Taking HIV to another level

CLUSTER 2.0

Beyond Comorbidities

New perspectives of neuropsychiatric interest

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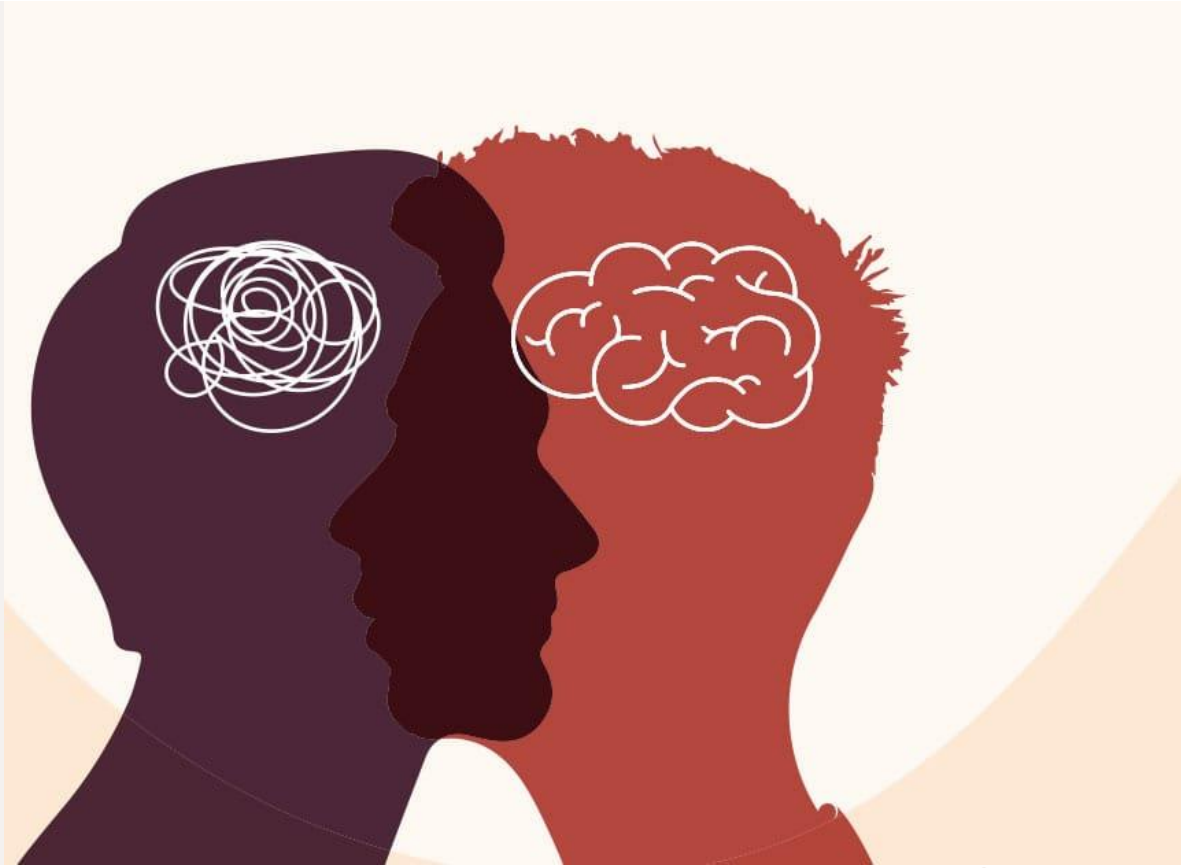
To the beloved memory of Margherita…

Disclosures

- MM received research grant from Gilead, fees as speakers and as advisory board member from ViiV Healthcare and Gilead Sciences, and fees as speakers from MSD and Angelini.

Agenda

- Prevalence of NP conditions in PLWH
- Focus on sleep
- Focus on Anticholinergics



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CENTRAL NERVOUS SYSTEM AND COGNITION (S SPUDICH, SECTION EDITOR)

Global Systematic Review of Common Mental Health Disorders in Adults Living with HIV

Jacqueline Hoare[1,2] · Tatum Sevenoaks[1] · Bulelwa Mtukushe[1] · Taryn Williams[1] · Sarah Heany[1] · Nicole Phillips[1]

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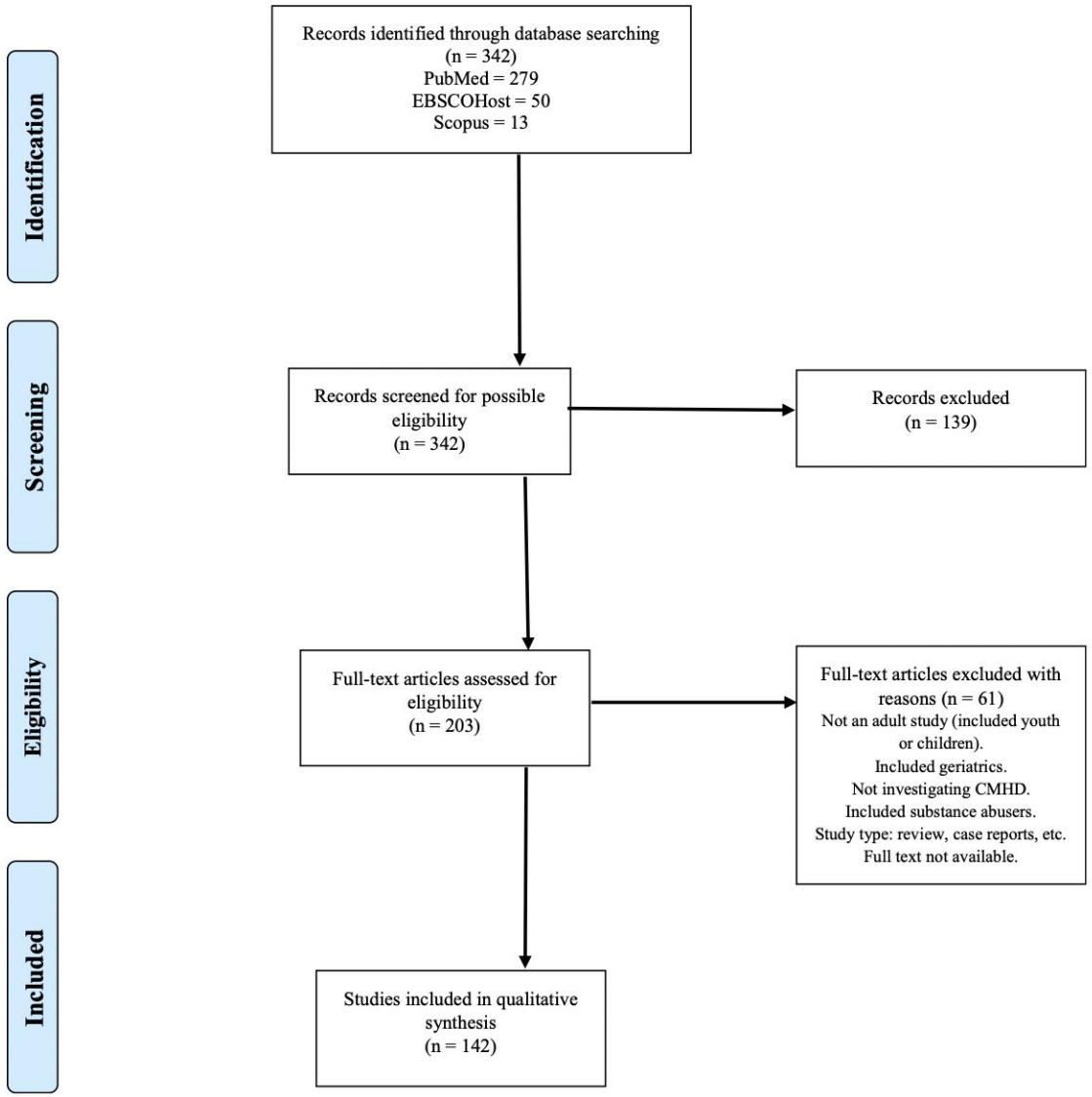
Abstract

Purpose of the review By reviewing the most recent common mental health disorders (CMHD) studies in people living with HIV (PLWH) (2018-2020), this review discusses the prevalence of CMHD, factors associated with CMHD in PLWH, mental health in PLWH from vulnerable groups, the impact of CMHD on HIV disease progression and adherence to antiretroviral therapy and the efficacy of different treatment approaches.

Recent findings After screening for eligibility 142 studies were included in the final systematic review. Only 27% of studies were conducted in Sub-Saharan Africa, which carries the highest burn of HIV disease globally. Despite the well-established increased risk of CMHD in PLWH, the current prevalence remains high, with studies reporting 28%-62% of PLWH having mental health symptoms.

Conclusion Despite the significant challenges that CMHDs present to successful HIV treatment, there are many mental health treatments and interventions which can improve outcomes in PLWH and opportunities to task-shift and integrate mental health care with HIV care.



	Type of study						
	CMHD treatment studies	CMHD impact on HIV disease progression	CMHD impact on adherence	CMHD prevelance in PLWH	CMHD in vulnerable groups living with HIV	Social factors associated CMHD in PLWH	Other
Region[a]	3/9/2/7/0	1/9/2/2/0	3/9/0/4/0	14/8/4/10/1	8/8/1/11/0	1/6/0/5/0	8/11/2/4/0
Total number of studies	18	12	19	39	29	12	26
N HIV+ sample[b]	2895	6570	39,861	106,898	9965	9308	16,978
HIV+ mean age (SD)[c]	41.4 (8.7)	41.3 (7.6)	41.0 (9.7)	39.0 (9.5)	24.5 (11.5)	37.3 (6.7)	--
Gender (N)							
Female	2678	2275	4469	32,773	6909	7347	7462
Male	3726	4999	8602	809,396	3584	2708	15,209
Transgender	3	0	157	420	41	0	17
Other	0	0	0	3	0	0	0
ARV status	Eleven studies included participants who were all on ARVs. Eight studies did not report the ARV status of the participants	Three studies did not report ARV status at all and three studies reported including participants who were all on ARVs	Only two studies reported including participants that were all on ARVs. All other studies had varying degrees of ARV adherence within their samples	The majority of studies did not report the participants ARV status (13 studies) and 8 studies reported that all of the participants included in the analysis were on ARVs	Twelve studies did not report participant ARV status. Seven studies reported that all included participants were on ARVs	Five studies did not report participant ARV status. Five studies included participants who were all on ARVs	Five studies did not report participant ARV status. Only 4 studies included studies with all participants being on ARVs
CMHD x ARVs[d]	Findings are inconsistent. One study reported no change in adherence as a function of CMHD. Another study reported that adherence improved when CMHD improved	Increased depressive symptoms were associated with worse ART adherence	Overall depression was associated with poor adherence. Some inconsistencies in other findings regarding duration on Arv and efavirenz	Overall, being of ARVs was associated with better MH outcomes	Not being on ARVs associated with poorer MH outcomes	Being virally suppressed was a protective factor against MH problems. Negative associations between ARVs and CMHD	Depression was associated with poor adherence and missed medical appointments. One study found no association between CMHD and ARVs

