

AGING IN HIV

BARCELONA – BUENOS AIRES

8TH EDITION

Antiretroviral therapy in older people and polypharmacy

Catia Marzolini

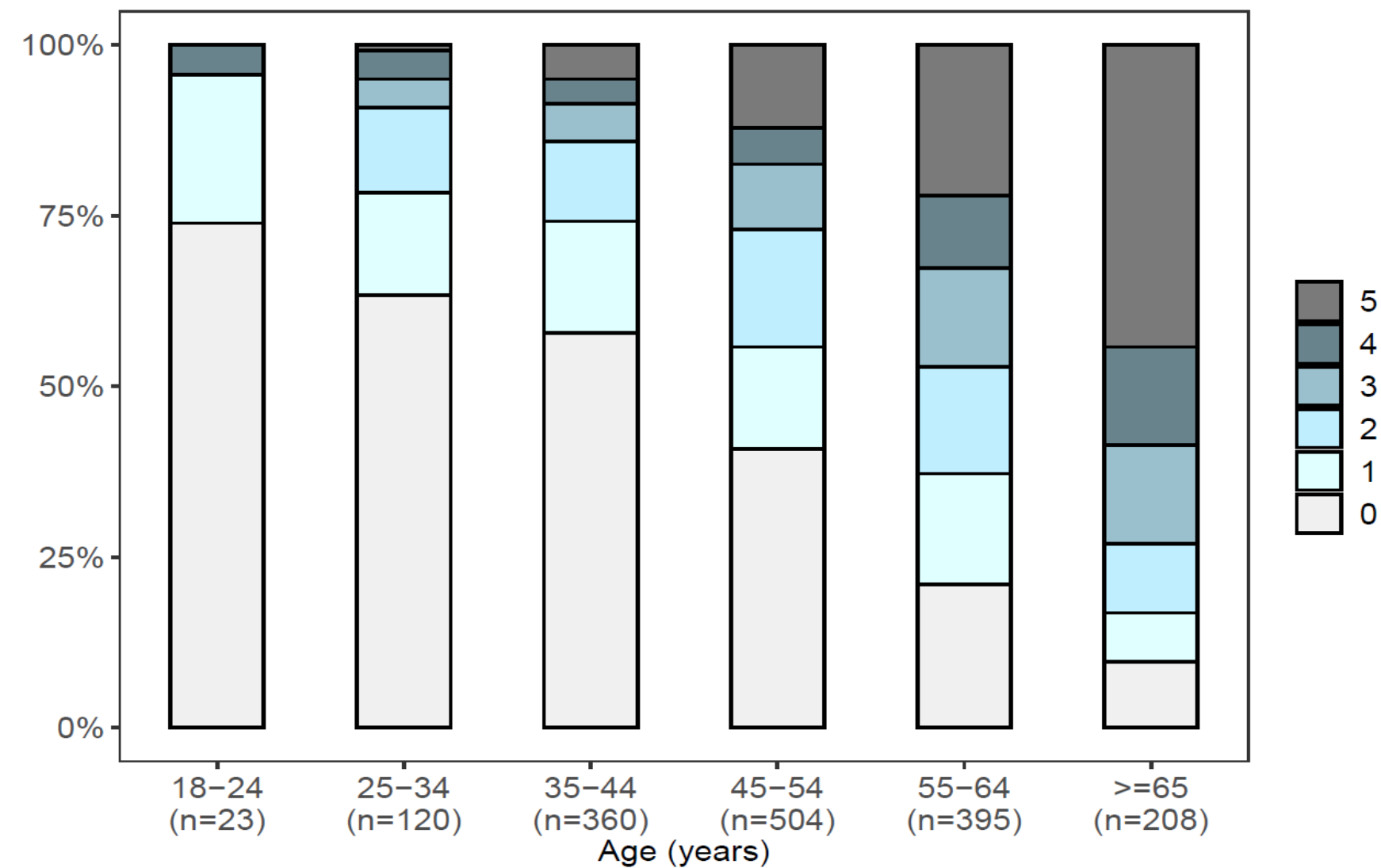


Aging of the HIV population and related pharmacological issues

- Globally, 7.5 million people with HIV are ≥ 50 years, representing about 20% of all people with HIV.

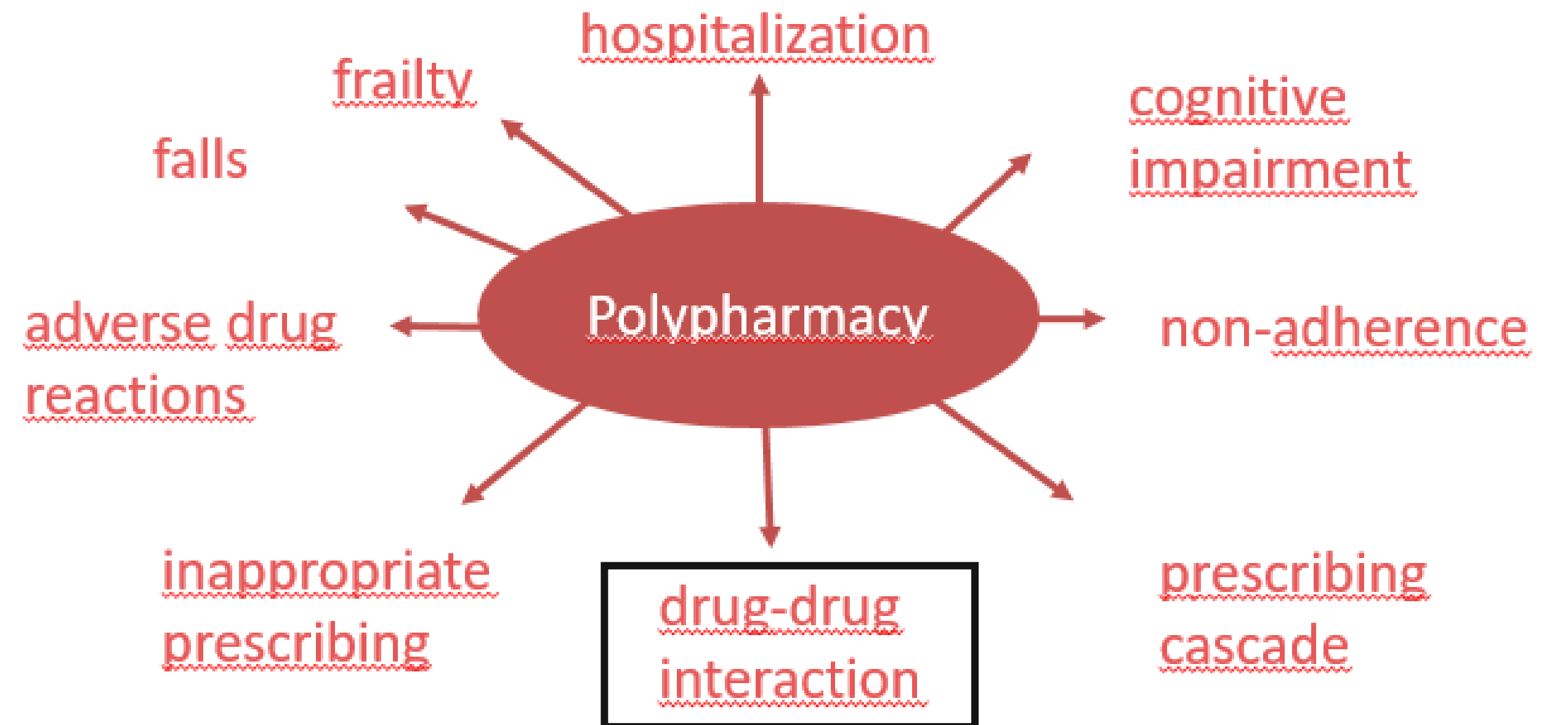
=> Increased number of comorbidities and comedications with aging

Number of non- HIV medications with age



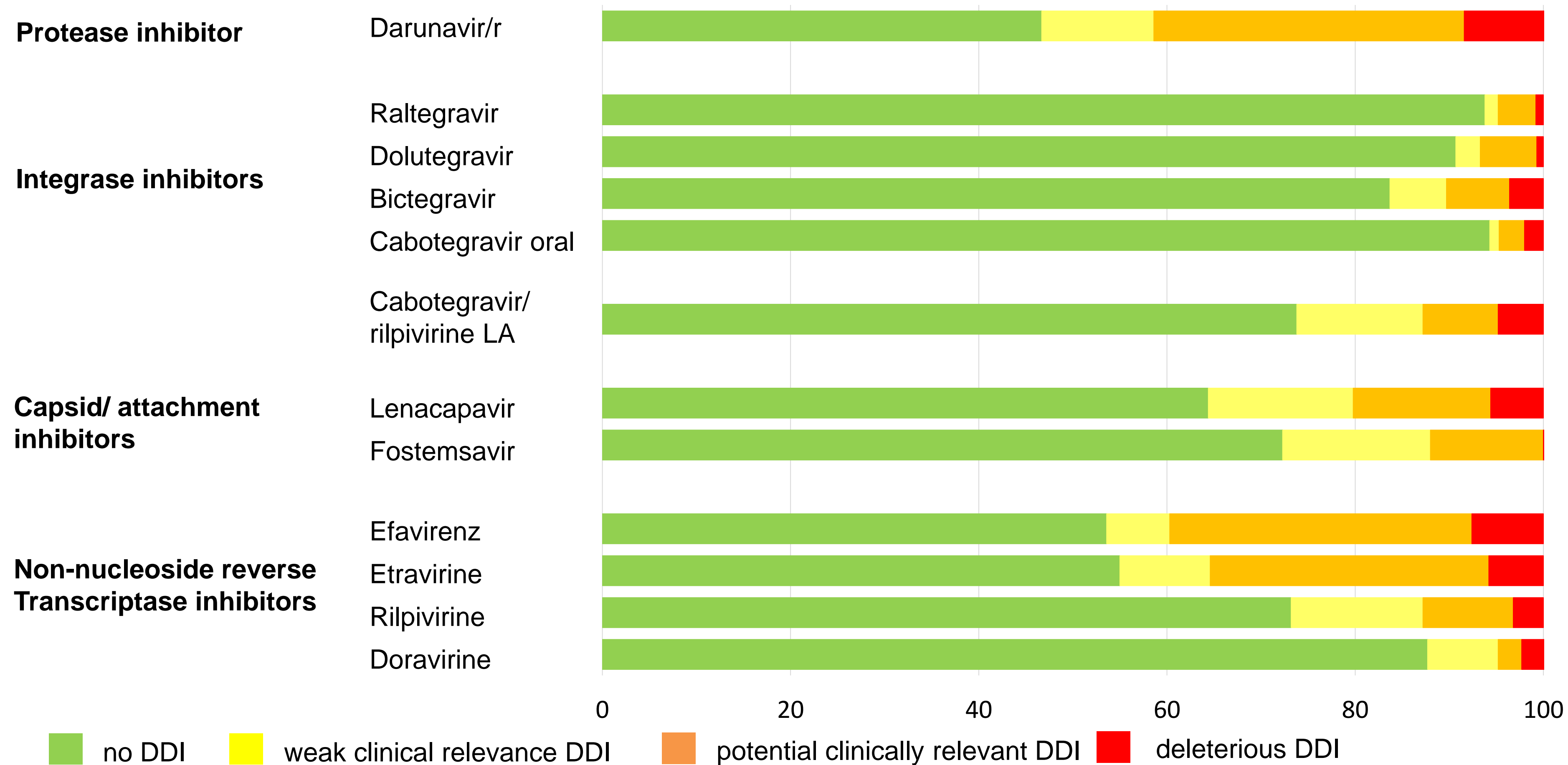
Polypharmacy defined as concurrent use of ≥ 5 medications.

