51.9%	NA	NA
Deutschmann E, 2021	Switzerland	9298	Observational ≥ 16 years from the Swiss HIV Cohort Study	6735(72) ^a	51(43-58) ^c	≥ 5 non-ART: 14%	Higher percentage of patients on polypharmacy in older age groups of PLWH	NA
Halloran MO, 2019	United Kingdom	1376 (1072 PLWH)	Observational, prospective Adult ≥ 20 years	≥ 50 years PLWH: 612(87.7) ^a < 50 years PLWH: 43(20-49) ^c	≥ 50 years PLWH: 56 (50-82) ^c < 50 years PLWH: 459(65.8) ^a < 50 years (PLWH): 180(48.1) ^a	≥ 5 non-ART: ≥ 50 years (PLWH): 459(65.8) ^a < 50 years (PLWH): 180(48.1) ^a	NA	NA
Jiménez-Guerrero L, 2018	Spain	242	Observational, retrospective Adult ≥ 50 years treated with ART	189(78) ^a	57.5 (54-62) ^c	≥ 5 outpatient prescriptions: 48.3%	NA	NA
Bastida C, 2017	Spain	197	Observational, cross-sectional Adult ≥ 65 years treated with ART and had a chronic medication record	157(79.7) ^a	71.2(5.4) ^d	≥ 5 drugs: 93%	NA	NA
Greene M, 2014	United States	89	Observational, retrospective Community dwelling adults ≥ 60 years treated with ART	84(94) ^a	63(60-82) ^e	≥ 5 non-ART: 66 (74) ^a ≥ 9 non-ART: 43 (48) ^a	NA	NA

ART: antiretroviral therapy, NA: not available/not applicable, PLWH: people living with HIV, aOR: adjusted odds ratio, aPR: adjusted prevalence ratio

^aValues are n (%) ^bValues are median (interquartile range) ^cValues are mean (SD) ^dValues are mean (range)

Table S2. Summary of studies reporting data on the prevalence of drug-drug interactions between ART and non-ART medication in PLWH affected by polypharmacy