	Type of study						
	CMHD treatment studies	CMHD impact on HIV disease progression	CMHD impact on adherence	CMHD prevelance in PLWH	CMHD in vulnerable groups living with HIV	Social factors associated CMHD in PLWH	Other
Summary of findings	All studies (18/18) investigated behavioral or psychosocial interventions. Only two integrated/collaborative care studies included psychopharmacology treatments. The majority of studies (15/18 or 83%) found an improvement in mental health symptoms after the intervention	Studies investigated the association of CMHD on CD4 cell count, viral load, inflammatory markers, HbA1C, D-dimer, cognitive decline, and symptomatic HIV	Only three studies found no association between CMHD and adherence. Thirteen studies found a significant inverse association between CMHD and adherence, such that poor mental health was strongly associated with poor adherence. Some studies found that when mental health improved, so too did adherence	The majority of studies found a significant increased risk of CMHD in PLWH. Depression and anxiety disorders are common co-morbid conditions. Lifetime and past week suicidal ideation was reported in 21–31% of PLWH	In all of the vulnerable groups, PLWH were at higher risk of CMHD. Vulnerable groups studied include: perinatal WLWH, low-income WLWH, survivors of sexual assault, transgender and gender-nonconforming people, gay and bisexual men, MSM, prisoners, and migrants	PLWH who are vulnerable to CMHD frequently face significant individual, structural, social, and biological challenges to accessing and adhering to ART. These factors may be sociodemographic, local environmental factors, social structures, individual factors, and HIV	In all except one, studies found that HIV was associated with negative MH-associated outcomes. For example, poorer resilience, developmental trajectories, negative life events, cognitive impairment, and common mental health problems

Notes: a: Region in the studies took place were classified as Asia/USA/Europe/SSA (sub-Saharan Africa)/other. b: Total number for HIV-infected participants included in all studies included in a specific category. c: Mean age and standard deviation for all studies that reported this information in a specific category. d: A description of overall findings for studies that reported an association between CMHD and ARVs or ARV adherence. Age standard deviation for all studies that reported this information in a specific category. Full texts were unavailable for 3 studies and were thus not extracted here

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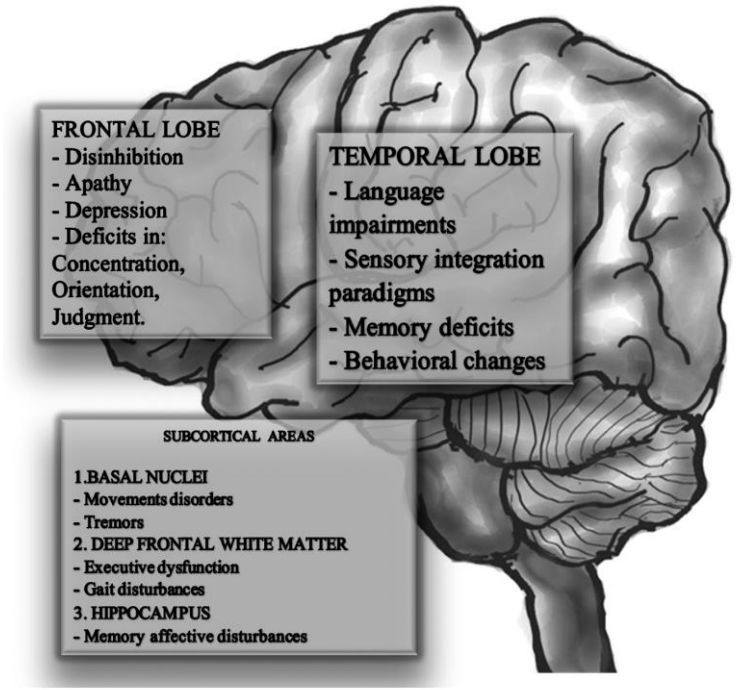
Review

Neuropsychiatric sequelae of medication non-adherence in people living with HIV

Debora Moreira[1], Rida Khan[2] and Paulo Marcelo Gondim Sales[3,*]

Psychiatric sequelae
↑Depression, ↑anxiety disorders, adjustment disorder, grief reaction
↑Manic episodes in bipolar disorder
Worsening of substance use disorders (Especially stimulants/cannabis) ↑PTSD, re-traumatization
Psychosis (Hallucinations, disorganization of behavior, delusions)



Neurological sequelae
CNS opportunistic infections: toxoplasma encephalitis, progressive multifocal leukoencephalopathy (JC virus), cytomegalovirus retinitis, herpes simplex virus retinitis, cryptococcal meningoencephalitis, primary CNS lymphoma, large B-cell lymphoma
Cardiovascular and cerebrovascular events: vascular dementia, thrombocytopenia Distal symmetric polyneuropathy
Asymptomatic neurocognitive impairment Mild neurocognitive disorder HIV-associated dementia

Theme 1: Social support

- Many participants described being socially isolated due to the physical manifestations of HIV-related illness or HIV treatment

Theme 2: Self-identity

- Internalized stigma accounted for 4.8% of the variance in cognitive-affective depression scores over and above the other variables

Theme 3: Poverty

- In several studies, participants also described how poverty and stigma were intertwined in a reciprocal and mutually reinforcing relationship

Theme 4: Coping

- Many participants reported low self-esteem, depressed mood, or anger related to their diagnosis, citing their inability to cope with their HIV status as the reason they failed to take their medications

Theme 5: Health systems

- Compassionate human capital elements could establish a supportive clinical environment for patients, while certain clinical programs could be designed to address care for the entire family

Depression

Screening and diagnosis of depression		
Who?	**How to screen?**	**How to diagnose?**
Consider screening at each routine HIV clinic visit, in view of the high prevalence of depression **Populations at particularly high risk** • Positive history of depression in family • Depressive episode in personal history • Older age • Adolescence • Persons with history of drug addiction, psychiatric, neurologic or severe somatic co-morbidity • Use of EFV • Use of neurotropic and recreational drugs • As part of investigation of neurocognitive impairment, see page 114 • Socially isolated	• Two questions: 1. Have you often felt depressed, sad or without hope in the last few months? 2. Have you lost interest in activities that you usually enjoy? • Rule out other medical conditions (such as hypothyroidism, hypogonadism, Cushing's syndrome, vitamin B12 deficiency) • Rule out depressive symptoms associated with ART (such as EFV) and non-ART medication (such as corticosteroids)	**Symptoms – evaluate regularly** **A.** At least 2 weeks of depressed mood OR **B.** Loss of interest OR **C.** Diminished sense of pleasure (+) **4 out of 7 of the following:** 1. Weight change of ≥ 5% in one month or a persistent change of appetite 2. Insomnia or hypersomnia on most days 3. Changes in speed of thought and movement 4. Fatigue 5. Feelings of guilt and worthlessness 6. Diminished concentration and decisiveness 7. Suicidal ideation or a suicide attempt(i) Assessment of the risk of suicide should be done with the following questions: • Are these just ideas? • Are they intrusive and how many? • How much control do you have over these ideas? • Have you made a plan? • Are you about to take action?

Degree of depression	Number of symptoms (see page 106: A, B or C + 4/7)	Treatment	Consultation with expert
No	< 4	No	
Mild	4	• Problem-focused consultation • Consider antidepressant treatment(i) • Recommend physical activity	• Always, if treating doctor is unfamiliar with use of antidepressants • If depression not responding to treatment • If person has suicidal ideation or psychotic symptoms (delusions or hallucinations) • In case of complex situations such as drug addiction, anxiety disorders, personality disorders, dementia, acute severe life events • Clinical improvement with antidepressants may take up to 4 weeks; there is no need to change antidepressants before this time. Dose increment of antidepressant may be considered
Intermediate	5-6	Start antidepressant treatment (i,ii,iii)	
Severe	> 6	Refer to expert (essential)(iv)	

i See Drug-drug Interactions between Antidepressants and ARVs
ii There is an increased risk of suicide and serious traffic accident in the first 15 days of antidepressant treatment; frequent monitoring in groups 5 and 6 is required during this period
iii In groups 4, 5 and 6, psychotherapeutic follow-up (e.g. cognitive behavioral therapy CBT) may be indicated (consult with expert advice)
iv Mental health professionals should always be consulted if there is a risk of suicide

If a person is diagnosed with depression, switching off EFV to another third ARV drug according to switch rules is recommended

Drug-drug Interactions between Antidepressants and ARVs

	Antidepressants	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	LEN	BIC	CAB/ RPV	DTG	EVG/c	RAL	TAF	TDF
NaSSA	mirtazapine	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔a	↔a	↔	↔	↔	↔a	↔	↑	↔	↔	↔
SSRI	citalopram	↑ a,b	↑ a,b	↑	↑	↑ a,b	↔	↓	↓	↓	↔a	↔a	↔	↔	↔	↔a	↔	↑	↔	↔	↔
	escitalopram	↑ a,b	↑ a,b	↑	↑	↑ a,b	↔	↓	↓	↓	↔a	↔a	↔	↔	↔	↔a	↔	↑	↔	↔	↔
	fluoxetine	↑	↑	↑	↑	↑a	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	fluvoxamine	↑	↑	↑	↑	↑a	↔	↔	↔	E	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	paroxetine	↑↓?	↑↓?	↑↓?	↓39%	↑↓?	↔	↔	↑3%	↔	↔	↔	↔	↔	↔	↔	↔	↑↓?	↔	↔	↔
	sertraline	↑	↓	↑	↓49%	↓a	↔	↓39%	↓	↓	↔	↔	↔	↔	↔	↔	↔	↓7%	↔	↑9%	↔
	vortioxetine	↑c	↑c	↑c	↑c	↑c	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑c	↔	↔	↔
SNRI	desvenlafaxine	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	duloxetine	↑	↑↓	↑	↑↓	↑↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	milnacipran	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	venlafaxine	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔a	↔a	D	↔	↔	↔a	↔	↑	↔	↔	↔
TCA	amitriptyline	↑	↑	↑	↑	↑ a,b	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	clomipramine	↑ a,b	↑ a,b	↑b	↑b	↑ a,b	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↑b	↔	↔	↔
	desipramine	↑a	↑a	↑	↑	↑5%a	↔	↔	↔	↔	↔a	↔a	↔	↔	↔	↔a	↔	↑	↔	↔	↔
	doxepin	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	imipramine	↑ a,b	↑ a,b	↑b	↑b	↑ a,b	↔	↓	↓	↓	↔a	↔a	↔	↔	↔	↔a	↔	↑b	↔	↔	↔
	nortriptyline	↑a	↑a	↑	↑	↑a	↔	↔	↔	↔	↔a	↔a	↔	↔	↔	↔a	↔	↑	↔	↔	↔
	trimipramine	↑a	↑a	↑	↑	↑a	↔	↔	↔	↔	↔a	↔a	↔	↔	↔	↔a	↔	↑	↔	↔	↔
TeCA	maprotiline	↑a	↑a	↑	↑	↑a	↔	↔	↔	↔	↔a	↔a	↔	↔	↔	↔a	↔	↑	↔	↔	↔
	mianserin	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔a	↔a	↔	↔	↔	↔a	↔	↑	↔	↔	↔
Others	agomelatine	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	bupropion	↔	↓	↔	↓	↓57%	↔	↓55%	↔	↓	↔	↔	↔	↔	↔	↔	↔	↑?	↔	↔	↔
	nefazodone	↑	↑	↑	↑	↑	E	↓E	↓E	↓E	E	E	E	E	E	E	↔	↑	↔	↔	↔
	phenelzine	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	reboxetine	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	St John's wort	Dd	Dd	Dd	Dd	Dd	Dd	Dd	Dd	Dd	Dd	Dd	Dd	Dd #	Dd	Dd	De	Dd	D	Dd	↔
	tranylcypromine	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	trazodone	↑ a,b	↑ a,b	↑	↑	↑ a,b	↔	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↑	↔	↔	↔