Consequences of polypharmacy



Autenrieh CS et al. PLoS One 2018; UNAIDS (data in 2019) available at <http://aidsinfo.unaids.org>; Pallela FJ et al. AIDS 2019, Pelchen-Matthews A et al. AIDS 2018; Courlet P et al. OFID 2019

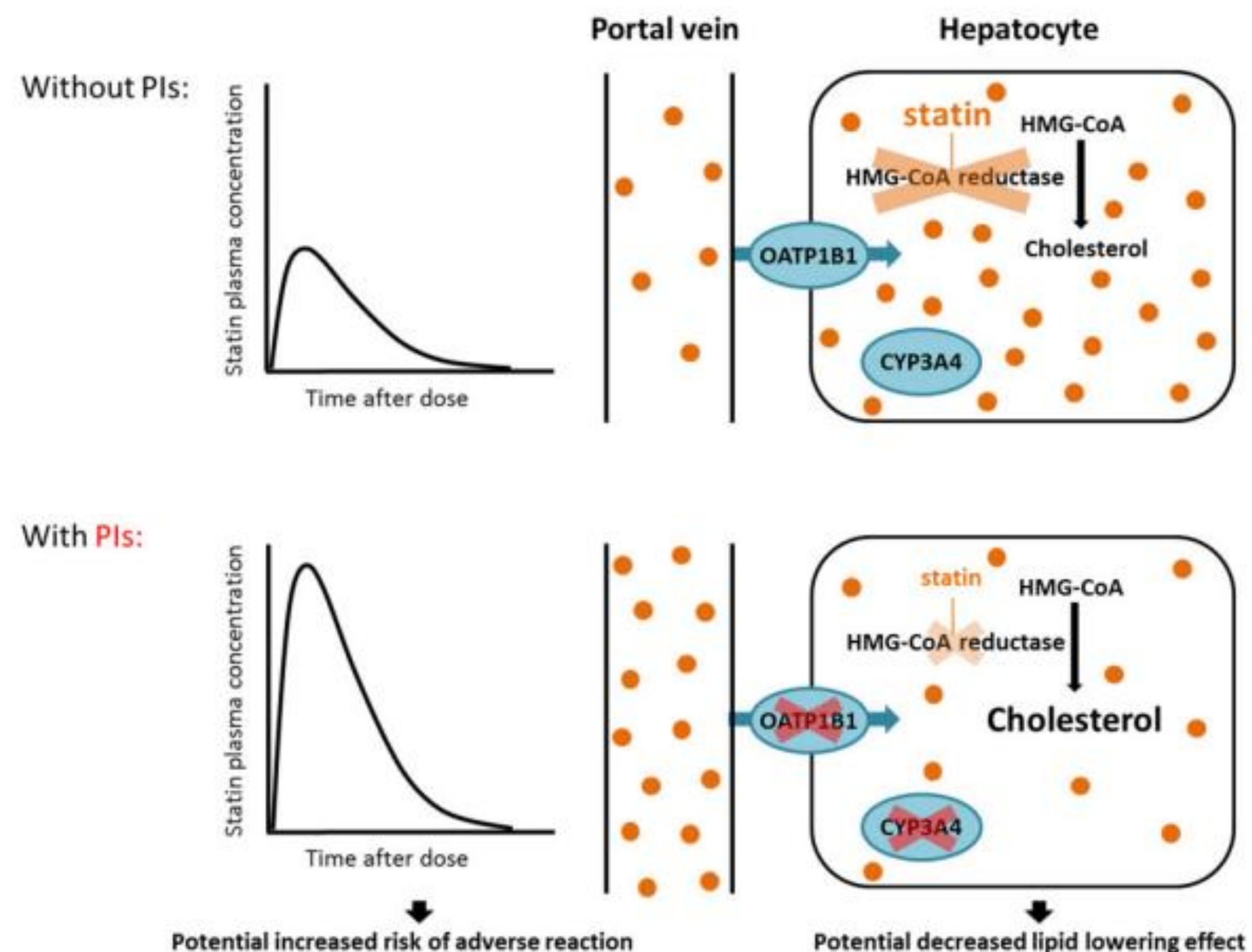
Drug interactions profiles of antiretrovirals considering 1000 medications



adapted from Back D & Marzolini C. J Int AIDS Soc 2020; www.hiv-druginteractions.org

Protease inhibitors are perpetrators of drug-drug interactions

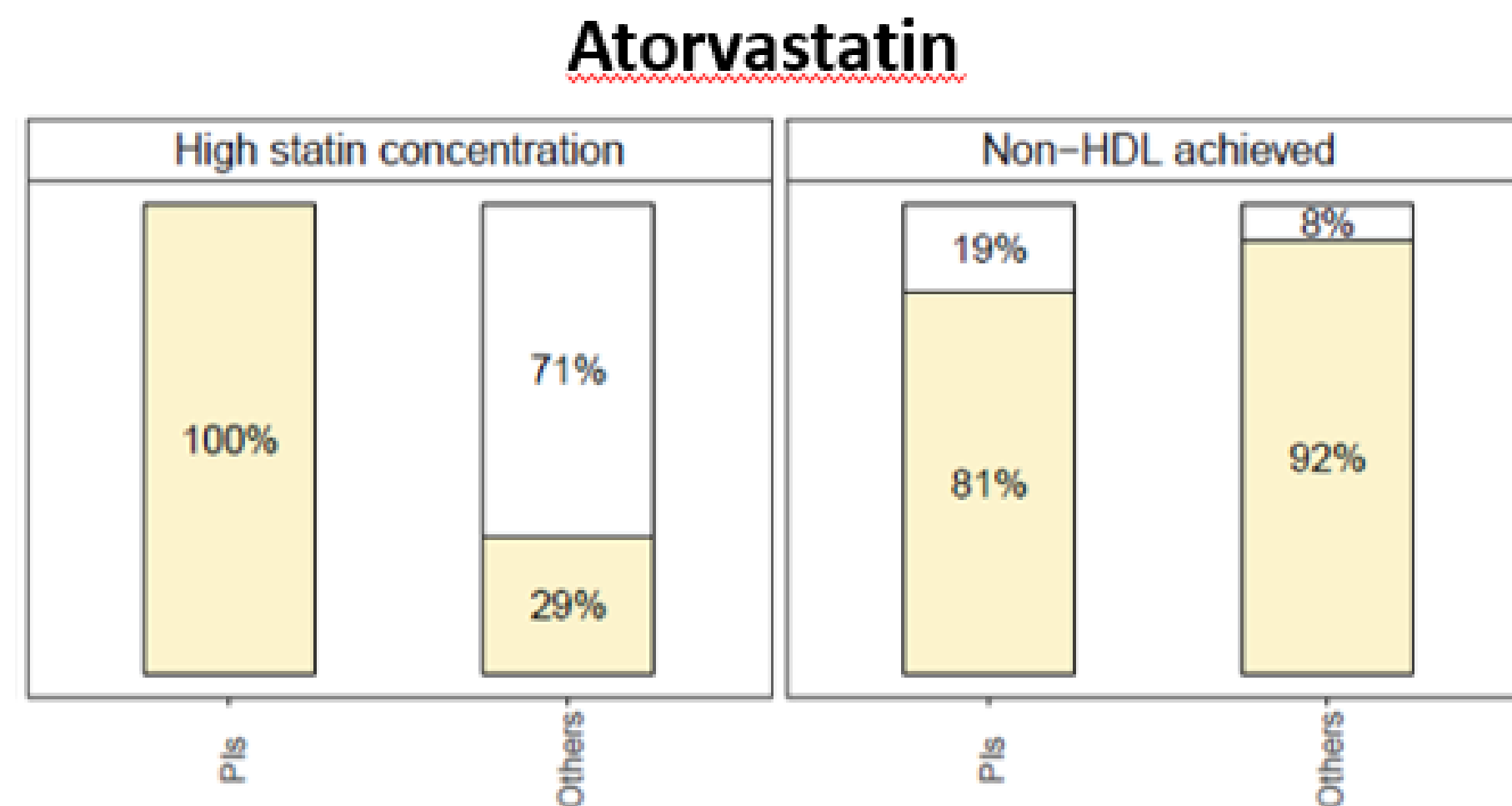
- Statins enter the liver (site of action and metabolic elimination) via hepatic transporter OATP1B1.
- Protease inhibitors inhibit OATP1B1: atazanavir > lopinavir > darunavir > ritonavir, cobicistat => PK/PD interaction.



www.hiv-druginteractions.org, Annaert P et al. Xenobiotica 2010; Courlet P et al. J Antimicrob Chemother 2020

Achievement of lipid targets in people with HIV on statin

- 175 people with HIV on antiretroviral treatment and receiving a statin.
- Individual non-HDL and total cholesterol target values set using the Framingham score and the European AIDS Clinical Society recommendations.



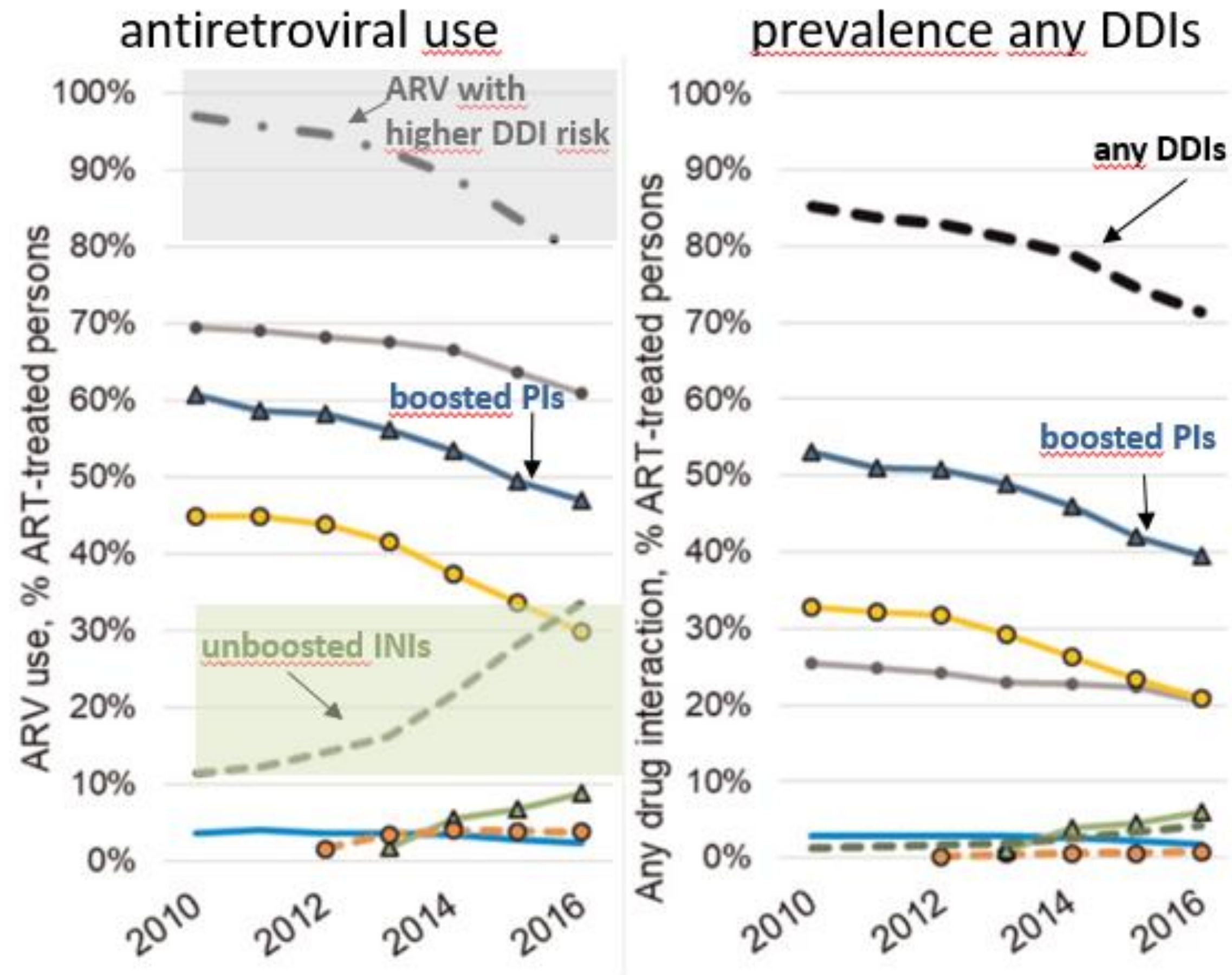
Yellow bars = % statin prescriptions with high statin plasma concentration and achievement of non-HDL-cholesterol targets. Others = treatment containing dolutegravir, raltegravir or rilpivirine.

- ⇒ Despite high concentrations of statins, non-HDL targets were less often achieved with protease inhibitors based regimens likely due to both their inhibitory effects on OATP1B1 and their unfavourable effects on lipids.
- ⇒ Unboosted antiretrovirals should be favoured in individuals with refractory dyslipidemia.

Courlet P et al. J Antimicrob Chemother 2020

Prevalence of drug-drug interactions over the years

Evolving patterns of drug-drug interactions in HIV cohort in British Columbia, Canada



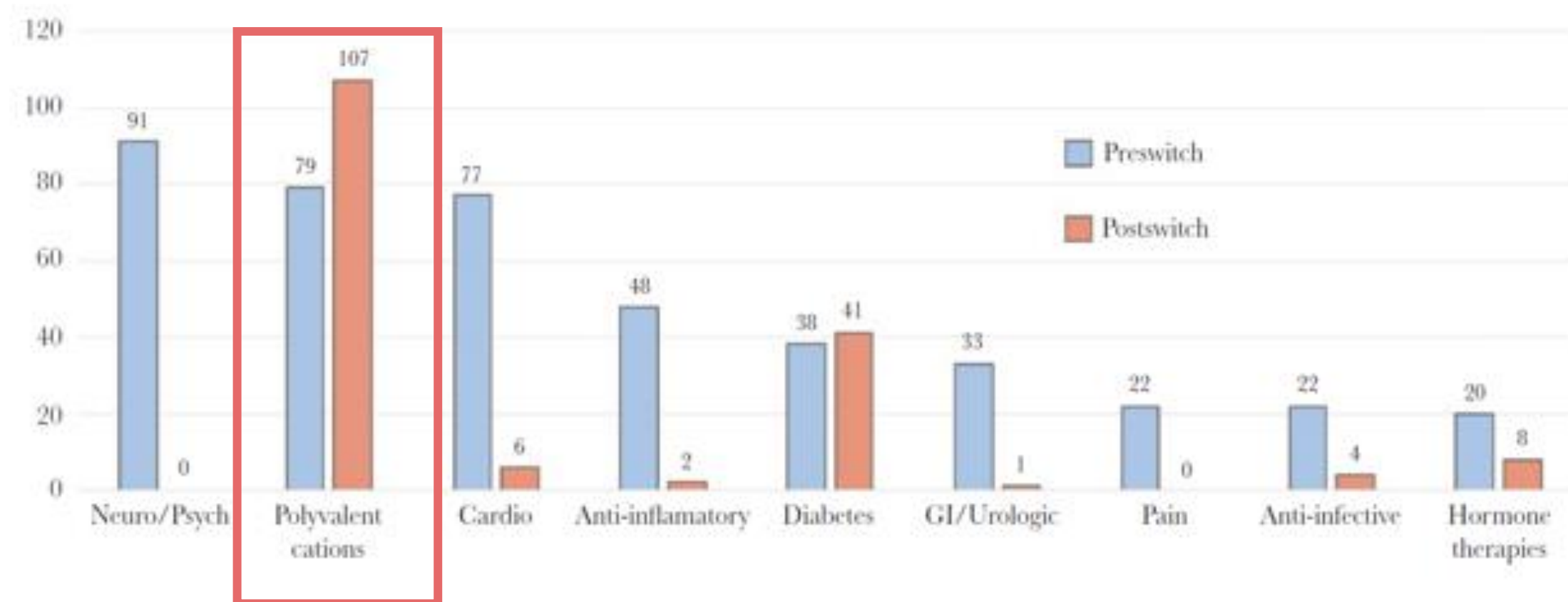
Lepik KJ et al. AIDS 2022

Drug interactions with unboosted integrase inhibitors

- Real-life studies evaluating prevalence of drug-drug interactions before and after switch to a bictegravir or dolutegravir containing regimen.

