P201

Tracing the evolution of polypharmacy and drug-drug interactions in people living with HIV

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INTRODUCTION

•**Increased Life Expectancy:** The advent of antiretroviral therapy has significantly improved life expectancy in people living with HIV. As a result, there is a growing proportion of ageing individuals within the HIV-positive population.[1,2]

•**Comorbidities & Polypharmacy:** Comorbidities increase with age, often requiring multiple medications, leading to a rise in polypharmacy.[1,2]

•**Evolving drug-drug interactions:** Frequent drug-drug interactions continue to evolve with the introduction of new antiretroviral drugs.[2,3]

MATERIALS AND METHODS

•**Study Design:** Retrospective cohort study.

•**Study Period:** January 2017 to December 2022.

•**Population:** 812 HIV-infected participants, aged over 18, with at least one annual consultation. The study was conducted at the University Hospital of Liège, Belgium

•**Data Analysis:** Both antiretroviral and non-antiretroviral treatments were reviewed for each participant. University of Liverpool HIV drug interactions database[4] was used to identify contraindicated drug-drug interactions (red flag).

RESULTS

Table 1 : Number of non ARV comedications

Table 2 : Number of contraindicated drug-drug interactions

(N = 812 participants with at least one consultation per year from 2017 to 2022).

	2017	2018	2019	2020	2021	2022	p-value
None	149 (18.3%)	124 (15.3%)	110 (13.6%)	121 (14.9%)	101 (12.4%)	93 (11.4%)	<0.0001 [a]
At least one	663 (81.7%)	688 (84.7%)	702 (86.4%)	691 (85.1%)	711 (87.6%)	719 (88.6%)	<0.0001 [a]
1-4	495	509	516	480	481	484	
≥ 5	168	179	186	211	230	235	<0.0001 [a]
Average ± SD	2.7 ± 2.8	2.9 ± 2.9	3.1 ± 3.1	3.2 ± 3.1	3.4 ± 3.2	3.5 ± 3.2	<0.0001 [b]
Median (Q1-Q3)	2 (1 – 4)	2 (1 – 4)	2 (1 – 4)	2 (1 – 5)	3 (1 – 5)	3 (1 – 5)	
Min - Max	0 - 17	0 - 18	0 - 23	0 - 21	0 - 23	0 - 20	

[a] Generalized Estimating Equations Model (GEE), [b] ANOVA mesures répétées

The number of comedications and polypharmacy significantly increased during the study period (p<0.0001).

	2017	2018	2019	2020	2021	2022	p-value
Number of participants	812	812	812	812	812	812	
Number (%) of participants with DDIs	31 (3.8)	29 (3.6)	20 (2.5)	19 (2.3)	24 (3.0)	18 (2.2)	0.064 [a]
Number of DDIs							
0	781 (96.2)	783 (96.4)	792 (97.5)	793 (97.7)	788 (97.0)	794 (97.8)	
1	24 (3.0)	20 (2.5)	12 (1.5)	13 (1.6)	15 (1.9)	13 (1.6)	
2	2 (0.2)	7 (0.9)	6 (0.7)	4 (0.5)	8 (1.0)	5 (0.6)	
3	2 (0.2)	2 (0.2)	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	
4	3 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	
5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	
Total number of DDIs	46	40	31	27	36	23	0.044 [b]

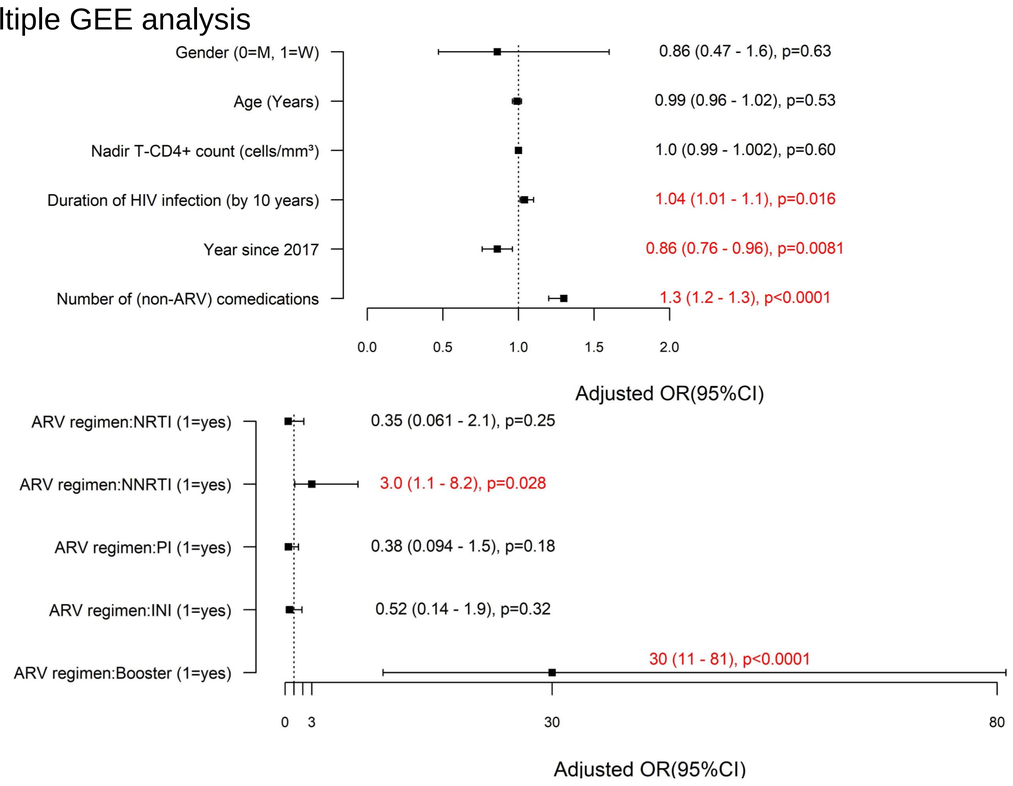
[a] Generalized Estimating Equations Model (GEE); [b] Linear model