Anxiety

Screening and diagnosis of anxiety		
Who?	**How to screen?**	**How to diagnose?**
Consider screening all persons with HIV at each routine clinic visit (in view of the high prevalence of anxiety) **Populations at particularly high risk** • Positive history of anxiety disorders in family • Anxious personality • Alcohol excess • As part of investigation of cognitive impairment, see page 114 • Multiple stressful life events (particular relevance during COVID-19 pandemic)	**Generalised Anxiety Disorder-2 (GAD-2) Screening tool**[(i)]**:** "Over the last 2 weeks, how often have you been bothered by the following problems?" • Feeling nervous, anxious or on edge • Not being able to stop or control worrying **Score each question and calculate sum:** 0. Not at all 1. Several days 2. More than half the days 3. Nearly every day	**If GAD-2 cut-off score of ≥ 3**, ask the following questions to diagnose General Anxiety Disorder: • excessive anxiety for more days than not over 6 months • difficulty controlling worry • associated with at least three of these symptoms (restlessness, fatigue, difficulty concentrating, irritability, muscle tension, sleep disturbances) • significant life impairment • not attributable to another substance or medical condition • not being better explained by another medical disorder **Rule out hyperthyroidism, hypoglycemia and hyperadrenocorticism. Exclude caffeine excess and use of stimulants (such as cocaine, crystal meth, amphetamines)** **Seek expert advice to diagnose panic disorders, social phobia and PTSD**

Degree of anxiety disorders	GAD-2 Score	Treatment	Consultation with expert
Minimal	< 3	Relaxation techniques	

Significant	≥ 3	• Recommend relaxation techniques
		• Consider benzodiazepines, mainly clonazepam or lorazepam for **a short period of time** (less than 4 weeks)
		• Consider antidepressant treatment with SSRI(i)
		• Consider psychotherapeutic intervention:
		  • Cognitive Behavioral Therapy
		  • Cognitive Behavioral Stress Management
		  • Mindfulness-based Cognitive Therapy
		  • Peer Support Counseling
			• Always, if treating doctor is unfamiliar with use of antidepressants
			• If anxiety not responding to treatment
			• If person has suicidal ideation
			• In case of complex situations such as drug addiction, personality disorders, acute severe life events
			• Clinical improvement with antidepressants may take up to 4 weeks; there is no need to change antidepressants before this time
			Dose increment of antidepressant may be considered

Generalized anxiety disorder		Start antidepressant treatment with SSRI and benzodiazepine if needed (to reduce anxiety faster)(i)(ii) Refer to mental health expert to start psychotherapeutic intervention	

Drug-drug Interactions between Anxiolytics and ARVs

Anxiolytics		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	LEN	BIC	CAB/ RPV	DTG	EVG/c	RAL	TAF	TDF
BZD	alprazolam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↑ ^	↔	↔	↔	↑	↔	↔	↔
	chlor-diazepoxide	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↑ ^	↔	↔	↔	↑	↔	↔	↔
	clonazepam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↑	↔	↔	↔
	lorazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	oxazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
SSRI	escitalopram	↑ a	↑ a	↑	↑	↑ a	↔	↓	↓	↓	↔ b	↔ b	↔	↔	↔	↔ b	↔	↑	↔	↔	↔
	paroxetine	↑↓?	↑↓?	↑↓?	↓39%	↑↓?	↔	↔	↑3%	↔	↔	↔	↔	↔	↔	↔	↔	↑↓?	↔	↔	↔
SNRI	duloxetine	↑	↑↓	↑	↑↓	↑↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	venlafaxine	↑ b	↑ b	↑	↑	↑ b	↔	↓	↓	↓	↔ b	↔ b	D	↔	↔	↔ b	↔	↑	↔	↔	↔
Others	buspirone	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↑ ^	↔	↔	↔	↑	↔	↔	↔
	hydroxyzine	↑ a,b	↑ a,b	↑ a,b	↑ a,b	↑ a,b	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↑	↔	↔	↔

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ORIGINAL RESEARCH

Neuropsychiatric Adverse Events Following Antiretroviral Therapy in People Living with HIV: A Real-World Study of Dynamic Trends and Risk Factors in Hangzhou, China

Wenhui Zhang[1,2,*], Yi Wang[2,3,*], Er Li[1], Dingyan Yan[1,2], Jianhua Yu[2], Mingli Zhu[4], Jinchuan Shi[2,*], Liping Zheng[1,*]

Purpose: Neuropsychiatric adverse events (NPAEs) occur frequently in people living with human immunodeficiency virus (PLWH) receiving antiretroviral therapy (ART). This study aimed to assess the dynamic trends and risk factors of NPAEs among PLWH in Hangzhou taking efavirenz (EFV)- or dolutegravir (DTG)- or elvitegravir (EVG)-based regimens.

Patients and Methods: A total of 287 ART-naive PLWH were included in this study, EFV (400mg)- (n = 122), EFV (600mg)- (n = 37), DTG- (n = 73), EVG-based (n = 47) and other ART regimens (n = 8) as the initial ART regimen were administered for 12 months. All data were collected at five time points within a 12-month follow-up. The Pittsburgh Sleep Quality Index and Hospital Anxiety and Depression Scale were used to evaluate sleep disorders and anxiety and depression symptoms, respectively. The dynamic trends and potential risk factors of NPAEs were investigated using a generalized linear mixed model.

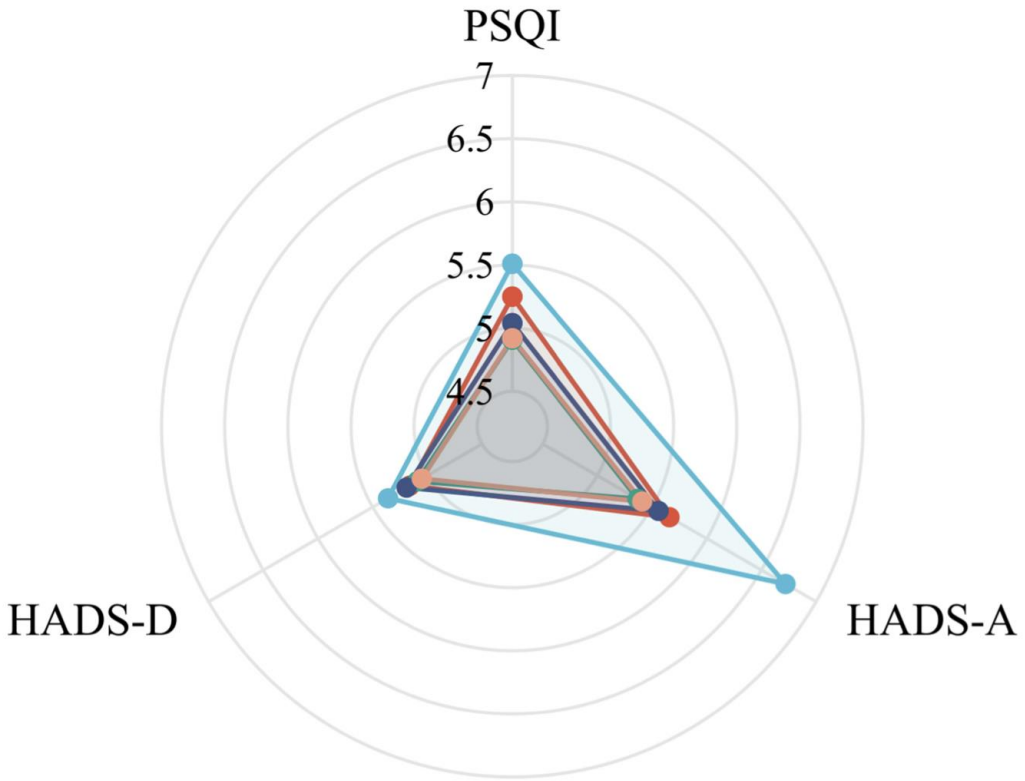
Results: Mean age was 29.4 (SD: 7.5) years with 97.2% males. After 12 months of ART, the prevalence of sleep disorders and anxiety decreased significantly, although only a slight improvement was observed for depression. In addition, there was a significant positive correlation between sleep disorders, anxiety, and depression. The risk factors for NPAEs differed slightly depending on the choice of ART regimen, but the seven factors most commonly associated with NPAEs were age, sex, marital status, education level, smoking status, body mass index, and WHO clinical stage. Treatment-induced changes in CD4-positive T-cell count and virological suppression did not depend on the particular choice of ART regimen.

Conclusion: The prevalence of sleep disorders and anxiety changed significantly over time on ART and the risks of these disorders were associated with seven common clinical and demographic factors.