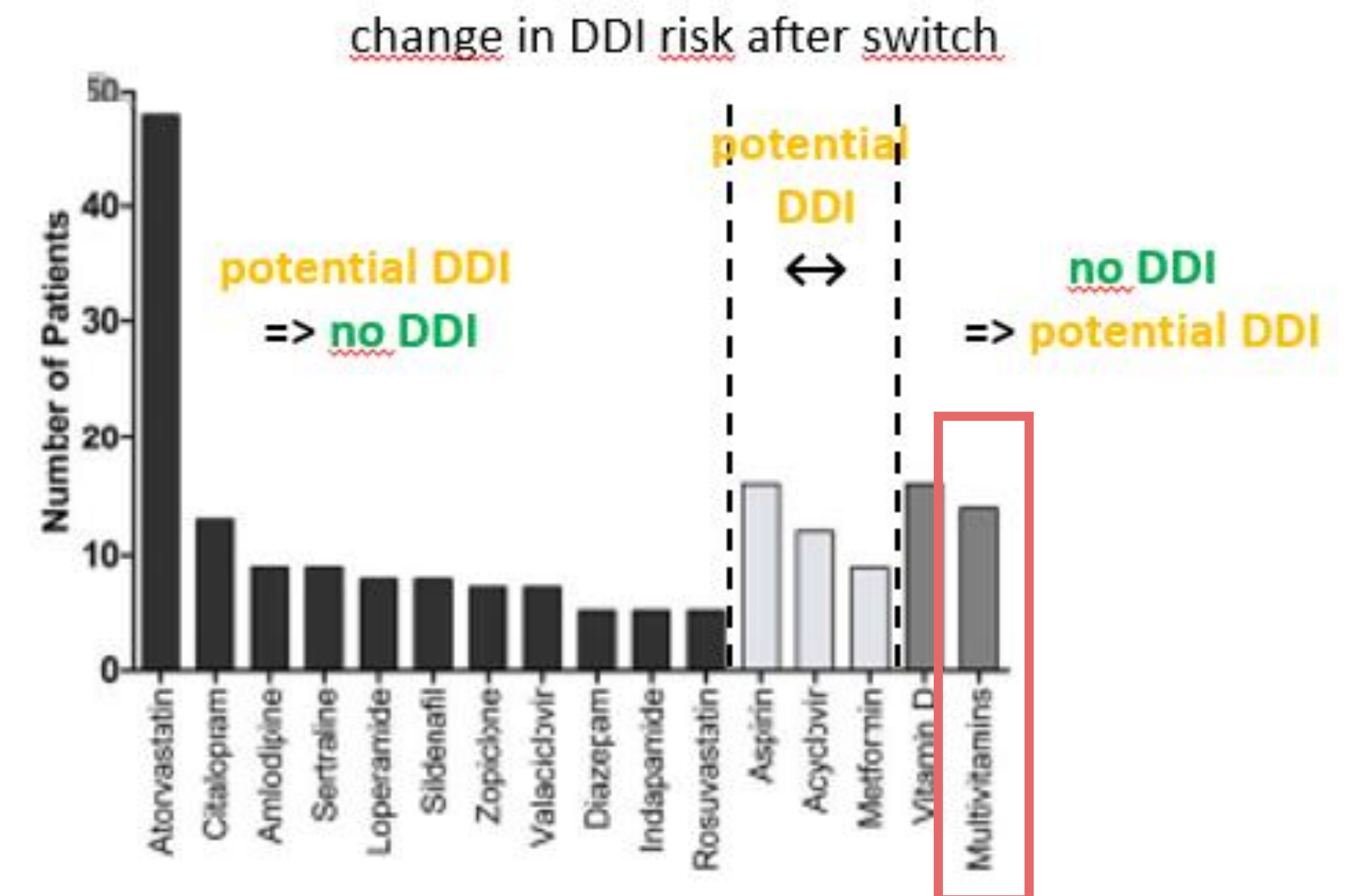
Prevalence interactions before and after switch to bictegravir/emtricitabine/tenofovir alafenamide

(n = 411 people with HIV)



Prevalence interactions before and after switch to bictegravir or dolutegravir containing regimens

(n = 151 people with HIV)



Schafer JJ et al. Open Forum Infect Dis 2020

Askari A et al. JAIDS 2023

Drug interactions with divalent cations are manageable

www.hiv-druginteractions.org



Integrase Inhibitors and Cations

EU SmPC ARV timing recommendations (related to co-medications intake)

Drug	Al/Mg antacids	Ca antacids	Multivitamins or supplements		
			Calcium	Iron	Magnesium
<u>Raltegravir</u>	Not recommended	No dose adjustment required Avoid with QD RAL	4h before or after Avoid with QD RAL	4h before or after Avoid with QD RAL	4h before or after Avoid with QD RAL
Elvitegravir	2–4h before/after	2–4h before/after	4h before or after	4h before or after	4h before or after
<u>Dolutegravir</u> Avoid if INI Resistant (EU)	2h before, 6h after	2h before, 6h after	2h before, 6h after	2h before, 6h after	2h before, 6h after
<u>Cabotegravir</u>	2h before, 4h after	2h before, 4h after	2h before, 4h after	2h before, 4h after	2h before, 4h after
<u>Bictegravir</u>	2h before, 2h after	No information in EU SmPC	Together without regard to food	Together with food or 2h before	With food

www.hiv-druginteractions.org/prescribing_resources/hiv-explainers-cations

Drug interactions with inducers remain an issue for most antiretrovirals

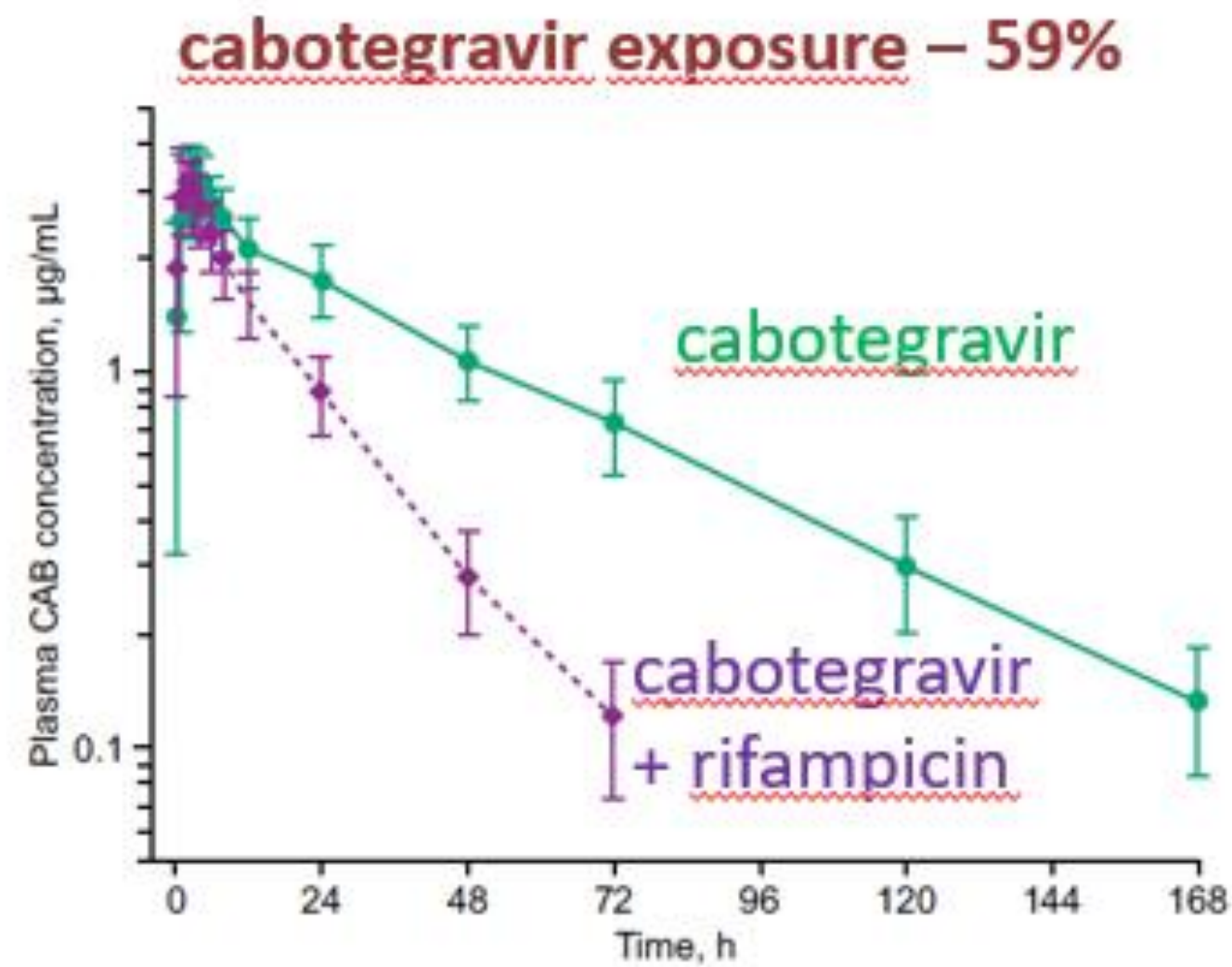
HIV drug	Rifampicin (strong inducer)		Rifabutin (moderate inducer)	
	PK interaction	Recommendation	PK interaction	Recommendation
Doravirine	AUC ↓88%/ C _{min} ↓97%	Do not coadminister	AUC ↓50%/ C _{min} ↓68%	Increase to 100 mg BID
Rilpivirine (oral)	AUC ↓80%/ C _{min} ↓89%	Do not coadminister	AUC ↓42%/ C _{min} ↓48%	Increase to 50 mg QD
Bictegravir	AUC ↓61%/ C _{min} ↓80%	Do not coadminister	AUC ↓38%/ C _{min} ↓56%	Do not coadminister
Cabotegravir (oral)	AUC ↓59%/ C _{min} ↓50%	Do not coadminister	AUC ↓23%/ C _{min} ↓26%	No significant DDI
Dolutegravir	AUC ↓57%/ C _{min} ↓86%	Increase to 50 mg BID	AUC ↓5%/ C _{min} ↓30%	No significant DDI
Raltegravir (400 mg BID)	AUC ↓40%/ C _{min} ↓61%	Increase to 800 mg BID, not recommended with raltegravir QD	AUC ↑5%/ C _{min} ↓20%	No significant DDI
CAB/RPV (injectable)	Not studied	Do not coadminister	Not studied	Do not coadminister
Lenacapavir	AUC ↓84%	Do not coadminister	Not studied	Do not coadminister
Fostemsavir	AUC ↓82%	Do not coadminister	AUC ↓20%/ C _{min} ↓41%	No significant DDI
TAF (25 mg)	TFV-DP AUC ↓36%	Standard dose as TFV-DP still 4 x higher than achieved with TDF alone	Not studied, recommendation based on rifampicin DDI	Standard dose as TFV-DP still 4 x higher than achieved with TDF alone
TDF	AUC ↓12%/ C _{min} ↓15%	No significant DDI	Not studied	No significant DDI

CAB = cabotegravir, RPV = rilpivirine, TAF: tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV-DP = tenofovir diphosphate (active entity)