The number of patients with at least one contraindicated interaction decreased, but this reduction was not statistically significant (p=0.064). The total number of drug-drug interactions decreased between 2017 and 2022 (p=0.044).

Figure 1: Factors influencing the presence of contraindicated interactions.

Figure 2: Influence of ARV type on the presence of DDIs

(N=812 participants with at least one consultation per year from 2017 to 2022) – Multiple GEE analysis



Boosters (cobicistat and ritonavir) significantly increased the risk of drug-drug interactions (p<0.0001). NNRTIs also increased the risk of drug-drug interactions (p=0.028).

The number of non-ARV co-medications increased the risk of DDIs (p<0.0001). A longer time since the first known HIV test increased the likelihood of presenting a drug-drug interaction (p=0.016). Over time (in years since 2017), the number of drug-drug interactions decreased (p=0.0081).

When adjusting the model for the number of non-ARV co-medications, the risk of CI interactions decreased over time (p=0.0081) but increased with the number of non-ARV co-medications (p<0.0001).

Table 3: Contraindicated drug-drug interactions: ARV treatments involved in interactions

Table 4: Contraindicated drug-drug interactions: Non-ARV treatments involved in interactions

(N=812 patients with at least one consultation per year from 2017 to 2022)

	Year					
	2017	2018	2019	2020	2021	2022
ARV implicated						
EFV/FTC/TDF	.	1	.	.	.	.
F/TAF	1	1	1	.	.	.
RPV	1	.	.	.	.	.
RPV/FTC/TDF	1	1	2	2	3	3
E/c/F/TAF	13	17	8	6	8	5
E/c/F/TAF/DRV	.	1	2	1	1	1
DOL/RPV	.	.	.	1	1	1
LPV/r	7	.	.	.	.	.
RPV/FTC/TAF	1	.	.	.	2	1
DRV/r	8	14	10	8	12	8
ATZ	3	2	1	2	1	.
ATZ/r	2	.	2	2	2	.
DRV/c	5	2	3	4	3	2
E/c/F/TDF	4	1	1	.	.	.
D/c/F/TAF	.	.	1	1	3	2
Total number of DDIs	46	40	31	27	36	23

	Year					
	2017	2018	2019	2020	2021	2022
Apixaban	.	.	.	.	1	2
Budesonide	.	1	.	.	.	.
budesonide (topic)	9	5	8	5	6	4
Carbamazepine	1	4	1	.	.	.
Clopidogrel	3	1	2	1	1	.
Domperidon	.	1	.	.	.	.
Esomeprazole	1	.	.	2	3	2
Flecainide	1	1	.	.	.	.
fluticasone (topic)	5	2	2	3	4	3
Haloperidol	1	.	.	.	.	.
Lercanidipine	5	5	7	6	6	3
Red yeast rice	4	2	1	.	.	.
mometasone (topic)	2	6	4	3	4	3
Omeprazole	1	1	1	2	1	0
Pantoprazole	4	2	2	1	3	3
birth control pill	.	1	.	.	.	.
Piroxicam	1	1	.	.	.	.
quetiapine	.	.	1	1	1	.
rivaroxaban	1	1	.	.	4	2
simvastatine	6	6	2	3	2	1
ticagrelor	1	.	.	.	.	.
Total number of DDIs	46	40	31	27	36	23

In 2022, 43.48% (10/23) of drug-drug interactions involved topical corticosteroids, while proton pump inhibitors contributed to 21.74% (5/23) of cases. Among antiretrovirals, DRV/r was associated with 34.78% (8/23) of the drug-drug interactions, and E/c/F/TAF accounted for 21.74% (5/23).

CONCLUSION

•The ageing population of people living with HIV and the increase in polypharmacy contribute to a higher risk of drug-drug interactions.

•Despite advances in antiretroviral treatments, a significant number of contraindicated drug-drug interactions persist.

•In our study, the total number of drug-drug interactions decreased from 2017 to 2022 (p=0.044)

•In 2022, the most involved drugs in drug-drug interactions were corticosteroids and proton pump inhibitors. Among antiretrovirals, DRV/r and E/c/F/TAF were the most frequently implicated.

•Clinicians must remain vigilant regarding drug-drug interactions, particularly in patients with polypharmacy. Implementing drug-drug interactions-checking tools is crucial to alert healthcare providers and reduce the number of contraindicated interactions.

References :

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