Keywords: sleep disorders, anxiety, depression, antiretroviral therapy, people living with HIV

Table 2 The Median Scores of Sleep Disorders, Anxiety and Depression at M0, M1, M3, M6 and M12 After ART Among PLWH

Parameters	Time point					*P* value	
	M0	M1	M3	M6	M12	r_s test	Friedman test
PSQI	5 (4.7)	5 (4.7)	5 (3.6)	5 (3.7)	5 (3.7)	0.001 (−0.086)	0.003
HADS-A	6 (4.9)	6 (3.8)	5 (2.8)	6 (2.8)	5 (2.8)	0.0001 (−0.099)	0.0001
HADS-D	5 (2.8)	5 (2.8)	4 (1.8)	5 (1.8)	4 (1.9)	0.137 (−0.04)	0.049



Research | Open access | Published: 22 April 2024

Stigma and mental health among people living with HIV across the COVID-19 pandemic: a cross-sectional study

Francesco Di Gennaro, Roberta Papagni, Francesco Vladimiro Segala ✉, Carmen Pellegrino, Gianfranco Giorgio Panico, Luisa Frallonardo, Lucia Diella, Alessandra Belati, Carmen Rita Santoro, Gaetano Brindicci, Flavia Balena, Davide Fiore Bavaro, Domenico Montalbò, Giacomo Guido, Lina Calluso, Marilisa Di Tullio, Margherita Sgambati, Deborah Fiordelisi, Nicolò De Gennaro & Annalisa Saracino

BMC Infectious Diseases **24**, Article number: 423 (2024) | Cite this article

1. **Hamilton Anxiety Rating Scale (HAM-A)**: This scale consists of 14 items, with scores ranging from 0 (not present) to 4 (severe anxiety), yielding a possible total score between 0 and 56 [22].
2. **Beck Depression Inventory (BDI-II)**: The BDI-II comprises 21 items, each scored from 0 to 3, resulting in a total score of 0 to 63. Higher scores indicate more severe depressive symptoms [23].
3. **Primary Care PTSD Screen for DSM-5 (PC-PTSD-5)**: This screening tool has 5 items scored as "yes" or "no" to identify the likely presence of PTSD [24].
4. **CAGE-AID questionnaire**: Adapted to include drug use, this instrument has 4 items scored with "yes" or "no" responses to screen for alcohol and substance misuse [25].

	Overall (*n* = 578)	Mental Disorders screening negative (*N* = *437*)	Mental Disorders screening positive (*N* = 141)	OR [95% CI]	*p*-value[1]
Gender, n (%)					
Male	426 (73.7)	334 (76.3)	92 (65.2%)	Ref.	Ref.
Female	147 (25.43)	102 (22.8%)	45 (31.9%)	1.18 [0.80;1.36]	-
Non-binary	4 (0.69%)	0 (0.93%)	4 (2.8%)	-	-
Age, median [IQR]	49 [37;56]	48.0 [36.0;56.0]	52.0 [41.0;57.0]	1.02 [0.99;1.04]	0.141
MSM (Men who have sex with men) n (%)	195 (33.74%)	100 (22.9%)	95 (67.3%)	2.94 [1.55;4.38]	0.001
Continent of origin, n (%)					0.840
Europe	559 (96.71%)	420 (95.8%)	139 (98.4%)	Ref.	Ref.
Africa	12 (2.08%)	10 (2.33%)	2 (1.59%)	-	-
America	7 (1.21%)	7 (1.86%)	0 (0.00%)	-	-
Tobacco smoke, n (%)	244 (42.21%)	166 (38.1%)	78 (55.6%)	2.02 [1.14;3.60]	0.015
Years of HIV (ys of diseases), n (%)	8 [4;20]	7.00 [3.00;15.5]	11.0 [5.00;23.0]	1.03 [1.00;1.06]	0.024
Substance use, n (%)	65 (11.25%)	47 (10.7%)	18 (12.7%)	1.23 [0.49;2.81]	0.648
HBV co-infection, n (%)	25 (4.33%)	18 (4.19%)	7 (4.76%)	1.18 [0.24;4.19]	0.814
HCV co-infection, n (%)	81 (14.01%)	57 (13.0%)	24 (17.5%)	1.42 [0.64;2.99]	0.379
COVID vaccination (number of doses), n (%)					
0–1	13 (2.25%)	9 (2.33%)	4 (3.17%)	Ref.	Ref.
2	49 (8.48%)	33 (7.44%)	16 (11.1%)	1.06 [0.17;9.81]	0.954
3	516 (89.27%)	395 (90.2%)	121 (85.7%)	0.67 [0.13;5.31]	0.659
On ART, n (%)	576 (99.65%)	437 (100%)	139 (98.4%)	-	0.227
ART regimen, n (%)					
2 NRTI + INSTI	248 (42.91%)	170 (39.0%)	78 (55.6%)	Ref.	Ref.
NRTI + PI	96 (16.61%)	76 (17.4%)	20 (14.3%)	0.58 [0.24;1.30]	0.195
NRTI + INSTI	78 (13.49%)	65 (15.0%)	13 (9.52%)	0.45 [0.16;1.33]	0.091
NRTI + NNRTI	92 (15.92%)	76 (17.4%)	16 (11.1%)	0.46 [0.17;1.08]	0.075
NNRTI + INSTI	53 (9.17%)	42 (9.86%)	11 (7.94%)	0.58 [0.18;1.57]	0.295
Others	11 (1.9%)	8 (1.41%)	3 (1.59%)	0.86 [0.03;7.69]	0.903
Dolutegravir-containing regimen, n (%)	144 (24.91%)	79 (18.1%)	65 (46.0%)	3.82 [2.08;7.05]	**< 0.001**
Previous SARS CoV-2 infection, n (%)	31 (5.36%)	29 (6.51%)	2 (1.59%)	0.26 [0.01;1.35]	0.126
Comorbidities, n (%)	294 (50.87%)	213 (48.8%)	81 (57.1%)	1.39 [0.79;2.48]	0.251
Diabetes, n (%)	29 (5.02%)	15 (3.26%)	14 (9.52%)	3.12 [1.35;9.97]	**0.002**
Hypertension, n (%)	64 (11.07%)	39 (8.84%)	25 (17.5%)	2.19 [0.94;4.85]	0.067
CKD, n (%)	19 (3.29%)	14 (3.26%)	5 (3.17%)	1.02 [0.14;4.51]	0.977
Dyslipidemia, n (%)	50 (8.65%)	32 (7.44%)	18 (12.7%)	1.82 [0.70;4.41]	0.211
Substance use, n (%)	61 (10.55%)	43 (9.77%)	18 (15.9%)	1.75 [0.74;3.89]	0.192
AIDS events, n (%)	225 (38.93%)	156 (35.8%)	69 (48.9%)	1.44 [1.15;2.38]	**0.002**
HIV-related hospitalization, n (%)	161 (27.85%)	132 (30.2%)	29 (20.6%)	0.61 [0.30;1.17]	0.136
Nadir CD4 count, cell/mm3 (median, Q1, Q3)	650 [230; 800]	677 [289;800]	560 [190;695]	1.00 [1.00;1.00]	**0.012**
Total Pill Burden (median, Q1, Q3)	1.00 [1.00;3.00]	1.00 [1.00;3.00]	2.00 [1.00;3.00]	1.04 [0.90;1.22]	0.574

Table 2 Logistic regression analysis (unadjusted and multiple adjusted estimates) for positivity to HAM-A, BDI-II, PTSD and CAGE-AID

	HAM-A positive (*n* = 91),	aOR [95%CIs]	CAGE-AID (*n* = 35)	aOR [95%CIs]	BDI-Positive (*n* = 104)	aOR [95%CIs]	PTSD (*n* = 29)	aOR [95%CIs]
Self-reported stigma, n (%)								
None (0–3)	26 (28.6)	Ref.	16 (45.7)	Ref.	44 (42)	Ref.	9 (28.6)	Ref.
Moderate (4–7)	28 (31.1)	1.76 [0.82;3.26*]	10 (28.6)	1.47 [0.71;3.25]	25 (24)	1.27 [0.55;2.79]	10 (35.7)	2.76[0.68;12.1]
Severe (8–10)	37 (40.3)	1.62 [1.28;2.57]*	9 (25.7)	0.68 [0.43;1.36]*	35 (34)	1.36 [0.62;1.73]	10 (35.7)	1.36[0.34;5.88]
Family stigma, n (%)	81 (88.6)	3.44 [2.18;5.97]**	31 (88.2)	2.42 [1.65;3.94]**	62 (60)	2.46 [1.52;4.73]**	22 (78.6)	4.12 [1.89;7.10]**
Social isolation, n (%)	82 (90.9)	4.56 [2.61;7.16]*	29 (82.4)	2.72 [1.55;4.84]*	66 (64)	2.65 [1.61;3.21]**	22 (78.6	3.52 [2.09;5.03]**
Perceived impact of COVID-19 pandemic on MH, n (%)								
None (0–3)	14 (15.9)	Ref.	13 (35.3)	Ref.	27 (26)	Ref.	8 (28.6)	Ref.
Moderate (4–7)	12 (13.6)	1.25 [0.38;4.01]*	10 (28.6)	1.47 [0.71;3.25]	25 (24)	1.38 [0.58;3.29]	2 (7.14)	0.38 [0.01;2.85]
Severe (8–10)	65 (70.5)	5.23 [2.28;13.7]**	16 (47.1)	1.64 [0.91;4.00]	52 (50)	2.05 [1.37;4.30]**	19 (64.3)	3.13 [1.26;8.36]*
DTG-based ART(Yes), n (%)	54 (59.1)	6.52 [3.30;13.2]*	14 (41.2)	2.30 [0.79;6.34]	54 (52)	4.76 [2.49;9.19]**	15 (50.0)	2.01 [1.02;7.02]*

[1] Mann-Whitney test or Fisher's exact test, as appropriate

Sleep

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Sleep disturbances and their correlation with cardiovascular risk, obesity, and mood disorders in people with HIV

Maria Mazzitelli [1], Mattia Trunfio [2 3], Ana Milinkovic [4 5], Eleonora Castelli [1], Lolita Sasset [1], Davide Leoni [1], Margherita Salvucci [5], Riccardo Cazzaro [5], Ilaria Calcinoni [5], Pietro Balducci [5], Gustavo Coelho Quirino Ribeiro [5], Giacomo Filagrana [6], Vincenzo Scaglione [1], Anna M Cattelan [1 7 8]

- Cross-sectional analysis in single centre cohort of PWH.
- Sleep quality assessed using by ESS, ISI, BQ, PSQI
- GAD-7 and PHQ-9
- Demographic, clinical and HIV-related data were collected, and Framingham and Data collection on Adverse effects of anti-HIV Drugs (DAD)-10 scores were computed in modelling associations with each SDs scale.