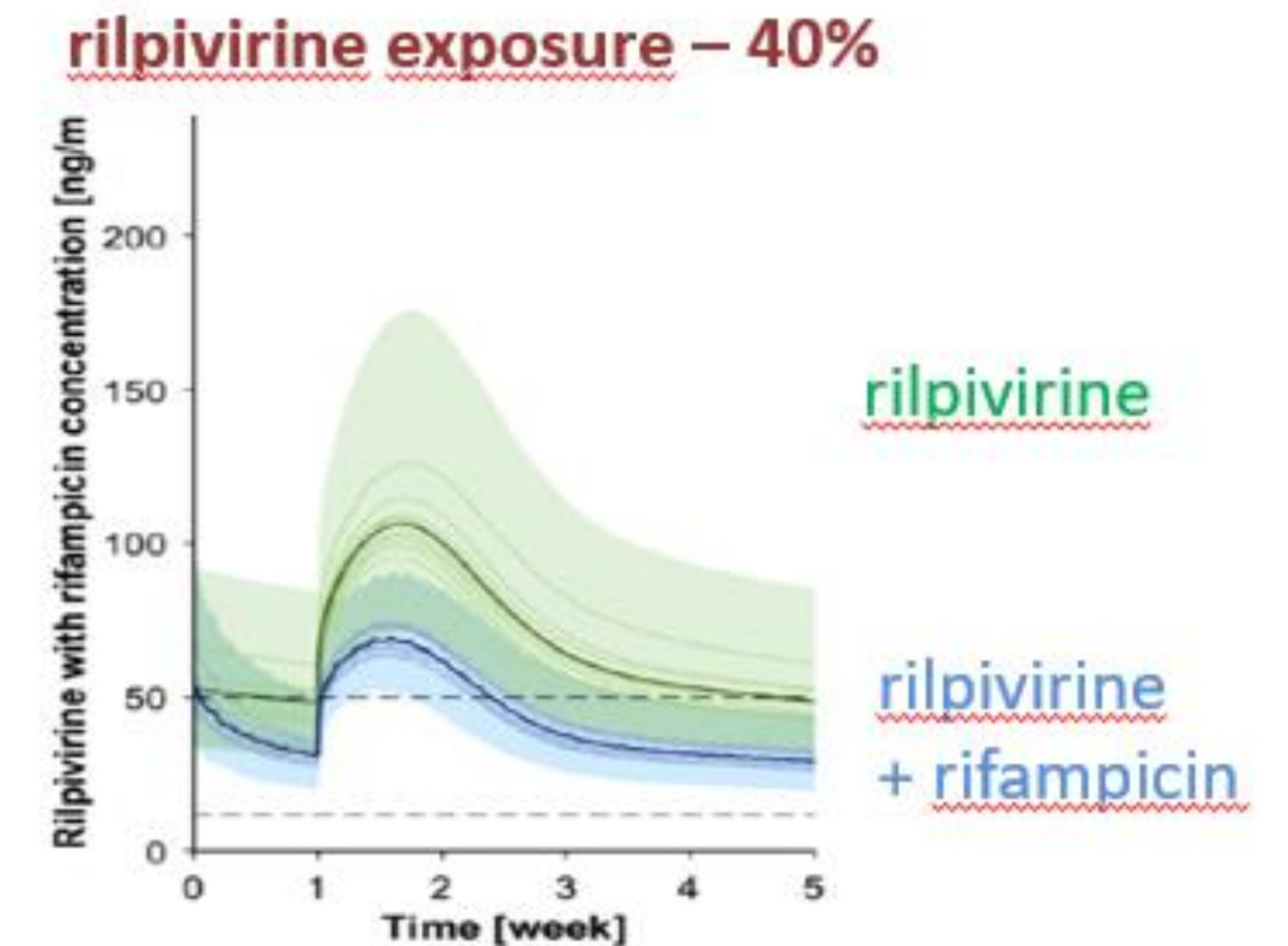
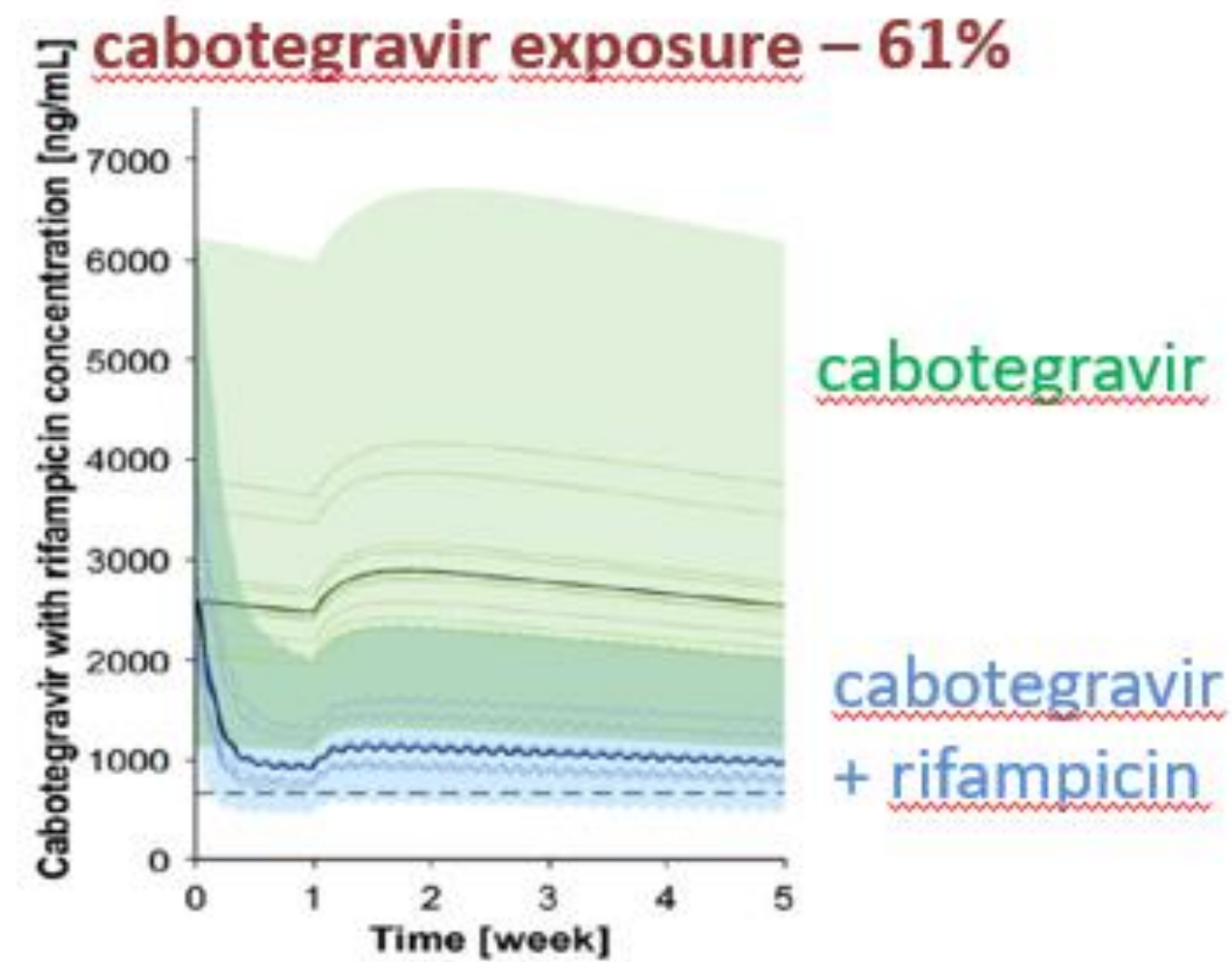
www.hiv-druginteractions.org

Drug interactions with intramuscular cabotegravir/rilpivirine

Oral cabotegravir + rifampicin



Intramuscular cabotegravir / rilpivirine (monthly administration) + rifampicin

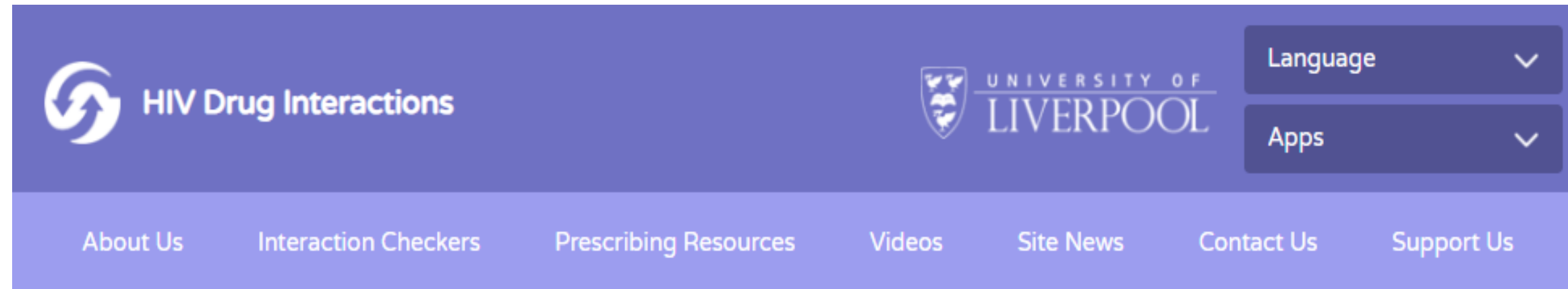


=> The interaction between intramuscular cabotegravir/rilpivirine and rifampicin cannot be overcome by reducing the dosing interval.

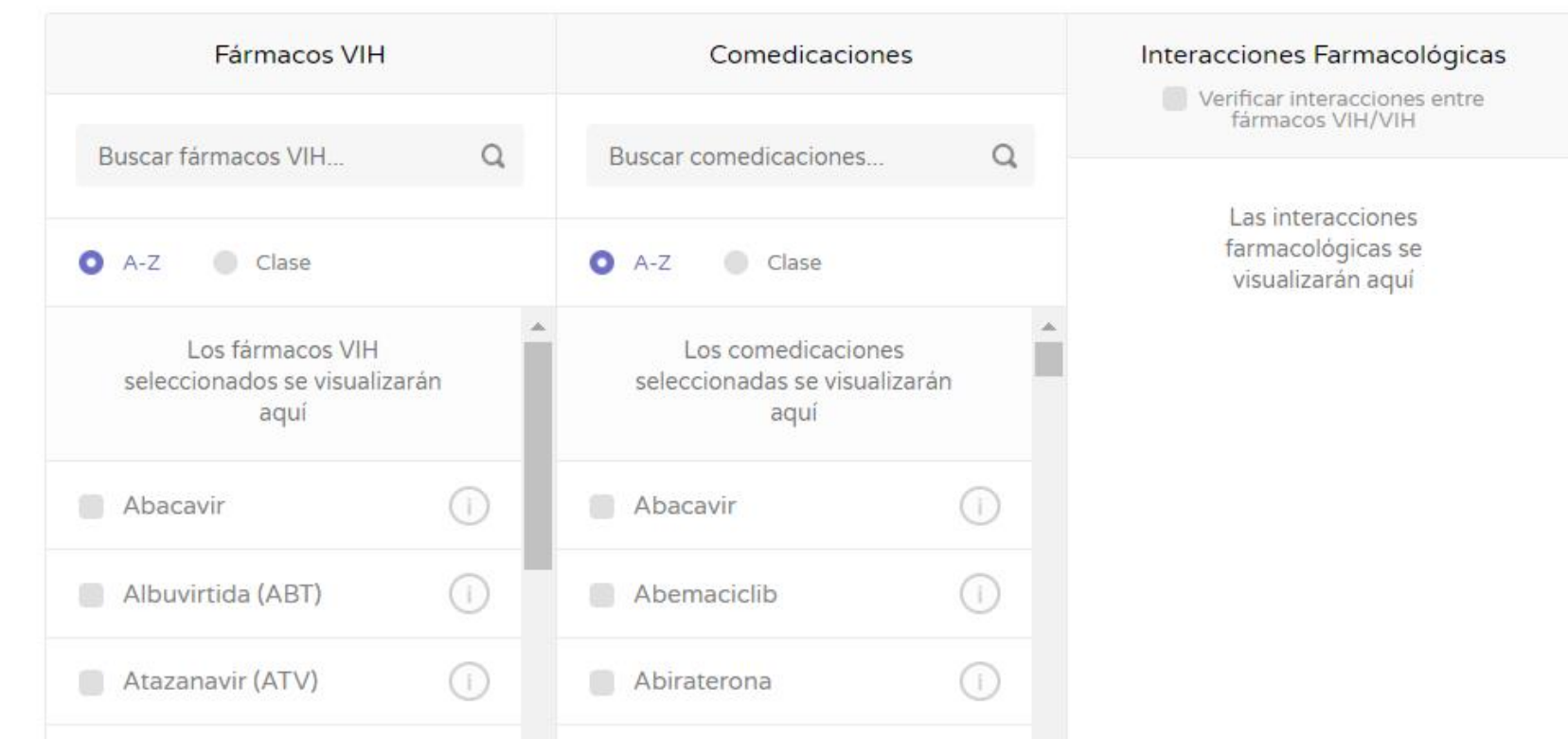
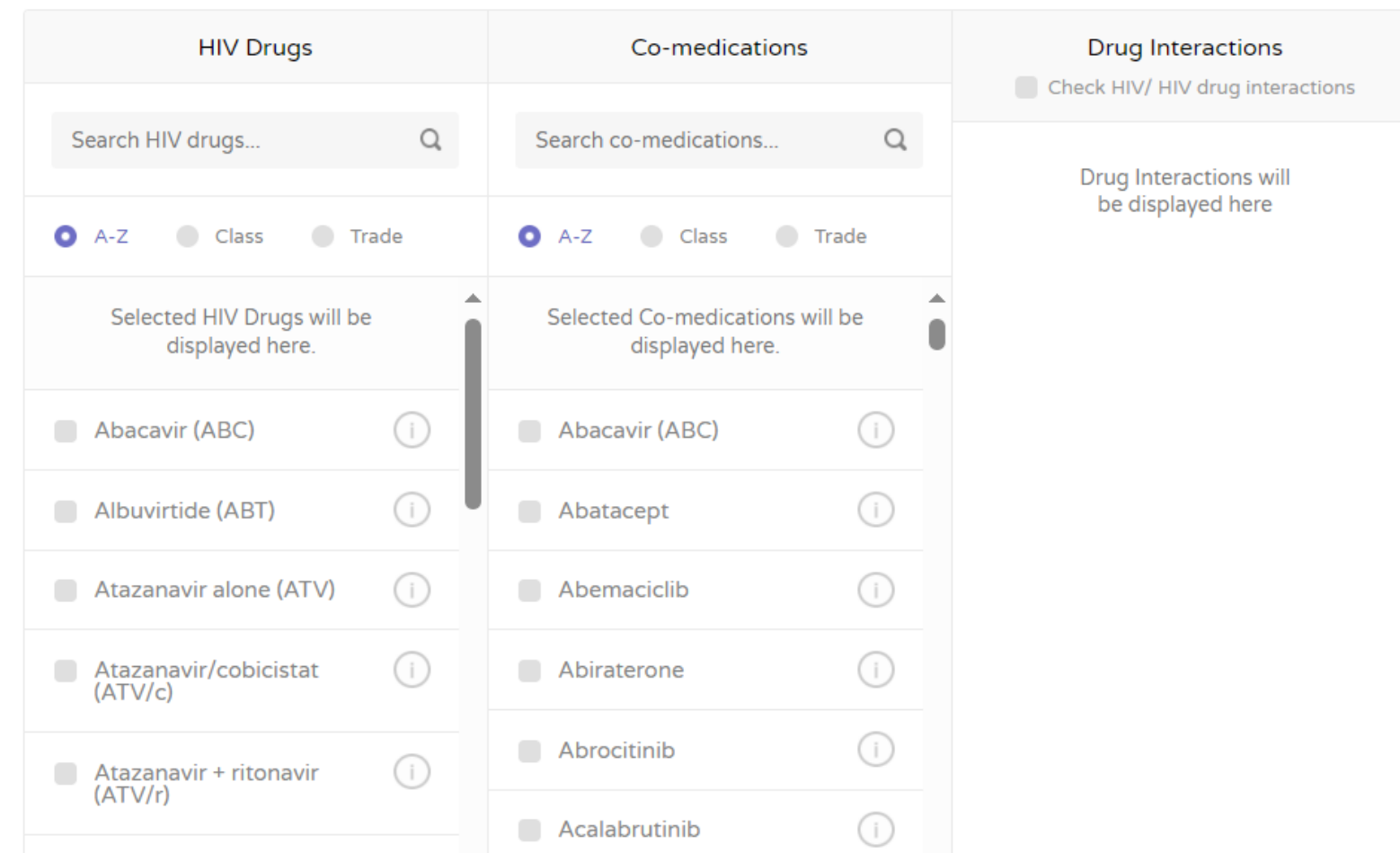
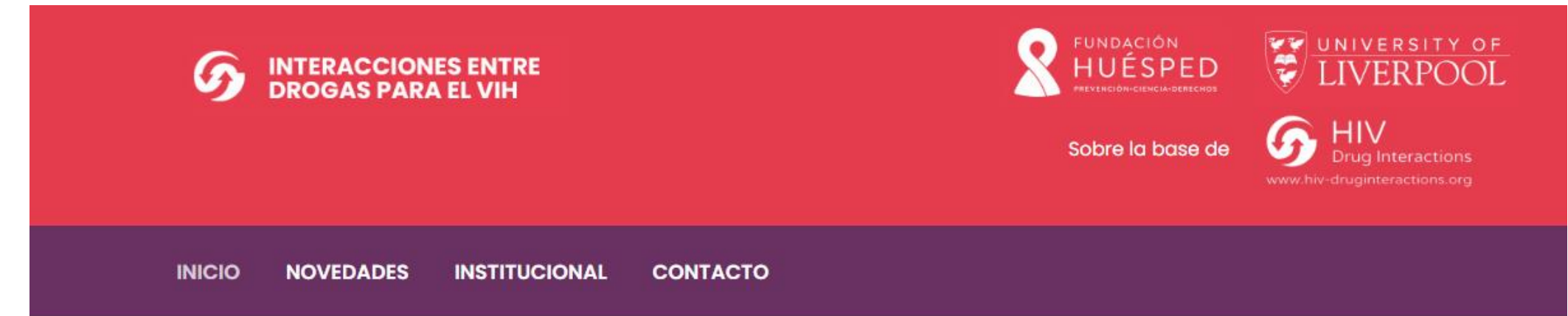
Ford SL et al. Antimicrob Agents Chemother 2017; Bettonte S et al. Clin Infect Dis 2023; www.hiv-druginteractions.org