First author, year	Country	Sample size	Study design and main patients' characteristics	Male, n (%)	Age (years)	Prevalence of polypharmacy in PLWH	Percentage of patients with at least one DDI	Classification of DDIs by severity	Other relevant findings
Zheng C, 2022	China	185	Observational, cross-sectional ≥ 50 years	137 (73.5) ^a	58.8 (50-84) ^b	≥ 5 medications: 40%	19.45%	Total number of DDIs: N = 45 Red flags: 1(2.2) ^a Amber flags: 37 (82.2) ^a Yellow flags: 7 (15.5) ^a	Higher percentage of potential DDIs in those patients with polypharmacy: 52% with polypharmacy and 6.1% without polypharmacy
El Moussaoui M, 2020	Belgium	1038 (2016) 911 (2012)	Observational, retrospective Outpatient adults treated with ART	2016: 574 (55.3) ^a 2012: 493 (54.1) ^a	2016: ≤ 50: 650(62.62) ^a 50-64: 320(30.83) ^a ≥ 65: 68(6.55) ^a 2012: ≤ 50: 647(71.0) ^a 50-64: 225(24.7) ^a ≥ 65: 39(4.3) ^a	≥ 5 non-ART: 2016: 20.13% 2012: 17.01%	NA	Percentage of patients affected by DDIs of different severities: 2012: Red flags: 37(4.1) ^a Orange flags: 349(38.3) ^a 2016: Red flags: 45(4.3) ^a Orange flags: 396(38.1) ^a Total number of DDIs: 2012: Red flags: 68(6) ^a Orange flags: 1070(94) ^a 2016: Red flags: 85(7) ^a Orange flags: 1137(93) ^a	NA
Kunimoto Y, 2021	Japan	71	Observational, cross-sectional Outpatient adults treated with ART for at least 48 weeks	67 (94.4) ^a	45 (21-79) ^c	≥ 5 non-ART: 35.2%	29.6%	Total number of DDIs: N = 44 Risk X (avoid combination): 3(6.8) ^a Risk D (consider therapy modification): 41(93.2) ^a	Higher median number of non-ART medications in the group of patients affected by potential DDIs: 6 vs. 3, p < 0.001 Higher percentage of potential DDIs in those patients with polypharmacy: 81% with polypharmacy and 26.7% without polypharmacy, p < 0.001 Potential DDIs that could reduce the effect of antiretrovirals in 21 cases
Murray MM, 2021	United States	621	Observational, cross-sectional ≥ 50 years treated with ART	521(83.9) ^a	≤ 15 medications: 57(54-62) ^c ≥ 15 medications: 59(55-65.5) ^c	NA	84%	Percentage of patients affected by DDIs of different severities: ≥ 15 medications: 58(98.3) ^a Potential: 48(82.8) ^a Do not coadminister: 10(17.2) ^a ≤ 15 medications: 464(82.6) ^a Potential: 432(93.1) ^a Do not coadminister: 32(6.9) ^a	Higher percentage of patients with at least one DDI in those patients taking a higher number of medications: ≤ 15 medications: 82.6% ≥ 15 medications: 98.3%
Funke B, 2021	Germany	453	Observational, cross-sectional Adult PLWH treated with ART	355(78.4) ^a	46 (18-86) ^c	≥ 4 medications: 21.2%	NA	Percentage of patients affected by DDIs of different severities: Potential: 41.5% Do not coadminister: 1.3%	NA
Loste C, 2020	Spain	91	Observational, cross-sectional ≥ 65 years receiving comprehensive geriatric assessment	74 (81.3) ^a	72.1 (5.6) ^d	≥ 5 non-ART: 59.3%	45.1%	Percentage of patients affected by DDIs of different severities: Red flags: 2(2.2) ^a Total number of DDIs: N= 86 Red flags: 3(3.5) ^a	NA
Ruellan AL, 2021	France	239	Observational, cross-sectional ≥ 65 years treated with ART receiving at least one comedication	187(78.2) ^a	69 (67-73) ^c	≥ 5 non-ART: 51.9%	25.1%	Percentage of patients affected by DDIs of different severities: Red flags: 17(7.1) ^a Orange flags: 48(20) ^a Yellow flags: 9(3.8) ^a Total number of DDIs: N= 126 (different DDIs: 72) Red flags: 23(31.9) ^a Amber flags: 41(56.9) ^a Yellow flags: 8(11.1) ^a	NA
Okoli C, 2020	United Kingdom	4630	Observational, cross-sectional Outpatient adults treated with ART	2609(56.3) ^a	47 (39-54) ^c	≥ 5 non-ART: 17%	NA	Total number of DDIs (red- plus amber-flag): N = 1498 Red flags: 40(2.7) ^a Amber flags: 1458(97.3) ^a	NA
Gimeno-Gracia M, 2020	Spain	74	Observational, cross-sectional Adult ≥ 65 years treated with ART	64(86.5) ^a	69 (66.7-72.0) ^b	Prescription of at least 6 active ingredients including ART: 71.6% Concomitant use of 11 active ingredients or more: 25.7%	55.4%	Percentage of patients affected by DDIs of different severities (the study described not only DDIs between non-ART and ART but also between non-ART): Potential: 55.4% Contraindicated: 12.2% Total number of DDIs: N= 110 Potential: 97(88.2) ^a Contraindicated: 13(11.8) ^a	NA
Deutschmann E, 2021	Switzerland	9298	Observational ≥ 16 years from the Swiss HIV Cohort Study	6735(72) ^a	51(43-58) ^c	≥ 5 non-ART: 14%	29% Of those receiving ≥ 1 comedication (n = 6324): 43%	Percentage of patients affected by DDIs of different severities (of those receiving ≥ 1 comedication, n = 6324): Red flags: 153(2) ^a Orange flags: 2093(33) ^a Yellow flags: 1259(20) ^a Total number of DDIs: N=5148 Red flags: 158(3.1) ^a Amber flags: 3311(64.3) ^a Yellow flags: 1679 (32.6) ^a	NA
Pontelo BM, 2020	Brazil	304	Observational, retrospective Outpatient adults	202 (66.4) ^a	< 50: 228(75) ^a ≥ 50: 72(23.7) ^a	≥ 5 medications: 23.3%	50%	Total number of DDIs: N = 465 Potential: 442(95.1) ^a Clinically significant: 23(4.9) ^a	Participants older than 50 years had a significantly higher number of DDIs A higher number of utilised non-ART was associated with a higher number of DDIs
Chen R, 2020	China	1804	Observational, prospective	1430(79.27) ^a	42.9(18-85) ^b	NA	19.15% of those taking comedications	Total number of potential DDIs: N=55 Do not coadminister (grade IV): 4(7.2) ^a	NA
Fernández Cañabate S, 2019	Spain	154	Observational, cross-sectional Outpatient adults ≥ 50 years treated with ART (collecting ART for at least 1 year)	123 (79.9) ^a	56.3(50-73) ^d	≥ 5 drugs including ART: 40.3%	NA	Percentage of patients affected by DDIs of different severities: Potential and Contraindicated: 52(33.7) ^a Week: 27(17.5) ^a Total number of DDIs: N=134 Potential plus contraindicated: 102(76.1) ^a - Potential: 96.1% - Contraindicated: 3.9% Weak: 32(23.9) ^a	NA
López-Centeno B, 2020	Spain	22 945	Observational, cross-sectional Dispensation registry of community and hospital pharmacies from the Madrid	78.3%	48(39-54) ^c	≥ 5 non-ART: 32.94%	NA	Percentage of patients affected by DDIs of different severities: Red flags: 3.18% Orange flags: 18.27% Yellow flags: 10.30% Green flags:	NA