Item/Parameter		**Overall population=721**
Sleep disorders*		
Overall, n (%)		555 (77)
Altered BO, n (%)		226 (31.3)
Altered ISI, n (%)		224 (31.1)
Altered ESS, n (%)		57 (7.9)
Altered PSQI, n (%)		435 (60.3)
Parasomnia, n (%)		3 (0.4)
Sleep movement disorders, n (%)		7 (1.0)
Bruxism, n (%)		3 (0.4)
*Each patient may have more than one		
Self-reported insomnia severity		
None, n (%)		258 (35.8)
Mild, n (%)		225 (31.2)
Moderate, n (%)		150 (20.8)
Severe/extremely severe, n (%)		88 (12.2)
Self-reported snoring, n (%)		349 (48,4)
Sleeping hours per night, hours, median (IQR)		7.0 (6.0-7.5)
Time to fall asleep>30 min, n (%)		218 (30.2)
Early awakening, n (%)		348 (42.3)
Issues in sleep maintenance, n (%)		391 (54.2)
Issues in falling asleep, n (%)		352 (48.9)
Afternoon nap (yes), n (%)		506 (70.2)
Drugs affecting sleep, n (%)	Antiretrovirals	364 (50.5%)
	Corticosteroids	12 (1.7%)
	Medical opioids/derivatives	32 (4.4%)
	Hypno-inducing drugs	62 (8.2%)
	Drugs with effect on the sleep-wake cycle	89 (12.3%)
FSS, altered, n (%)		112 (15.5)
Self-reported wellness (0-10), median (IQR)		7 (6-8)

Characteristic		Study population (n=721)
Demographics		
Age, years, median (IQR)		53 (44-59)
Male sex, n (%)		518 (71.8)
Ethnicity, n (%)	Caucasian	613 (85.0)
	Black African	74 (10.3)
	Others	34 (4.7)
Education and behaviours		
Education, years, median (IQR)		13 (8-13)
Smoker, n (%)		338 (46.9)
Regular physical exercise, n (%)		196 (21.2)
Alcohol use disorders, n (%)		64 (8.9)
HIV-related parameters		
Acquisition routes, n (%)	MSM	379 (52.6)
	Heterosexual	250 (34.7)
	IVDU	78 (10.8)
	Others	14 (1.9)
Length of HIV infection, years, median (IQR)		15 (7-24)
cART, n (%)	Dual therapy (DTG+3TC)	261 (36.2)
	2NRTI-INI	179 (24.8)
	2NRTI-nNRTI	204 (28.3)
	2NRTI-PI	72 (10.0)
	Others	5 (0.7)
Current CD4 count, cells/mmc, median (IQR)		638 (474-811)
Nadir CD4 count, cells/mmc, median (IQR)		299 (160-459)
Past AIDS episodes, n (%)		130 (18.0)
Detectable plasma HIV-RNA (>50 copies/ml), n		28 (3.9)
Coinfections*, n (%)	HBsAg	75 (10.4)
	HCV Ab (+)	126 (17.5)
	Positive HCV-RNA, n	34 (4.7)
Comorbidities* and polypharmacy		
Autoimmune disorders, n (%)		54 (7.5)
Cancer, n (%)		105 (14.6)
Chronic kidney disease, n (%)		57 (7.9)
Chronic obstructive pulmonary disease, n (%)		44 (6,1)
Diabetes, n (%)		68 (9.4)
Dyslipidaemia, n (%)		214 (29.7)
Ischemic heart disease, n (%)		51 (7.1)
Hypertension, n (%)		239 (33.1)
Liver cirrhosis, n (%)		24 (3.3)
Neurological diseases, n (%)		107 (14,8)
Obesity, n (%)		161 (22.3)
Osteoporosis, n (%)		139 (19.3)
Multimorbidity (yes), n (%)		469 (65.0)
N comorbidities/patient, median (IQR)		2 (1-4)
Polypharmacy (yes), n (%)		145 (20.1)
N comedications/patient (excluding antiretrovirals), median (IQR)		2 (1-4)

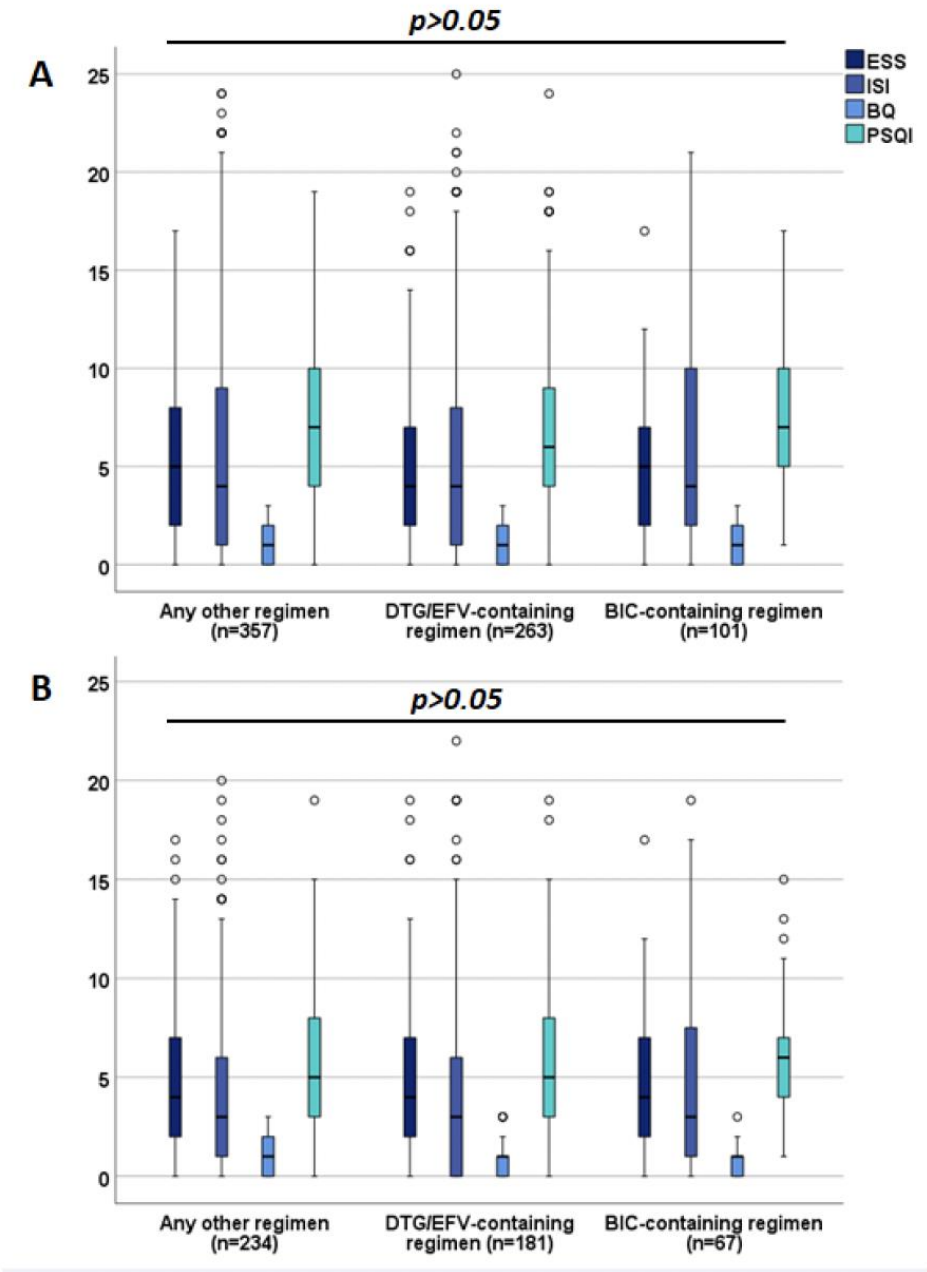
*Each patient may have more than one

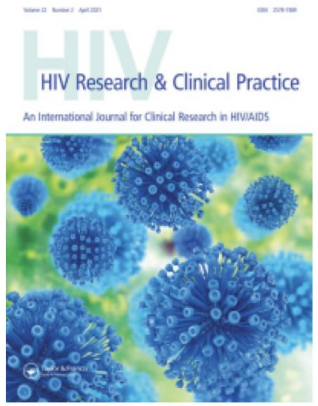
ACCEPTED

- *76.9% had SDs*
- *60.3%, 31.3%, 31.1% and 7.9% at PSQI, BQ, ISI, and ESS, respectively.*
- *Anxiety and depression were detected in 28.3% and 16.1% participants, respectively.*
- *BQ score was independently associated with high BMI (p<0.001), Framingham risk>10% (p<0.001), and both DAD-10R and -10F*

score>10% (p<0.001 and p=0.031).

- *PSQI and ISI scores were independently associated with depression and anxiety (p<0.001).*
- *No association between SDs and specific antiretroviral regimens, nor HIV-related parameters was detected.*





HIV Research & Clinical Practice

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Impact of switching to injectables cabotegravir and rilpivirine on sleep disturbances in a cohort of people living with HIV

Maria Mazzitelli, Elena Agostini, Eleonora Vania, Nicolò Presa, Lolita Sasset, Davide Leoni, Samuele Gardin, Vincenzo Scaglione & Annamaria Cattelan

ABSTRACT

Background: Recently, injectable cabotegravir/rilpivirine (ICAB/RPV) became available for HIV treatment. However, there are no real-life data on the impact of switching to ICAB/RPV on sleep disturbances (SD). Therefore, we aimed at assessing and investigating this aspect in our cohort.

Methods: A SD multidimensional assessment (Epworth Sleepiness scale, Insomnia severity Index, Berlin Questionnaire, and Pittsburg Sleep Quality Index, PSQI) was performed to all people who consented before starting ICAB/RPV and 12 wk after the switch. Demographics, life-style habits, laboratory, and clinical data were collected from medical health records.

Results: To June 2023, 46 people were included, 76.1% males, with a median age of 48.5 (IQR: 41–57), 50% had multimorbidity, 13% was on polypharmacy. Median age with HIV and CD4 + T cell count nadir were 10 (5–19.5) years and 360 (205–500) cell/mm^3, respectively. The reason to start a long-acting strategy was person's choice in all cases. Baseline antiretroviral regimens were mostly: tenofovir alafenamide/emtricitabine/rilpivirine (39.1%) and dolutegravir/lamivudine (32.6%). No significant changes were observed in any of the scores for each questionnaire, but for a worsening PSQI. 37% people reported a subjectively improved sleep quality, even if statistically significant changes were not observed in almost all the sleep parameters.

Conclusions: To the best of our knowledge, this is the first study exploring impact of switching to ICAB/RPV on SD. Despite integrase inhibitor have been associated with SD, we did not observed a negative impact on sleep quality after the switch to ICAB/RPV. More studies and with larger number of people are necessary to confirm our results.