HIV drug interactions websites

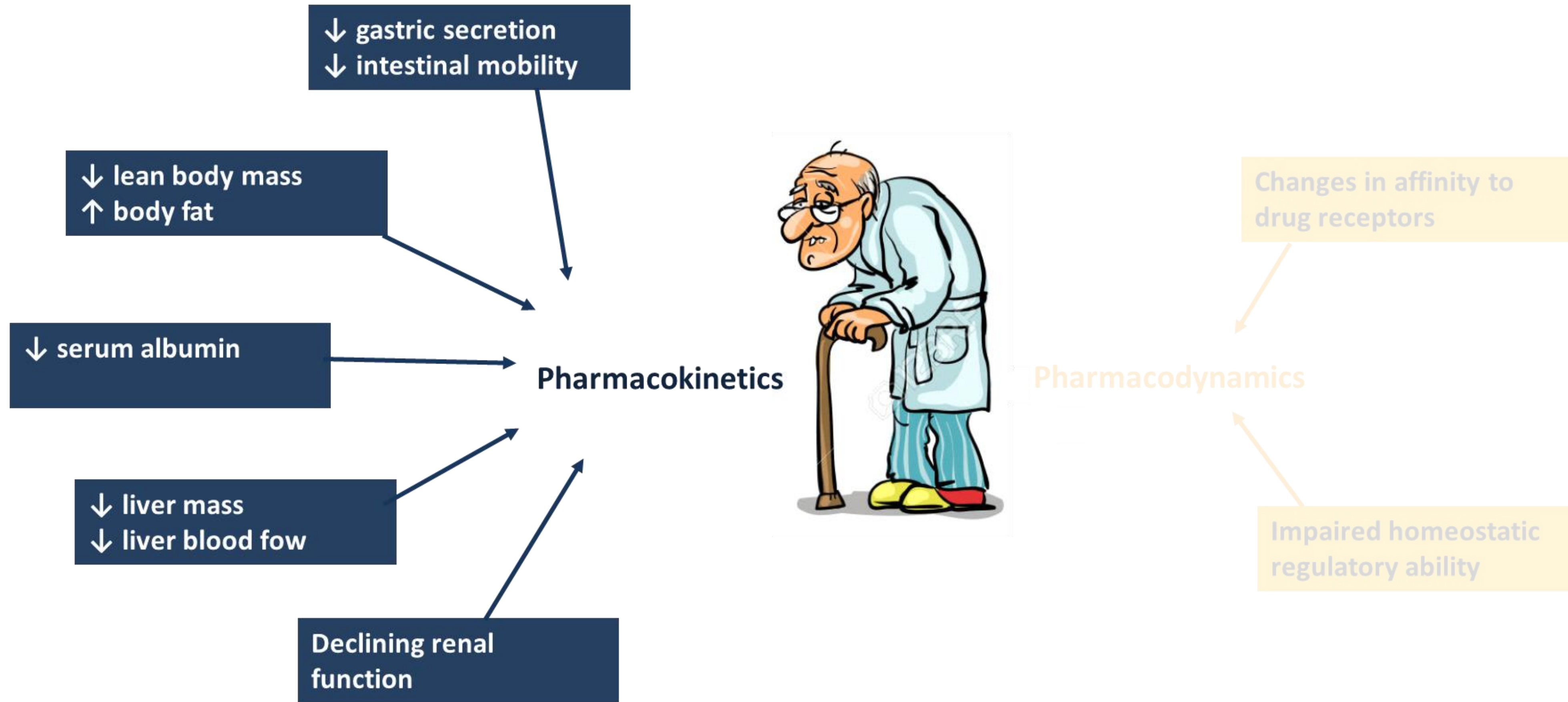
www.hiv-druginteractions.org



<https://interaccioneshiv.huesped.org.ar>



Physiological changes with aging



Back D & Marzolini C. J Int AIDS Soc 2020; Calcagno A et al. Expert Opin Drug Metab Toxicol 2021

Effect of aging on antiretroviral drug pharmacokinetics

Antiretroviral class	Reference	Age (years)	Antiretroviral exposure
Protease inhibitors	Dumond et al. (2013)	55-65	ritonavir: ↑ 19%
			atazanavir/r: ↑ 12%
	Courlet et al. (2020)	56-80	darunavir/r: ↑ 14%
	Winston et al. (2013)	20-80	↑
Integrase inhibitors	Elliot et al. (2019)	60-79	dolutegravir: ↑ 8%
	Courlet et al. (2020)	56-80	dolutegravir: ↑ 5%
	Stader et al. (2021)	50-85	bictegravir ↑ 1%
Non-nucleoside reverse transcriptase inhibitors	Dumond et al. (2013)	55-65	tenofovir: ↓ 9%
			emtricitabine: ↑ 53%
			efavirenz: ↑ 5%
	Courlet et al. (2020)	56-80	lamivudine: ↑ 11%

=> Age related physiological changes do not impact antiretroviral pharmacokinetics to a clinically significant extent. No a priori dose adjustment is needed in absence of severe comorbidities.

=> Effect of aging on the pharmacokinetics of intramuscular cabotegravir/rilpivirine remains to be evaluated.

Stader F et al. Br J Clin Pharmacol 2021; Courlet P et al. AIDS 2020; Stader F et al. Clin Pharmacol Ther 2021
Dumond J et al. HIV Med 2013; Elliot E et al. Clin Infect Dis 2019; Winston A et al. J Antimicrob Chemother 2013

Effect of aging on the PK of intramuscular cabotegravir/rilpivirine

Factors such as exercise and blood flow in the muscle can impact the release of drug from the depot.

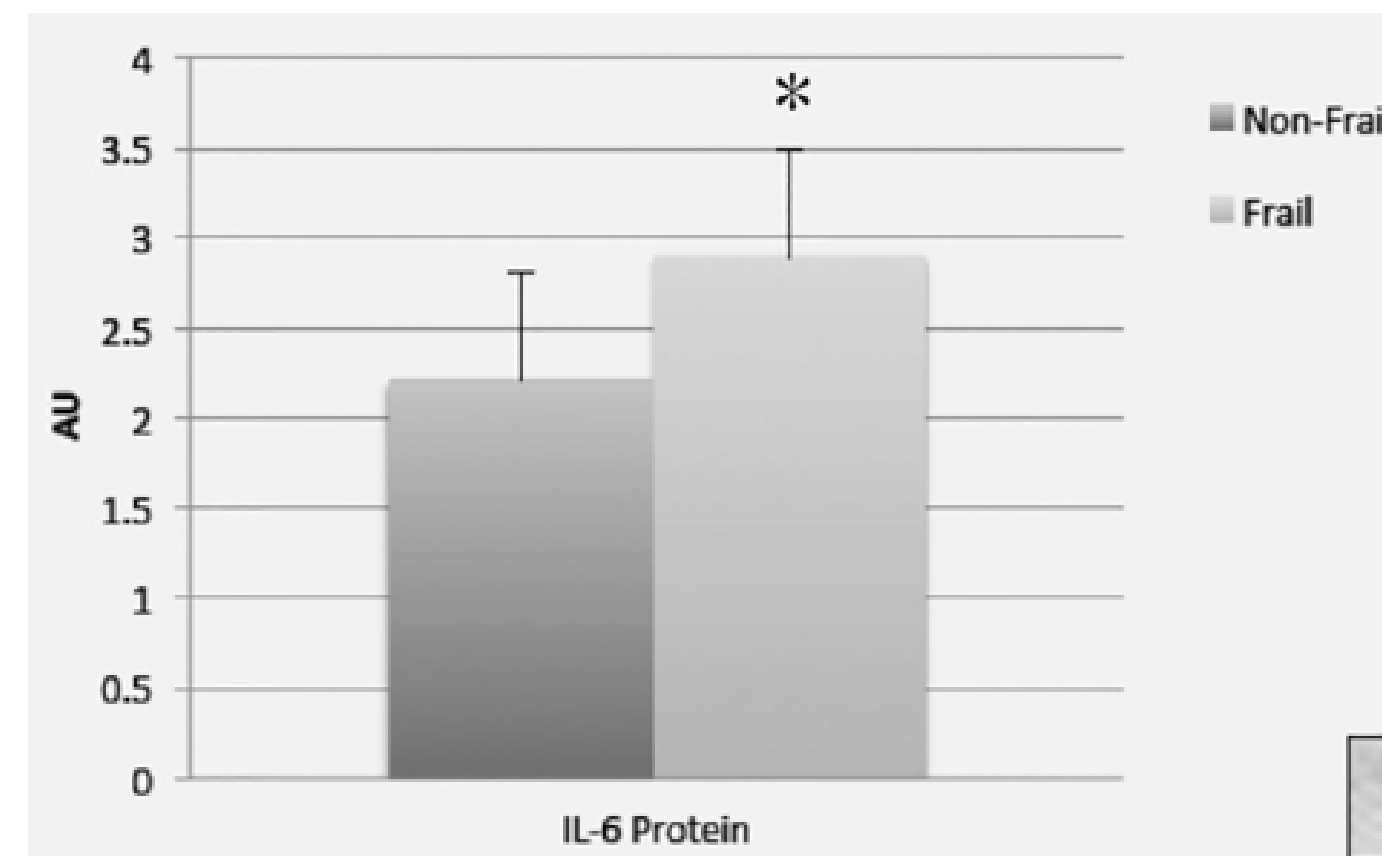
physical activity
muscle mass
blood flow

} reduced with aging => impact on cabotegravir/rilpivirine PK?

When comparing muscle biopsies in age-matched and non-obese BMI-matched frail and non-frail elderly adults:

frail group showed increased intramuscular adipose tissue, decreased lean tissue and elevated IL-6 protein compared non-frail group => impact on cabotegravir/rilpivirine PK?