			Regional Health Service including paediatric patients					51.48% Grey flags: 0.11%	
Halloran MO, 2019	United Kingdom	1376 (1072 PLWH)	Observational, prospective Adult ≥ 20 years	≥ 50 years PLWH: 612(87.7) ^a < 50 years PLWH: 302(80.8) ^a	≥ 50 years PLWH: 56 (50-82) ^c <50 years PLWH: 43(20-49) ^c	≥ 5 non-ART: ≥50 years (PLWH): 459(65.8) ^a <50 years (PLWH): 180(48.1) ^a	≥ 50 years (PLWH): 400 (57.3) ^a < 50 years (PLWH): 121 (32.4) ^a	Total number of DDIs: ≥ 50 years (PLWH, n=913): Contraindicated: 25(2.7) ^a Potential: 888 (97.3) ^a < 50 years (PLWH, n=201): Contraindicated: 4 (2) ^a Potential: 197 (98) ^a	NA
Jiménez-Guerrero L, 2018	Spain	242	Observational, retrospective Adult ≥ 50 years treated with ART	189(78) ^a	57.5 (54-62) ^c	≥ 5 outpatient prescriptions: 48.3%	45.5%	Percentage of patients affected by DDIs of different severities: Severe: 34(14) ^a Total number of DDIs: Moderate: 197(81) ^a Severe: 46(18.9) ^a	NA
Bastida C, 2017	Spain	197	Observational, cross-sectional Adult ≥ 65 years treated with ART and had a chronic medication record	157(79.7) ^a	71.2(5.4)d	≥ 5 drugs: 93%	65%	Percentage of patients affected by DDIs of different severities: Severe: 6.6%	Total number of DDIs, n=259: Pharmacokinetic: 92% Pharmacodynamic: 8%
Greene M, 2014	United States	89	Observational, retrospective Community dwelling adults ≥ 60 years treated with ART	84(94) ^a	63(60-82) ^e	≥ 5 non-ART: 66 (74) ^a ≥ 9 non-ART: 43 (48) ^a	NA	Percentage of patients affected by DDIs of different severities: X (Avoid combination): 10(11) ^a D (Consider therapy modification): 67(70) ^a Total number of DDIs, n=152: X (Avoid combination): 9(6) ^a D (Consider therapy modification): 142(93,4) ^a	NA
Holtzman C, 2013	United Kingdom	3810	Observational, cross-sectional Outpatient adults treated with ART	3001 (79) ^a	<u>Median age:</u> 46 <u>Age groups:</u> ≤40: 1189 (31.20) ^a 40-49: 1615 (42.38) ^a ≥50: 1006 (26.40) ^a	≥ 5 non-ART: 39%	NA	Percentage of patients affected by DDIs of different severities: Contraindicated: 267(7) ^a Moderate: 1267(33) ^a	NA

ART: antiretroviral therapy, DDI: drug-drug interaction; NA: not available/not applicable, PLWH: people living with HIV. ^aValues are n (%) ^bValues are mean (range), ^cValues are median (interquartile range), ^dValues are mean (SD), ^eValues are median (range).