Table 2. Sleep metrics and results from screening for sleep disturbances at the baseline and at follow-up.

Item/parameter	Baseline, ($n = 46$)	Follow-up ($n = 46$)	P value
Sleep disorders*			
Overall, n (%)			
None	29 (63)	26 (56.5)	0.512
2 or more positive categories in BQ, n (%)	9 (19.5)	7 (15.2)	0.748
ISI >15, n (%)	6 (13)	4 (8.7)	0.739
ESS > 10, n (%)	7 (15.2)	2 (4.4)	0.157
PSQI> 5, n (%)	6 (13)	20 (43.5)	0.002
Parasomnia, n (%)	1 (2.2)	1 (2.2)	1
*Each patient may have more than one			
Scoring for each questionnaire, median (IQR)			
BQ score, median (IQR)	1 (0–2)	1 (1–2)	0.41
ISI score, median (IQR)	5 (3–7)	6 (3–7)	0.26
ESS score, median (IQR)	7 (5–8)	6 (5–8)	0.23
PSQI score, median (IQR)	4 (3–5)	7 (5–7)	0.001
Self-reported insomnia severity			
None, n (%)	21 (45.6)	24 (52.2)	0.676
Mild, n (%)	12 (26.1)	17 (36.9)	0.369
Moderate, n (%)	8 (17.4)	3 (6.5)	0.197
Severe/extremely severe, n (%)	5 (10.9)	2 (4.4)	0.434
Self-reported snoring, n (%)	19 (41.3)	18 (39.1)	1
Sleeping hours per night, hours, median (IQR)	7 (6–8)	7.0 (7–8)	0.214
Time to fall asleep > 30 min, n (%)	12 (26)	10 (8.8)	0.807
Early awakening, n (%)	18 (39.1)	12 (26)	0.260
Issues in sleep maintenance, n (%)	21 (45.6)	11 (23.9)	0.048
Issues in falling asleep, n (%)	19 (41.3)	12 (26)	0.185
Afternoon nap (yes), n (%)	34 (73.9)	28 (60.9)	0.266
Overall use of hypno-inducing drugs, n (%)	4 (8.7)	6 (13)	0.739
Self-reported wellness (0–10), median (IQR)	8 (7–9)	8 (7–9)	0.388
How would you rate the overall quality of your sleep?			
Improved	–	17 (37)	–
Unchanged	–	29 (63)	–
Worsened	–	0 (0)	–

Outcome of a multidimensional intervention for insomnia in a cohort of people living with HIV

POSTER ID: 3316

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BACKGROUND

- No studies specifically assessed interventions for improving sleep quality (SQ) in people with HIV (PWH). We introduced a multidimensional program for SQ in the routine management at our outpatient clinic and assessed its impact on PWH suffering from insomnia.

METHODS

- Following up a study on sleep disorders[1] in our cohort we implemented an interventional study in adult PWH with subthreshold (≥8), moderate (≥15), or severe (≥22) insomnia at the Insomnia Severity Index (ISI). Quality of sleep, depression (PHQ9), and well-being were assessed at baseline and after 6 months. Participants received sleep hygiene counselling and underwent tailored interventions as shown in the study flow (Fig1A). Participants were categorized into three groups based on their adherence to prescribed interventions: fully adherent, partially adherent (attended at least one intervention when more than one was prescribed), and non-adherent (FA-PA-NA). The impact of interventions on insomnia was assessed by mixed-effects models for repeated measures and paired tests for longitudinal data (e.g., Wilcoxon, Friedman).

RESULTS 1/2

- Among 730 PWH screened, 277 had altered ISI score, and 175 eventually participated (Figure 1A). 65.7% were male, median age and CD4+ T cell count were 51 years and 650 cell/μL, 95.4% PWH had HIV-RNA<50 cp/mL (demographic and clinical data in Table 1).
- 94.8%, 91.0% and 2.8% of participants were referred to psychologist, psychiatrist, and neurologist, and 30.3% and 20.5% had indication to hypo-inducing drugs/antidepressants and psychotherapy/cognitive-behavioral therapy.
- Seventy-seven participants (44.0%) were NA, 16 (9.1%) PA, and 82 (46.9%) FA, with no relevant baseline differences detected in demographics and clinical parameters among them.

Table 1. Main demographics and clinical characteristics of study population at baseline

Variable		Study population (n=175)
Age, years, median (IQR)		51 (44-59)
Male gender, n (%)		115 (65.7)
Caucasian, n (%)		150 (85.7)
Route of acquisition, n (%)	Males who have sex with males	85 (48.6)
	Heterosexuals	63 (36.0)
	Past intravenous drug users	27 (15.4)
Years with HIV, years, median (IQR)		17 (9-27)
Antiretrovirals, n (%)	Dual	61 (34.8)
	INI-based	51 (29.1)
	NNRTI-based	45 (25.7)
	PI-based	17 (9.7)
	Others	1 (0.6)
Current CD4+ count, cells/mmc, median (IQR)		650 (487-798)
Nadir CD4+ count, cells/mmc, median (IQR)		290 (171-462)
Previous AIDS, n (%)		36 (20.6)
HIV-RNA <50 copies/ml, n (%)		167 (95.4)
Positive HBsAg, n (%)		16 (9.1)
Positive HCV-RNA, n (%)		11 (6.3)
Polypharmacy, n (%)		43 (24.6)
Comorbidities, n (%)	Cancer	34 (19.4)
	Chronic kidney disease	11 (6.3)
	Ischemic heart disease	8 (4.6)
	Lipodystrophy	24 (13.7)
	Hypertension	57 (32.6)
	Obesity	37 (21.1)
	Cirrhosis	8 (4.6)
	Diabetes	15 (8.6)
	Chronic obstructive pulmonary disease	18 (10.3)
	Anxiety	87 (49.7)
	Depression	67 (38.3)
	Central nervous disorders	29 (16.6)
N. comorbidities per subject, median (IQR)		3 (2-5)
Multimorbidity, n (%)		137 (78.3)

Legend to table 1. INI= integrase inhibitor, PI= protease inhibitor, NNRTI= non-nucleos(t)ide reverse transcriptase inhibitor, NRTI= nucleos(t)ide reverse transcriptase inhibitor, IQR=interquartile range, n= number

Figure 1A. Study flow chart from the sampling frame, through the screening/enrolment, and the interventions prescribed and eventually attended

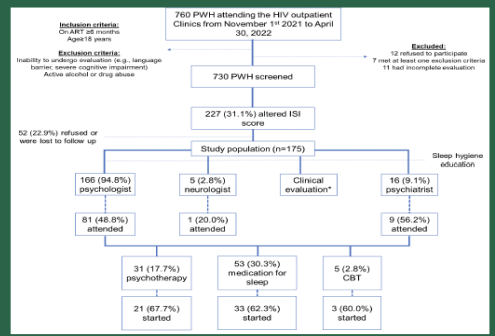
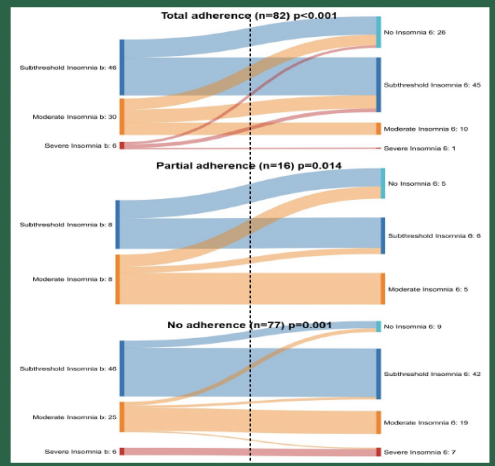


Figure 1B. Trajectories from baseline to follow-up of ISI score according to intervention adherence.



RESULTS 2/2

- Baseline ISI categories and their trajectory over time are shown in Figure 1B: all the groups had an improvement in ISI score and in the distribution of insomnia categories; the highest effect size was in FA (Z=-5.8, p<0.001 vs -2.1, p=0.035 in PA, and -2.6, p=0.010 in NA). Perceived wellness and sleep hours per night increased in all individuals but more relevantly in FA (Z=4.3 and Z=4, both p<0.001).
- After adjusting by age, sex, and baseline ISI, PHQ9 and adherence to interventions were the only independent factors associated with ISI overtime: compared to NA, ISI decreased in FA (aβ -1.24 [-2.09; -0.38], p=0.005) and showed a trend of reduction in PA (aβ -0.71 [-2.21; 0.78], p=0.349).

Sleep quality may significantly influence everyone's quality of life. That is why screening for sleep disturbances and implementing targeted multidimensional services (psychologists, psychiatrists, pneumologists, neurologists, medications) aiming at improving conditions such as insomnia can greatly enhance the PWH well-being.

CONCLUSIONS

A real-life outpatient multidimensional management of SQ based on sleep hygiene and individual-tailored interventions proved to be effective in improving the overall SQ and wellness in PWH suffering from insomnia. Therefore, such kind of approach should be integrated into daily clinical practice with specific multidisciplinary services in HIV clinics.