	Frail	Non-Frail
n	8	16
Age (years)	83.3 (79.5–87.0)	78.1 (75.05–81.07)
BMI (kg/m ²)	25.0 (22.2–27.7)	23.9 (22.5–25.3)
PASE	58.6 (30.6–86.6)	215.0 (185.0–245.0) *
MPPT	16.3 (9.8–22.7)	35.2 (34.5–35.8) *
% Lean	81.9 (77.9–86.1)	88.3 (87.3–89.4) *
% IMAT	18.0 (13.9–22.1)	11.7 (10.6–12.7) *



Stader F et al. Clin Pharmacokinet 2019; Addison O et al. J Nutr Health Aging 2014

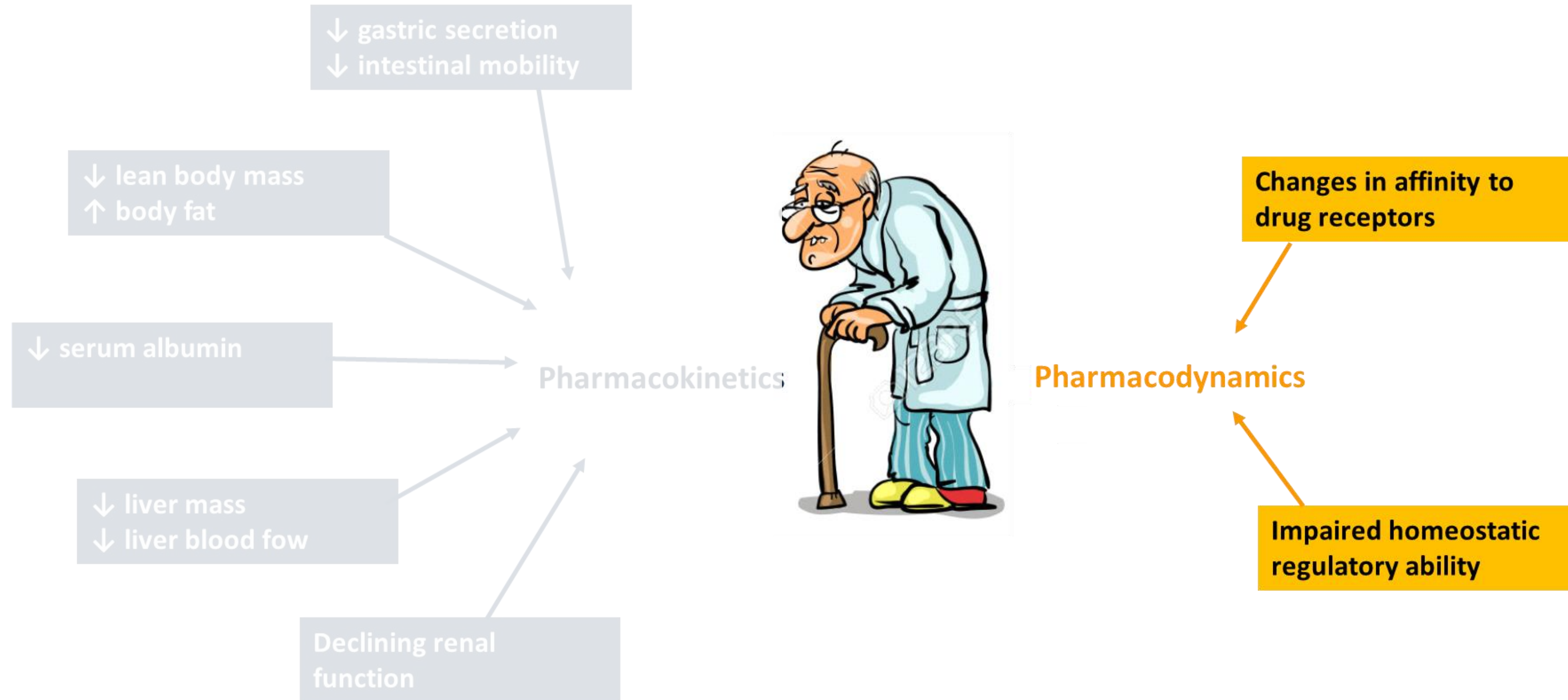
Effect of aging on non-HIV drug pharmacokinetics

Drugs	AUC-Ratio elderly/young	
	observed	predicted
Midazolam	0.97	1.08
Metoprolol	0.97	1.04
Lisinopril	1.24	1.18
Amlodipine	1.38	1.31
Rivaroxaban	1.52	1.52
Repaglinide	1.79	1.62
Atorvastatin	1.38	1.32
Rosuvastatin	1.03	1.24
Clarithromycin	1.53	1.48
Rifampicin	1.74	1.56

⇒ Exposure of HIV and non-HIV drugs increases progressively with aging due to a decrease in clearance as a result of decreased hepatic blood flow and glomerular filtration.

Stader F et al. Clin Pharmacokinet 2020; Stader F et al. Br J Clin Pharmacol 2021

Physiological changes with aging



Back D & Marzolini C. J Int AIDS Soc 2020; Calcagno A et al. Expert Opin Drug Metab Toxicol 2021

Virologic outcomes for older PWH initiating ART in RCTs

ART regimen	Efficacy of initial ART in PLWH aged ≥ 50 years vs < 50 years
DTG + 3TC	GEMINI: no difference at 48 or 96 weeks [1,2]
DTG + XTC/(TDF or TAF)	GEMINI: no difference at 48 or 96 weeks [1, 2] GS-1490: no difference at 144 weeks [3]
DTG/ABC/3TC	GS-1489: no difference at 144 weeks [3] SINGLE: no difference at 48 weeks [4] ARIA: no difference at 48 weeks [5]
BIC/FTC/TAF	GS-1498 and GS-1490: no difference at 144 weeks [3]
CAB/RPV LA	FLAIR and ATLAS-2M: no difference at 96 weeks [6]

=> Efficacy of most commonly prescribed ART-regimens seem not to be different in older compared to young PLWH.

1. Cahn P et al. Lancet 2019; 2. Cahn P et al. JAIDS 2020; 3. Mills A et al. CROI 2020 abstract 477; 4. Walmsley S et al. NEJM 2013; 5. Orrell C et al. Lancet HIV 2017; 6. Elliot ER et al. AIDS 2022

Tolerability of LA cabotegravir/rilpivirine in older compared to young PWH

Sub-analysis of CARISEL study showed that safety and tolerability of LA cabotegravir/rilpivirine was similar in participants aged <50 y (n = 301) and ≥50 y (n = 129) through 12 months.

Adverse reactions through 12 months

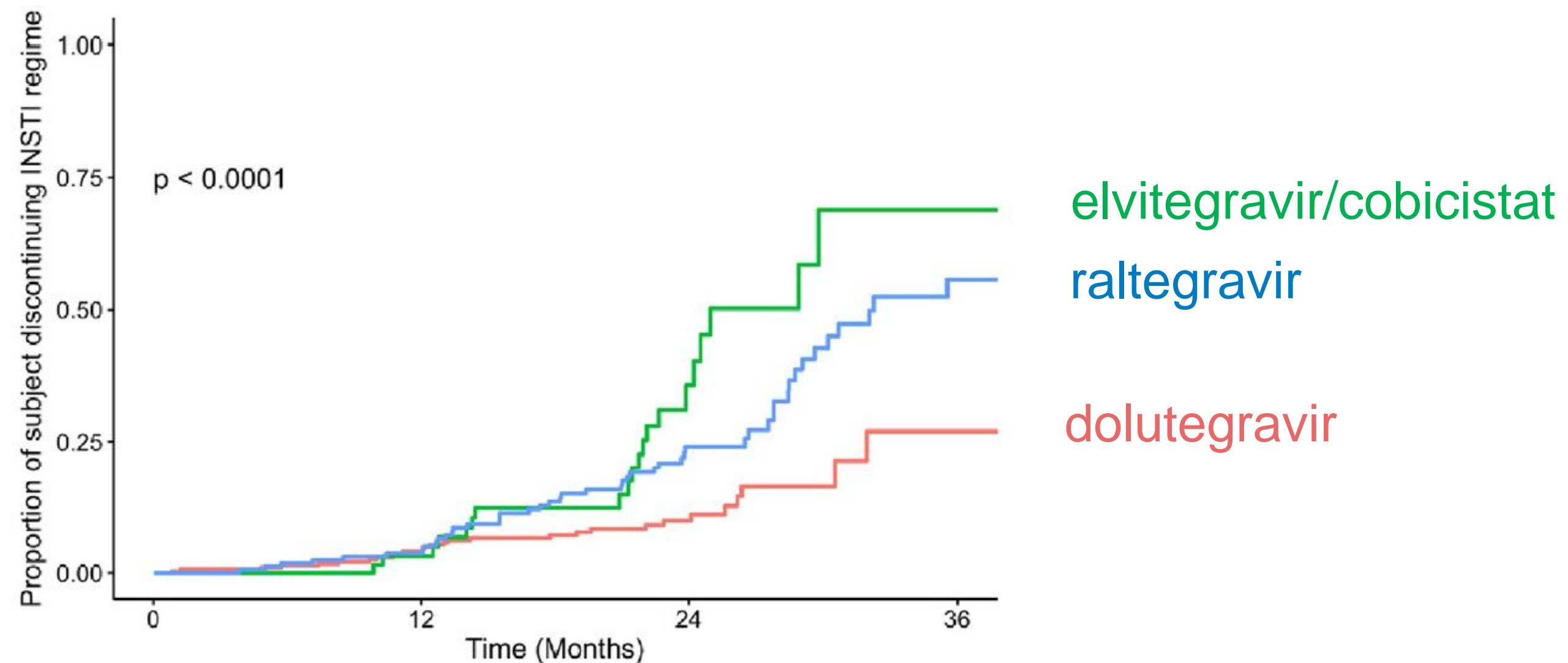
Parameter, n (%)	Sex at birth		Age (years)		Race			
	Female (n=109)	Male (n=321)	<50 (n=301)	≥50 (n=129)	White (n=336)	Black (n=76)	Asian (n=9)	Other races (n=9)
Any AEs*	105 (96)	314 (98)	294 (98)	125 (97)	331 (99)	71 (93)	8 (89)	9 (100)
Any Grade ≥3	12 (11)	37 (12)	36 (12)	13 (10)	37 (11)	9 (12)	3 (33)	0
Drug-related AEs	98 (90)	291 (91)	276 (92)	113 (88)	308 (92)	64 (84)	8 (89)	9 (100)
Excluding ISRs	41 (38)	115 (36)	105 (35)	51 (40)	131 (39)	17 (22)	5 (56)	3 (33)
Grade ≥3	5 (5)	20 (6)	17 (6)	8 (6)	19 (6)	5 (7)	1 (11)	0
AEs leading to treatment withdrawal	10 (9)	32 (10)	26 (9)	16 (12)	32 (10)	7 (9)	3 (33)	0
SAEs†	4 (4)	11 (3)	11 (4)	4 (3)	12 (4)	1 (1)	2 (22)	0
Drug related excluding ISRs‡	0	1 (<1)	1 (<1)	0	0	0	1 (11)	0

Ghosn J et al. EACS Conference 2023

Tolerability of LA cabotegravir/rilpivirine in older compared to young PWH

- Inclusion of 822 participants (median age 70 years) in the GEPP0 cohort.
- 6.4%, 21.1% and 22.9% participants discontinued dolutegravir, raltegravir and elvitegravir/cobicistat respectively. Discontinuation mainly due to treatment simplification.

Proportion of subjects discontinuing the integrase inhibitor based regimen



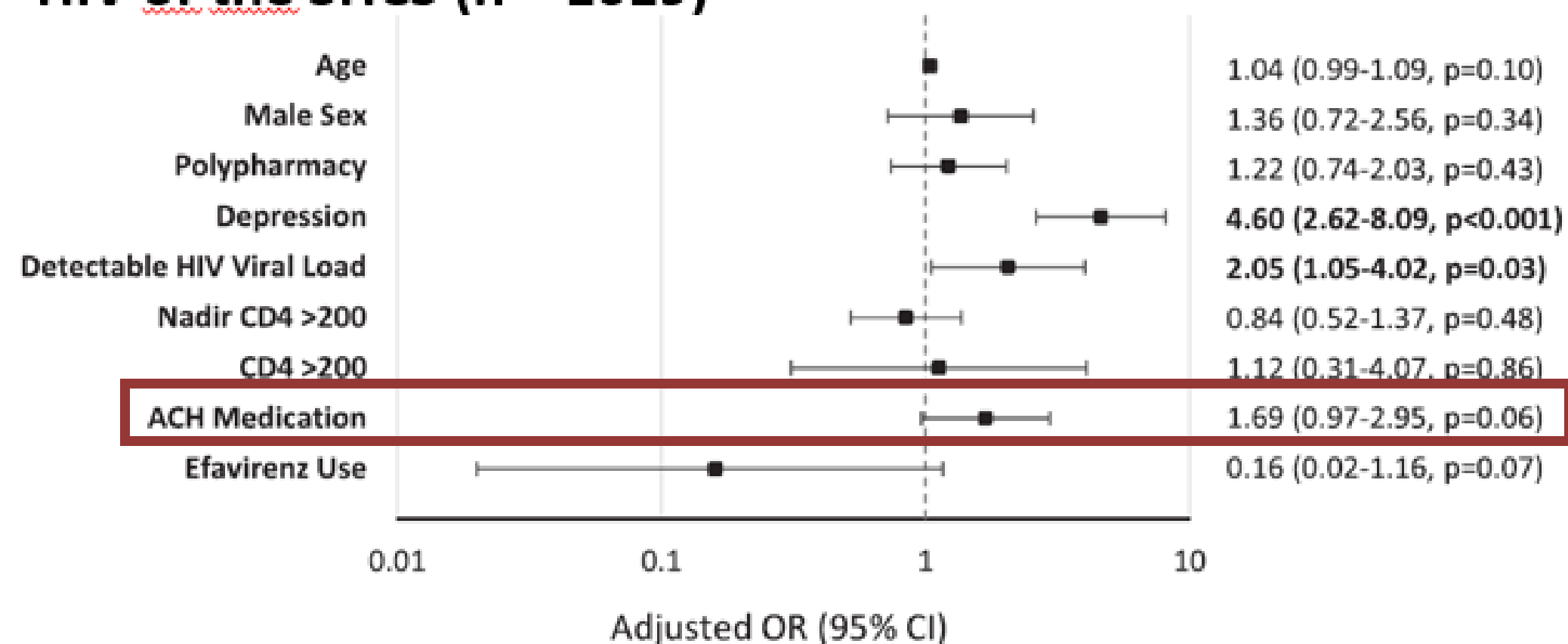
=> Integrase inhibitor based regimens showed a good tolerability/durability of more than 2 years in geriatric patients.

Foca E et al. PLoS One 2021

Anticholinergic medications and cognitive impairment/falls

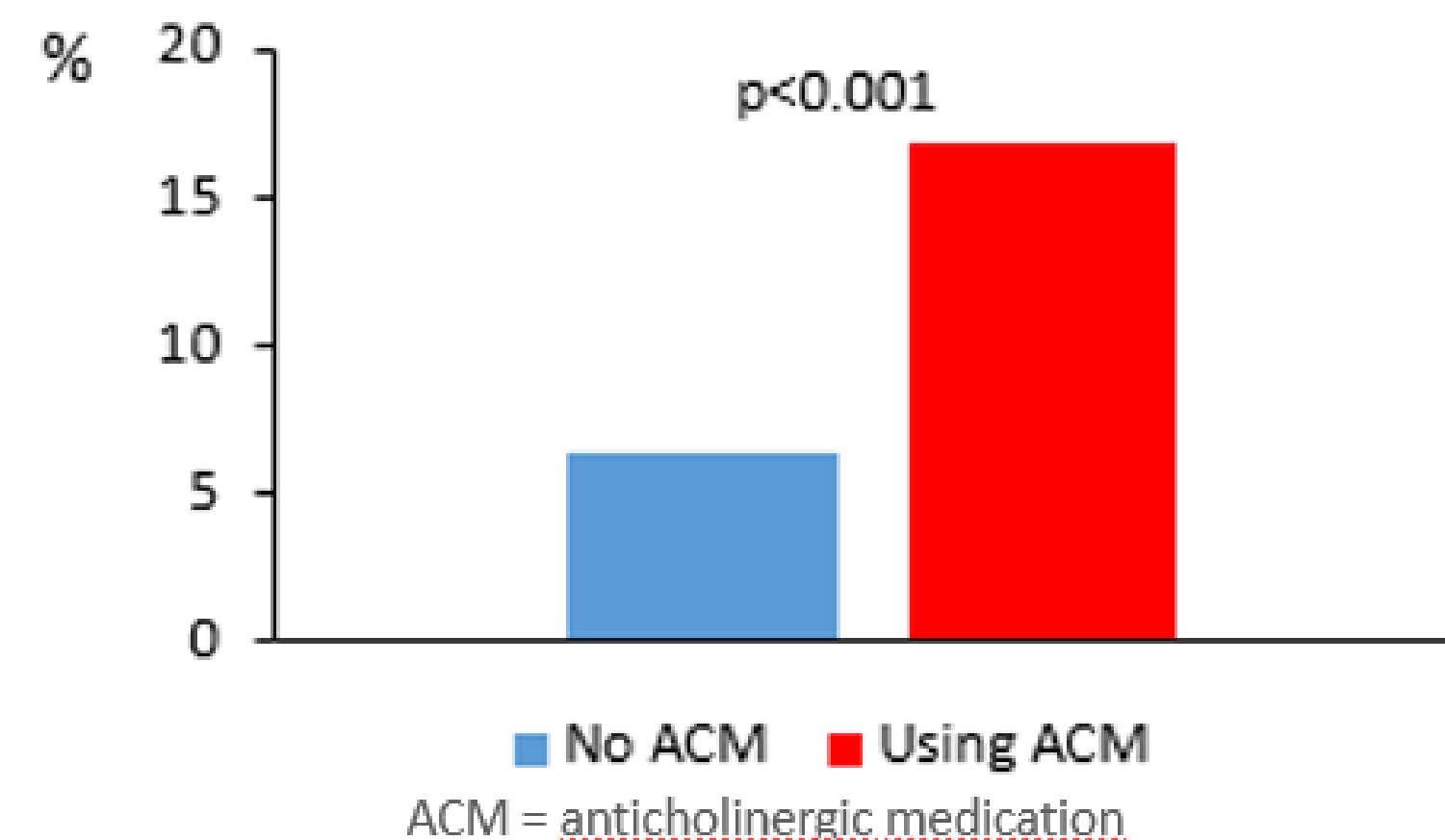
Older individuals are more sensitive to anticholinergic medications due to a decrease in cholinergic receptors in the brain. Drugs with anticholinergic properties can impair cognition, increase the risk of falls.

Anticholinergic medication use and self-reported neurocognitive impairment in older people with HIV of the SHCS (n = 1019)



- => Trend with being on >1 anticholinergic medication and self-reported neurocognitive impairment.
- => In a second analysis of the SHCS, anticholinergic medication use was associated with motor skills deficits.

People with HIV reporting recurrent falls

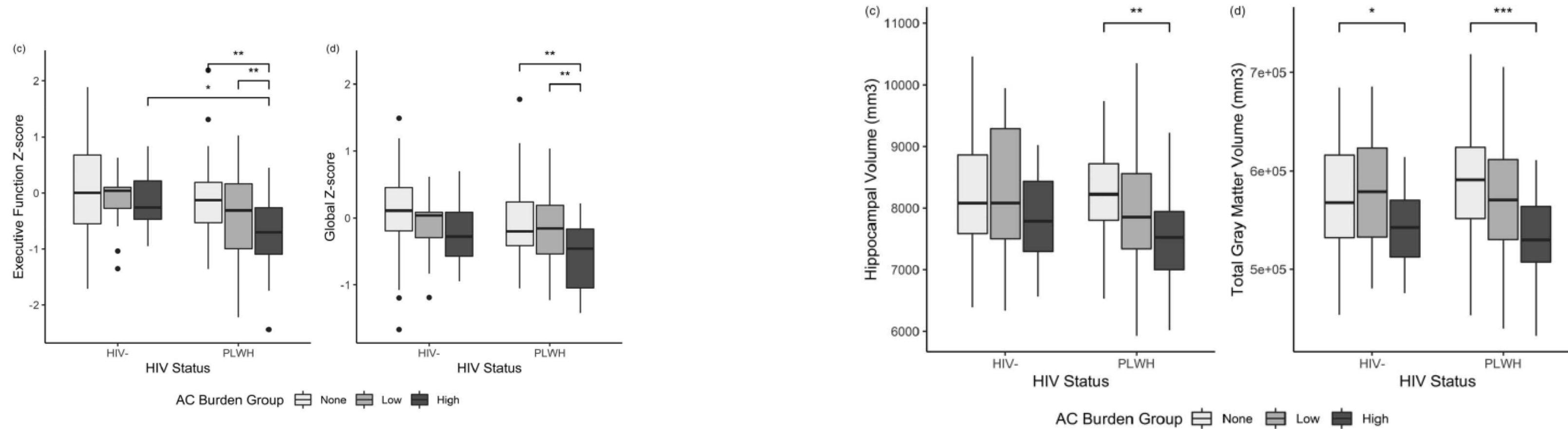


- => Association between use of anticholinergic medication and higher odds of recurrent falls.

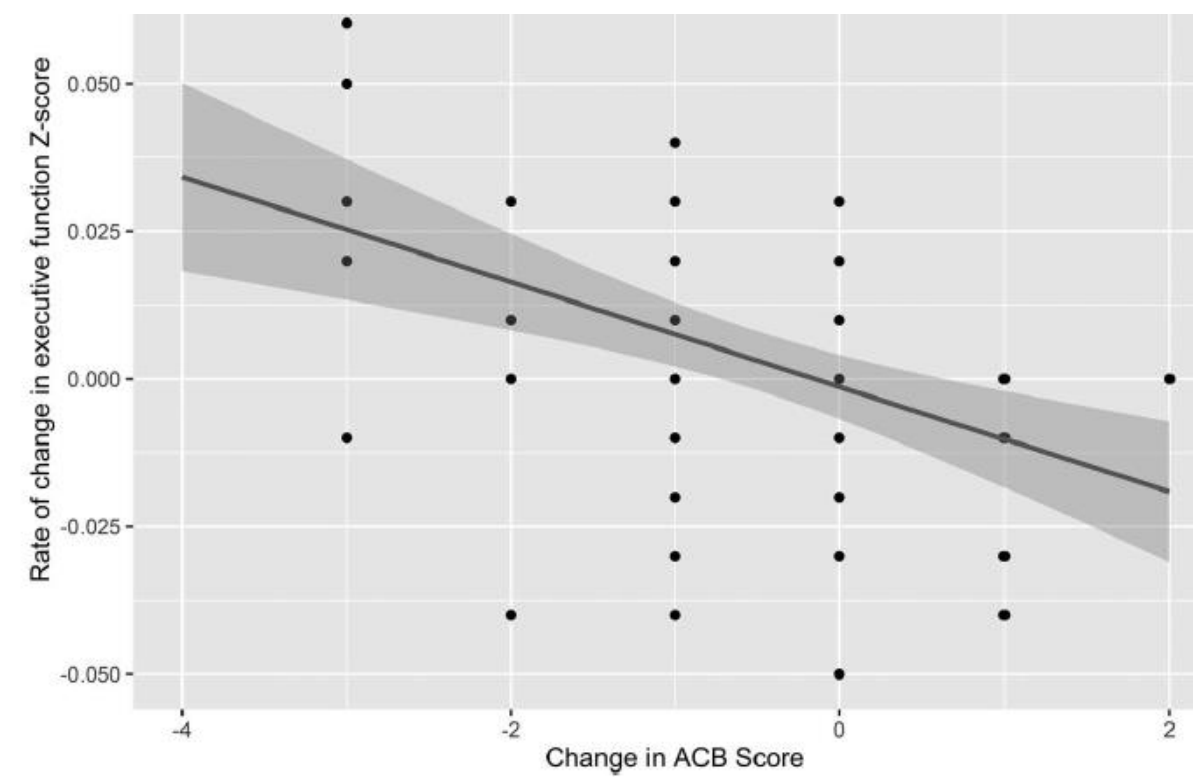
Jakeman B et al. J Antimicrob Chemother 2022; Jakeman B et al. Open Forum Infect Dis 2022; Doctor J et al. HIV med 2023

Drugs with anticholinergic effects and cognitive performance

Anticholinergic burden and cognitive performance/ brain volumes



Impact of reduction in anticholinergic burden and executive function



Cooley SA et al. AIDS 2021

Anticholinergic medications

Examples of anticholinergic medications

amitriptyline	clozapine	imipramine	promethazine
atropine	darifenacin	nortriptyline	scopolamine
chlorpheniramine	diphenhydramine	olanzapine	thioridazine
chlorpromazine	doxepin	oxybutynin	tolterodine
clomipramine	hydroxyzine	paroxetine	trimipramine

Online anticholinergic burden calculator

<https://www.acdcalc.com>

Jakeman B. et al. J Antimicrob Chemother 2022

Prescribing errors in older people with HIV

Reference	Country	N	ACH medication	Inappropriate medication
Cantarelli et al. Farm Hosp 2020	Spain	78	47%	
Contreras Macias et al. Rev Esp Quimioter 2021	Spain	19		47%
Courlet et al. OFID 2019	CH	996		31%
Doctor et al. Top Antivir Med 2022	UK	699	28%	
Fernandez Fradejas et al. Enferm Infect Microbiol Clin 2022	Spain	73		59%
Gallardo et al. Eur J Hosp Pharm 2019	Spain	237		78%
Greene et al. J Am Geriatr Soc 2014	USA	89		38%
Guaraldi et al. Antivir Ther 2017	Italy	123		38%
Jakeman et al. J Antimicrob Chemother 2022	Switzerland	1019	20%	
Jakeman et al. OFID 2022	Switzerland	981	14%	
Lao Dominguez et al. Farm Hosp 2021	Spain	251	45%	
Livio et al. J Antimicrob Chemother 2021	Switzerland	175		67%
Lopez Ceteno et al. HIV Med 2020	Spain	1292		37%
Loste et al. Br J Clin Pharmacol 2021	Spain	91		88%
Mazzitelli et al. AODS 2019	UK	790	27%	
McMillan et al. Can J Gen Int Med 2022	Canada	951		60%
Mercadal-Orfila et al. AIDS Care 2022	Spain	223	31%	
Onteniente Candela et al. Farm Hosp 2019	Spain	210		47%
Onteniente Candela et al. Eur J Hosp Pharm 2019	Spain	120		47%
Vinuesa-Hernando et al. Int J Clin Pharm 2021	Spain	30		63%
Zhan Zhou et al. Farm Hosp 2018	Spain	75		55%

Interventions to limit polypharmacy and prevent prescribing errors

1) Medication reconciliation

- Establish list of current prescription & over-the-counter drugs to be updated at each medical visit

2) Periodic medication review

Questions to consider when reviewing a prescription

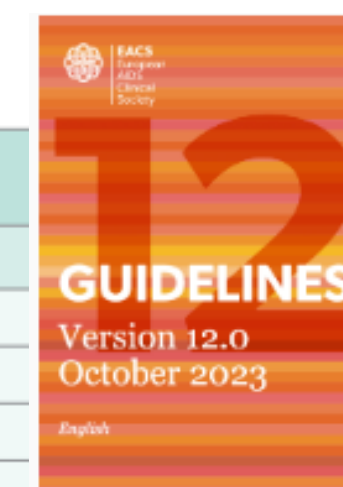
- Is there an indication for the medicine?
- Is the medicine appropriate for elderly PLWH? → Beers/STOPP&START criteria
- Is the dose correct (e.g. adjusted for renal function)?
- Is there a significant drug-drug interaction? (favor unboosted ARV)
- Is there a significant drug-disease interaction?
- Is the duration of treatment acceptable?
- Is there any missing medicine?
- Is the person able to manage his/her own medicines or does he/she need assistance?