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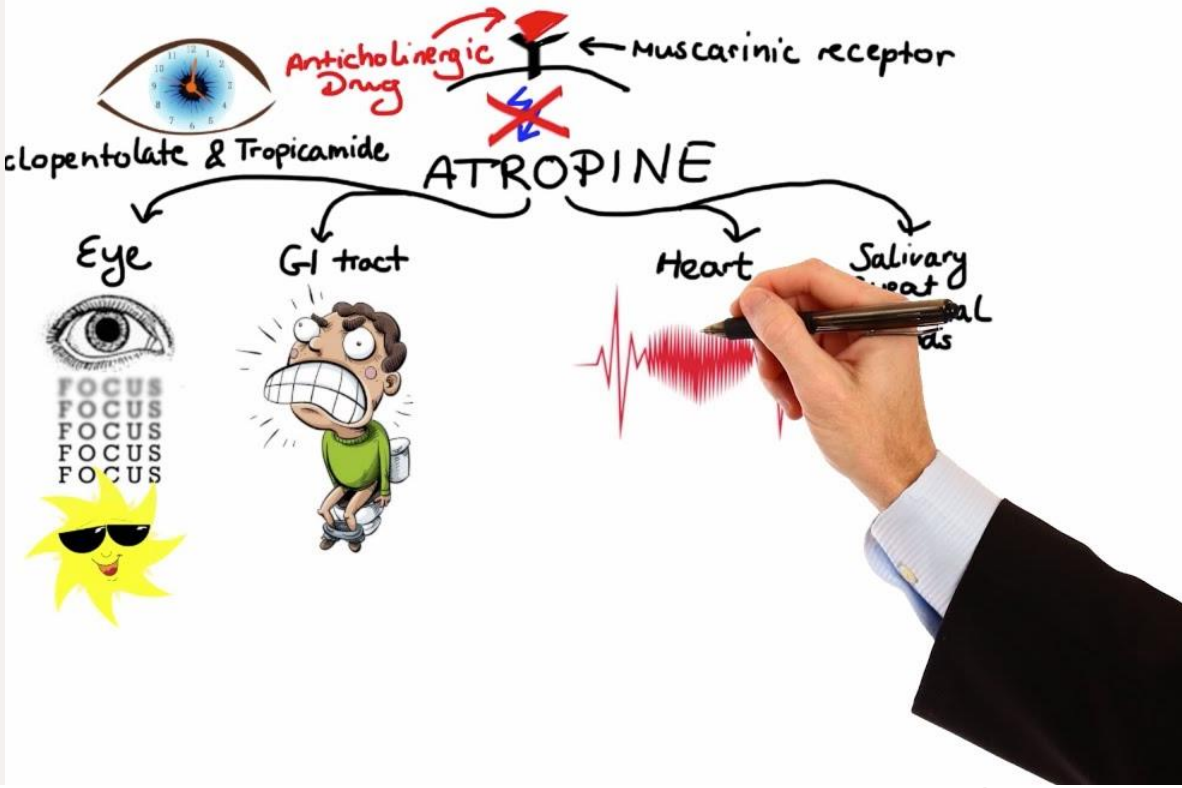
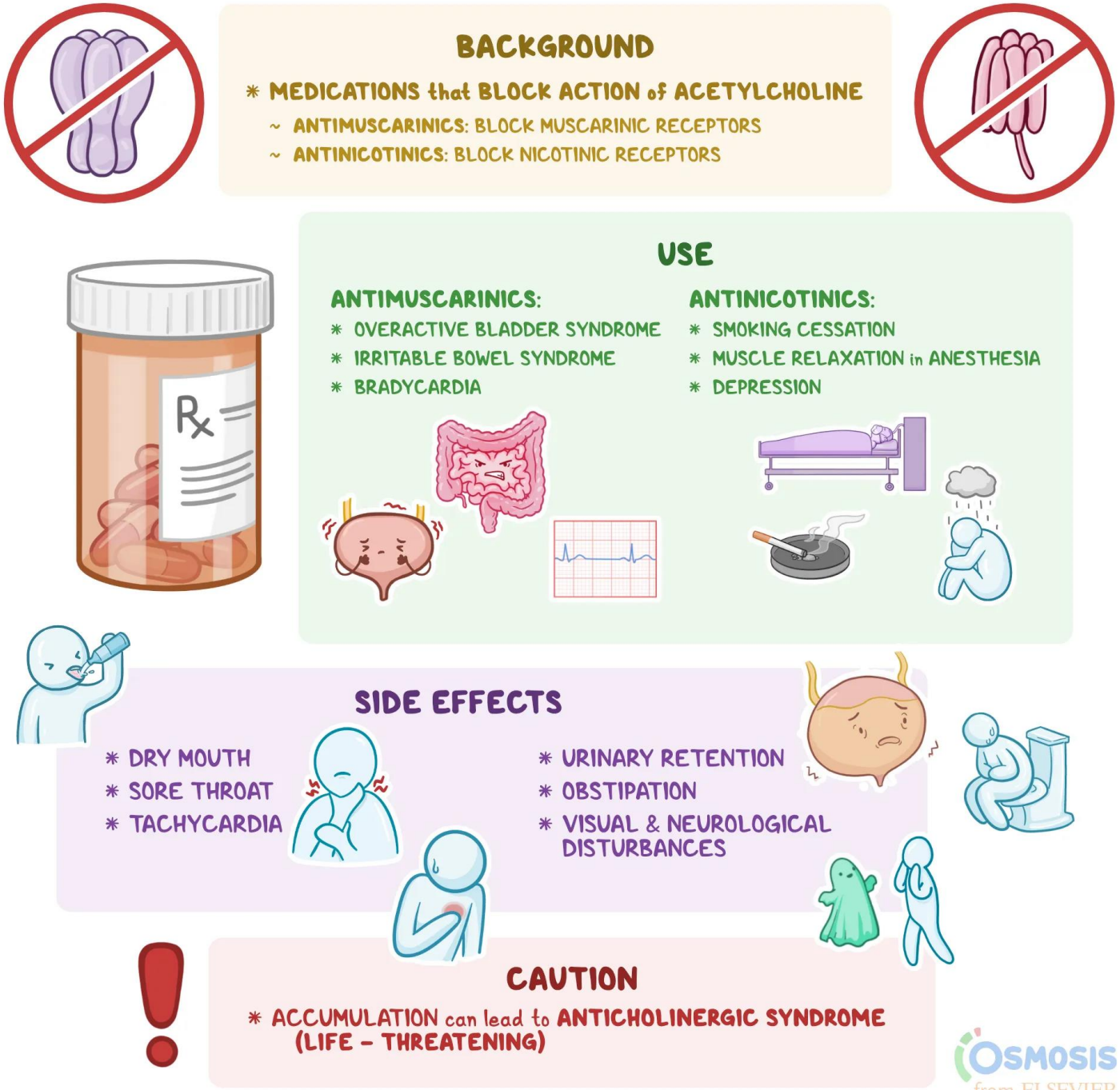
1. Mazzitelli M. et al. Sleep disturbances and their correlation with cardiovascular risk, obesity, and mood disorders in people with HIV. AIDS, 2023 May 1;37(6):925-934. doi: 10.1097/QAD.0000000000003493

Anticholinergic



What is AC?



Antihistamines

- Brompheniramine*
- Carbinoxamine*
- Chlorpheniramine*†
- Clemastine*
- Cyproheptadine†
- Dexbrompheniramine
- Dexchlorpheniramine
- Dimenhydrinate*
- Diphenhydramine*†
- Doxylamine
- Hydroxyzine*†
- Meclizine*
- Promethazine*†
- Pyrilamine*† (mepyramine)
- Triprolidine

Antiparkinson

- Benztropine*†
- Trihexyphenidyl*

Antiarrhythmic

- Disopyramide

Antimuscarinics

- Darifenacin*
- Fesoterodine
- Flavoxate*
- Oxybutynin*†
- Solifenacin
- Tolterodine*
- Trospium

Antidepressants

- Amitriptyline*†
- Amoxapine
- Clomipramine*
- Desipramine*
- Doxepin*
- Imipramine*†
- Nortriptyline*
- Paroxetine*
- Protriptyline*
- Trimipramine*

Muscle Relaxants

- Cyclobenzaprine
- Orphenadrine*

Antispasmodics

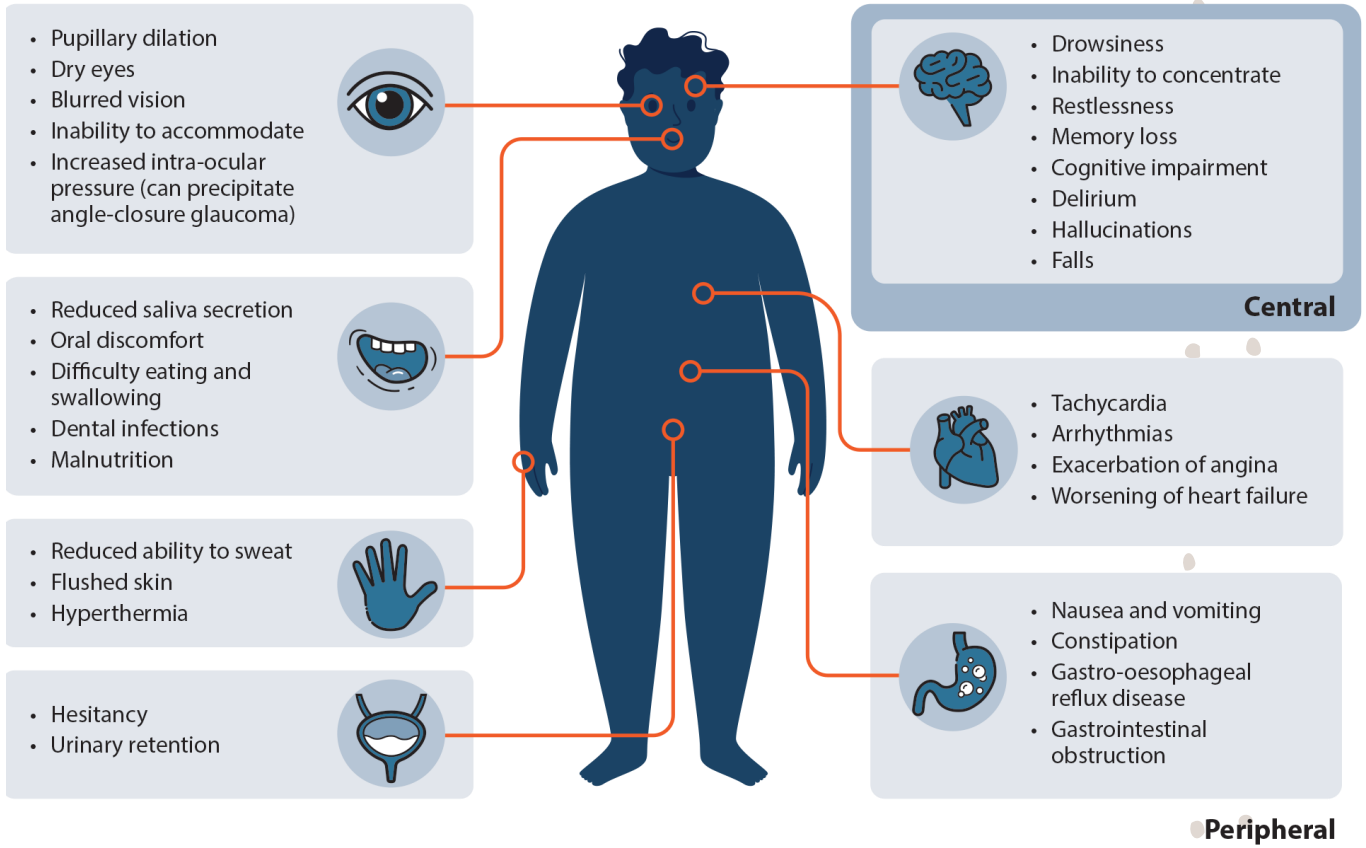
- Atropine*†
- Belladonna alkaloids
- Clidinium-chlordiazepoxide
- Dicyclomine*
- Homatropine†
- Hycoscyamine*†
- Methscopolamine
- Propantheline*
- Scopolamine*

Antipsychotics

- Chlorpromazine*†
- Clozapine*
- Loxapine
- Olanzapine
- Perphenazine†
- Thioridazine*†
- Trifluoperazine†

Antiemetics

- Prochlorperazine
- Promethazin*†



Multicenter Study > AIDS. 2019 Dec 1;33(15):2439-2441.
doi: 10.1097/QAD.0000000000002403.