Selected Top 10 Drug Classes To Avoid in Older Persons with HIV

Drug class	Problems/alternatives
First generation antihistamines e.g., clemastine, diphenhydramine, doxylamine, hydroxyzine	Strong anticholinergic properties, risk of impaired cognition, anticholinergic adverse reactions (dry mouth, constipation, retention). Alternatives: cetirizine, desloratadine, loratadine
Tricyclic antidepressants e.g., amitriptyline, clomipramine, doxepin, imipramine, trimipramine	Strong anticholinergic properties, risk of impaired cognition, anticholinergic adverse reactions (dry mouth, constipation, retention). Alternatives: citalopram, escitalopram, mirtazapine, v
Benzodiazepines Long and short acting benzodiazepines e.g., clonazepam, diazepam, midazolam Non-benzodiazepines hypnotics e.g., zolpidem, zopiclone	Elderly are more sensitive to their effect, risk of falls, impairment, drug dependency. Use with caution, at the lowest effective dose and for the shortest duration. Alternatives: non-pharmacological treatment of sleep
Atypical antipsychotics	Anticholinergic adverse reactions, increased risk of s

Selected Non-ARV Drugs Requiring Dosage Adjustment in Renal Insufficiency

Therapeutic class and drugs	CL _{CRT} threshold for adjustment ^{a,b}	Additional information ^c
ANTIBACTERIALS^d		
Fluoroquinolones		
Ciprofloxacin	≤ 60 mL/min	
Delafloxacin	< 30 mL/min	iv dosage: 200 mg every 12 hours; oral dosage: 450 mg every 12 hours
Levofloxacin	≤ 50 mL/min	
Ofloxacin	≤ 50 mL/min	
Cephalosporins		
Cefpodoxime	≤ 40 mL/min	
Ceftazidime	≤ 50 mL/min	
Cefepime	≤ 50 mL/min	



EACS guidelines, version 12 October 2023

Drug to deprescribe in older PWH in presence of certain conditions

Deprescribing = planned and supervised process of dose reduction or stopping of medications that may be causing harm or no longer provide benefit.

Drug class	Conditions for which deprescribing should be considered	Problems caused by drug class	Alternatives or information on how to stop drug
Acetylcholinesterase inhibitors e.g. donepezil, rivastigmine	History of persistent bradycardia (< 60 beats/min), heart block, or recurrent syncope or coadministration of beta-blocker, digoxin, diltiazem, verapamil	Increase the risk of cardiac conduction failure, syncope and injury	Taper gradually, consider halving the dose every 4 weeks
Antipsychotics e.g., haloperidol, lurasidone, paliperidone, perphenazine	Parkinson	Severe extra-pyramidal symptom	quetiapine, clozapine
Aspirin	Low cardiovascular risk and/or advanced age and/or high risk of gastrointestinal bleeding (e.g., concurrent use of NSAIDs, SSRIs, corticosteroids) and/or prior gastrointestinal disease and/or coadministration of a second anti-platelet or anticoagulant (continued beyond the recommended duration)	Risk of bleeding	No need to taper
Biphosphonates e.g., alendronate, ibandronate, risedronate, zoledronate	Low risk of fracture or history of 5 years of continuous treatment with a bisphosphonate	Biphosphonates keep showing a benefit in non-vertebral fractures in the 5 years after an initial treatment particularly if the T score is above -2.5. Prolonged use increases the risk of osteonecrosis of the jaw, hypocalcemia and/or severe vitamin D deficiency.	No need to taper
Opioids e.g. codeine, fentanyl, morphine, oxycodone, tramadol	Chronic non-cancer pain	Tolerance to analgesic effect of opioids with long-term use. Associated with adverse psychological effects, higher risk of death from drug overdose with opioids.	Multidisciplinary pain management program. Written and verbal instructions should be provided to patients and families to educate about the tapering protocol that will minimize the withdrawal symptoms
Proton pump inhibitors (PPIs) e.g. esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole	Uncomplicated peptic ulcer disease	Long-term use is linked with increased risk of fracture, enteric infections, mineral deficiencies	Use low dose of PPI -> if symptoms well controlled -> use PPI on demand -> if symptoms well controlled -> stop PPI
Selective serotonin re-uptake inhibitors (SSRIs) e.g., citalopram, fluoxetine, paroxetine, sertraline	Current or recent significant hyponatremia (i.e. serum Na+ <130 mmol/L)	Syndrome of inappropriate antidiuretic hormone secretion (SIADH) and aggravation hyponatremia	agomelatine, bupropion, mianserin, trazodone. Note: tricyclic antidepressants should be avoided as associated with a higher risk of adverse effects (e.g., life-threatening arrhythmias and heart block)



EACS guidelines, version 12 October 2023

69-year old man

HIV infection
(since 2004)

HIV medications

Bictegravir 50 mg QD
Emtricitabine 200 mg QD
Tenofovir alafenamide 25 mg QD

Immunological/virological parameters

HIV VL: <20 copies/mL
CD4: 519 cells/mm³

Co-morbidities

Neurocognitive disorders
Depression
Gout
Gastro-esophageal reflux
Urticaria
Dyslipidemia

Co-medications

Hydrochlorothiazide 25 mg QD
Escitalopram 10 mg QD
Allopurinol 300 mg QD
Pantoprazole 20 mg QD
Clemastine 1 mg BID
Atorvastatine 20 mg QD

Serum chemistry

eGFR 80 ml/min/1.73
Potassium : 3.3 mmol/L
Glucose: 5 mmol/L
Total cholesterol: 5.0 mmol/L
HDL cholesterol: 1.6 mmol/L
LDL cholesterol: 2.1 mmol/L

Blood pressure: 115/75 mmHg

69-year old man

Step 1
Check indication

HIV infection
(since 2004)

HIV medications
Bictegravir 50 mg QD
Emtricitabine 200 mg QD
Tenofovir alafenamide 25 mg QD

Immunological/virological parameters
HIV VL: <20 copies/mL
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Co-morbidities

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Co-mediations

Hydrochlorothiazide 25 mg QD
Escitalopram 10 mg QD
Allopurinol 300 mg QD
Pantoprazole 20 mg QD
Clemastine 1 mg BID
Atorvastatine 20 mg QD

Serum chemistry

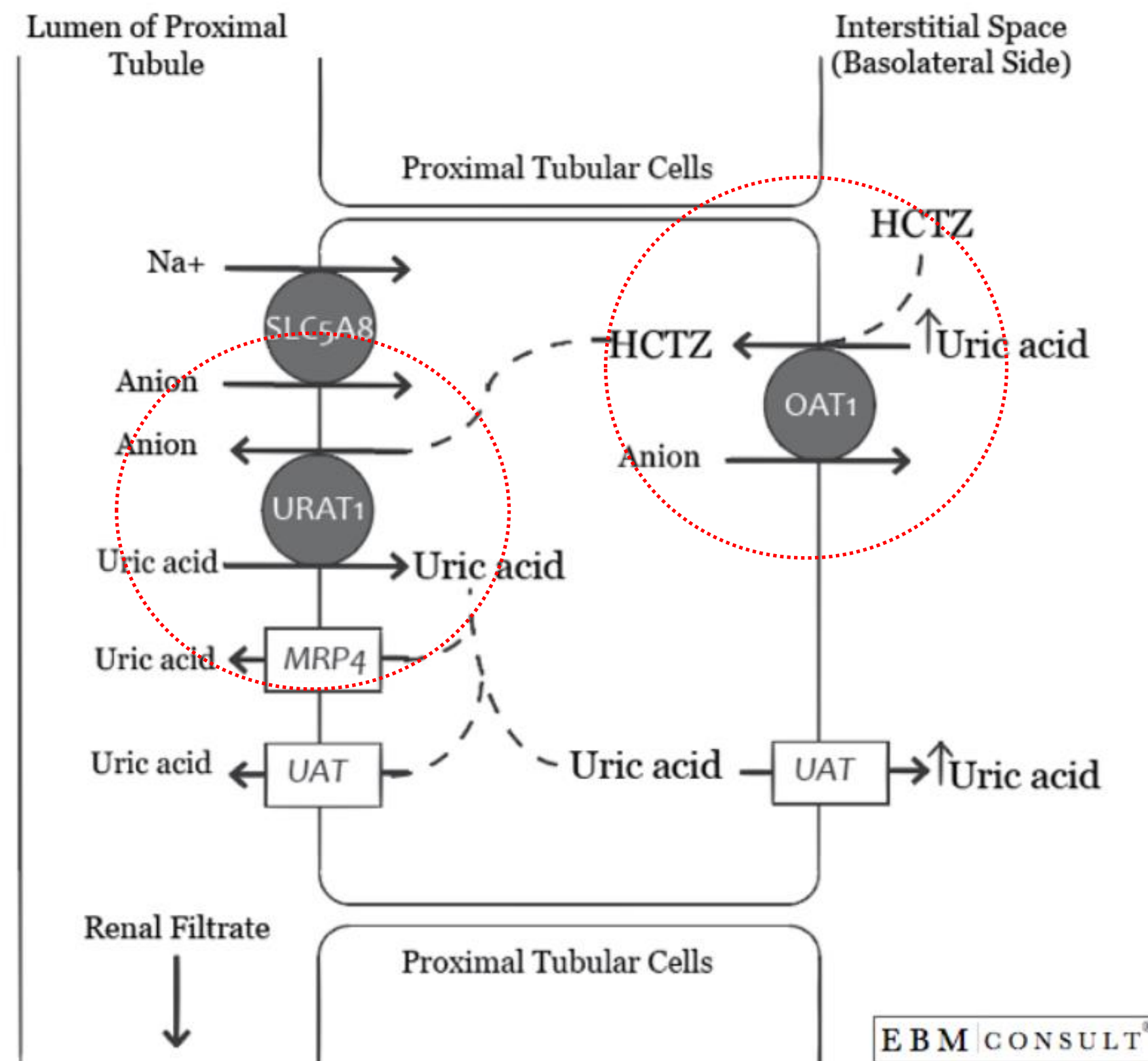
eGFR 80 ml/min/1.73
Potassium : 3.3 mmol/L
Glucose: 5 mmol/L
Total cholesterol: 5.0 mmol/L
HDL cholesterol: 1.6 mmol/L
LDL cholesterol: 2.1 mmol/L

Blood pressure: 115/75 mmHg


- No indication for hydrochlorothiazide, patient has no hypertension
- Hydrochlorothiazide can increase uric acid levels

Interaction between hydrochlorothiazide and uric acid

Hydrochlorothiazide recognized as organic acid and serves as substrate for moving uric acid intracellularly from renal filtrate



Competition between hydrochlorothiazide and uric acid for renal elimination via OAT1

www.hiv-druginteractions.org 

Common Prescribing Cascades to Avoid in Elderly PLWH

Produced July 2019

Thiazide diuretics → Hyperuricemia; gout → Allopurinol; colchicine

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69-year old man

Step 2
Check
Inappropriate drug

HIV infection
(since 2004)

HIV medications
Bictegravir 50 mg QD
Emtricitabine 200 mg QD
Tenofovir alafenamide 25 mg QD

Immunological/virological parameters
HIV VL: <20 copies/mL
CD4: 519 cells/mm³

www.hiv-druginteractions.org 

Top Ten Drug Classes to Avoid in Elderly PLWH

Produced July 2019

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Co-mor
Neuroc
Depres
Gout
Gastro-
Urticari
Dyslipic

• Conc
clem
Repl

Drug class	Problems	Alternatives
First generation antihistamines e.g., Clemastine Diphenhydramine Doxylamine Hydroxyzine	Strong anticholinergic properties, risk of impaired cognition, delirium, falls, peripheral anticholinergic adverse reactions (dry mouth, constipation, blurred vision, urinary retention).	Cetirizine Desloratadine Loratadine
Tricyclic antidepressants e.g., Amitriptyline Clomipramine Doxepin Imipramine Trimipramine	Strong anticholinergic properties, risk of impaired cognition, delirium, falls, peripheral anticholinergic adverse reactions (dry mouth, constipation, blurred vision, urinary retention).	Citalopram Escitalopram Mirtazapine Venlafaxine

69-year old man

Step 3
Check DDIs/dose

HIV infection
(since 2004)

HIV medications

Bictegravir 50 mg QD
Emtricitabine 200 mg QD
Tenofovir alafenamide 25 mg QD

Immunological/virological parameters

HIV VL: <20 copies/mL
CD4: 519 cells/mm³

	BIC/FTC/TAF
Allopurinol	◆
Aspirin (Analgesic)	◆
Atorvastatin	◆
Escitalopram	◆
Loratadine	◆
Pantoprazole	◆

Summary

- Age related physiological changes increase the exposure of antiretrovirals however to an extent that does not warrant dose adjustment.
- Virologic response and tolerability of antiretroviral treatment is similar in elderly compared to younger PWH. However, age related pharmacodynamic changes may affect the effect of other drugs.
- Polypharmacy often unavoidable in elderly, avoid unnecessary/inappropriate polypharmacy.

Future research/developments

- Impact of frailty on drug pharmacokinetics/pharmacodynamics.
- Impact of eliminating unnecessary/inappropriate medications on the quality of life.
- Prediction of drug-drug interactions with antiretrovirals using AI.
- Computerized prescription systems integrating several screening tools to efficiently assist with identification and prevention of prescribing errors.

Dziękuję Mauruuru Спасибо Dankie D'Akujem хвала.
Obrigado Gracías Merci
Sagolun Danke Arigatô Kiitos Kösönöm Kiitos Rahmat
Tak Merci Arigatô Thank You You
Xièxie Matondo Obrigado Teşekkür Ederim Sagolun Mahalo
Grazie Chokrane Efharisto Chokrane
квала Toda Tak Danke Dank Je Takk
Hvala Faleminderit Terima Kasih