Polypharmacy and evaluation of anticholinergic risk in a cohort of elderly people living with HIV

Maria Mazzitelli [1], Ana Milinkovic, Branca Pereira, James Palmer, Timothy Tong, David Asboe, Marta Boffito

- 790 attended the clinic (Jan 2009- July 2019)
- 92.8% male, 84.2% white.
- Mean age was of 55.8 (5.6) years; the main risk
- 87.1% MSM, 95.2% HIV RNA < 50 Cp/ml
- 44.7% patients were on polypharmacy
- severe polypharmacy was reported 7.9%) cases

Table 1. Anticholinergic risk results for the two scales.

Level of anticholinergic risk	Anticholinergic burden scale *n* (%)	Anticholinergic risk score *n* (%)
0 (no risk)	697 (88.2)	711 (90)
1–2 (intermediate)	68 (8.6)	57 (7.2)
>0 = 3 (high)	25 (3.2)	22 (2.8)

- The most commonly used drugs used were:

  Statins (46.1%),
  antihypertensives (33.3%),
  antidepressants (15.9%),
  proton pump inhibitors (10.8%).

> J Antimicrob Chemother. 2024 Jan 3;79(1):66-77. doi: 10.1093/jac/dkad348.

Use of different anticholinergic scales and their correlation with anticholinergic symptom burden in a cohort of people living with HIV

Maria Mazzitelli [1], Mattia Trunfio [2 3], Alessandra Coin [4], Lolita Sasset [1], Jacopo Farina [4], Monica Brundu [1], Vincenzo Scaglione [1], Maria Devita [5], Giuseppe Sergi [4], Anna M Cattelan [1 6]

Affiliations + expand

PMID: 37965917 PMCID: PMC11032244 (available on 2024-11-15) DOI: 10.1093/jac/dkad348

Variable		Overall population (*N* = 721)
Age, years, median (IQR)		53 (44–59)
Male sex, *n* (%)		519 (72.0)
Caucasian, *n* (%)		613 (85.0)
Route of acquisition, *n* (%)	MSM	379 (52.6)
	Heterosexual	250 (34.7)
	IVDU	78 (10.8)
	Other	14 (1.9)
Years living with HIV, median (IQR)		15 (7–24)
cART, *n* (%)	Dual	261 (36.2)
	INI-based	179 (24.8)
	NNRTI-based	204 (28.3)
	PI-based	72 (10.0)
	Others	5 (0.7)
Boosted regimens (cobicistat all), *n* (%)		131 (18.2%)
Current CD4 count, cells/mm^3, median (IQR)		638 (474–811)
Nadir CD4 count, cells/mm^3, median (IQR)		299 (160–459)
Previous AIDS-defining conditions,, *n* (%)		130 (18.0)
HIV-RNA > 50 copies/mL, *n* (%)		28 (3.9)
Positive HBsAg, *n* (%)		75 (10.4)
Positive HCV-RNA, *n* (%)		34 (4.7)
Number of drugs with anticholinergic properties, median (IQR)		0 (0–0)
Number of non-antiretroviral drugs, median (IQR)		2 (1–4)
Polypharmacy, *n* (%)		152 (21.1)

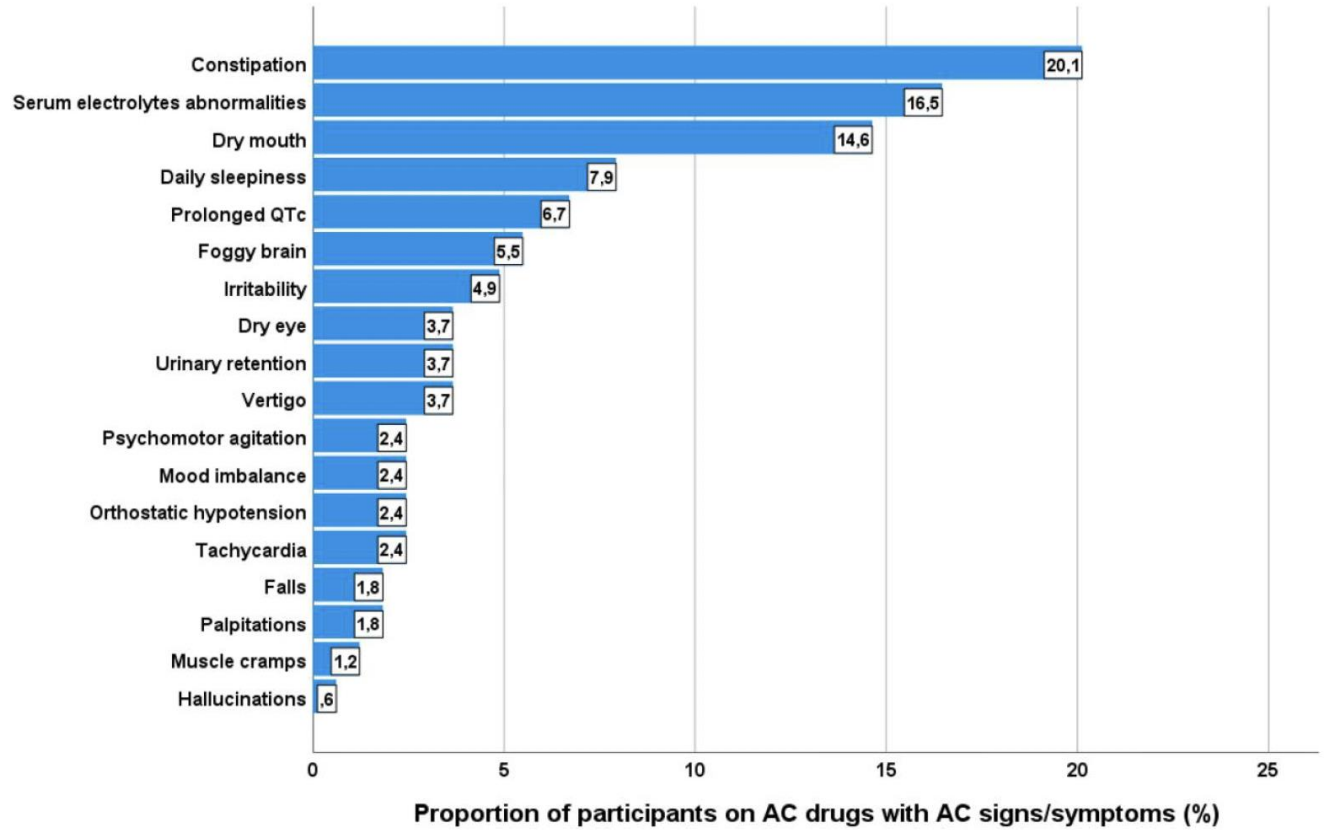
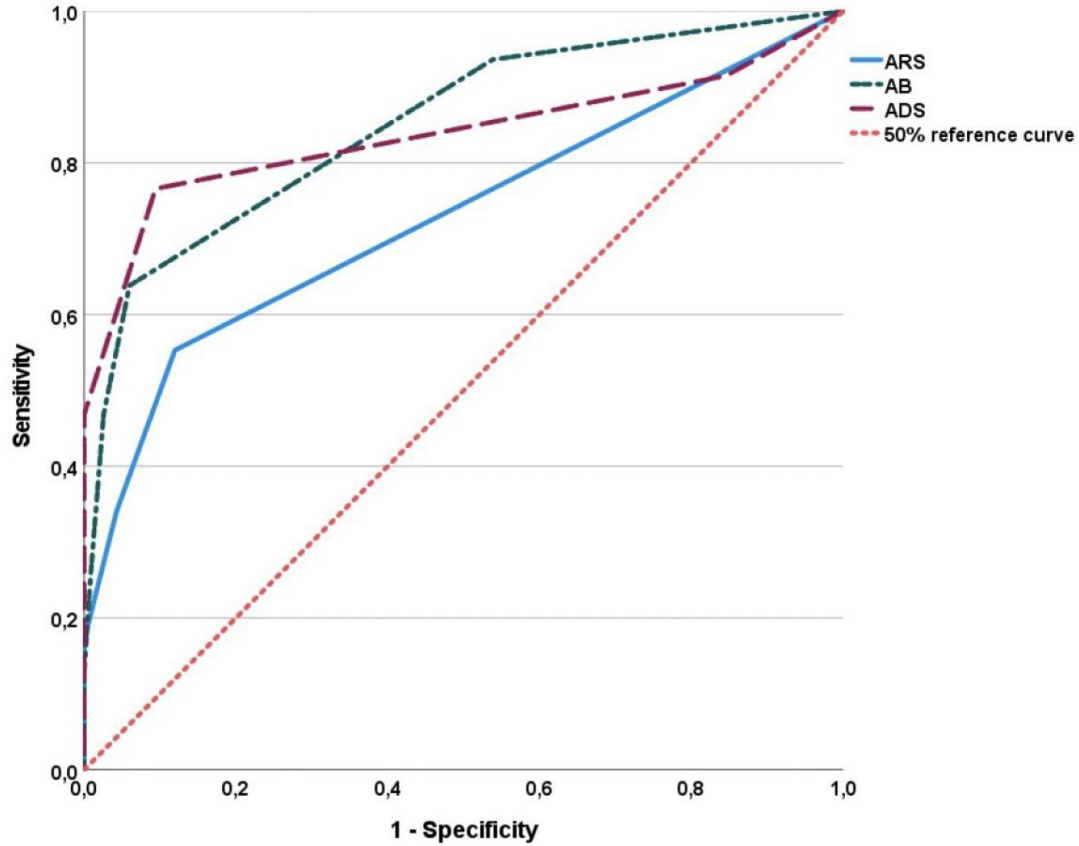


Table 3. Accuracy of ARS, ABS and ADS scales according to different cut-offs in participants on AC drugs ($N = 164$)

Cut-off	Sensitivity	Specificity	LR+	LR–	CCR
ARS					
≥1	55.3%	88.0%	4.6	0.51	78.7%
≥2	34.0%	95.7%	7.9	0.69	78.0%
≥3	17.0%	100%	—	0.83	76.2%
≥4	8.5%	100%	—	0.91	73.8%
ABS					
≥1	93.6%	46.2%	1.7	0.14	59.8%
≥2	63.8%	94.0%	10.7	0.38	85.4%
≥3	46.8%	97.4%	18.2	0.54	82.9%
≥4	25.5%	99.2%	29.9	0.75	78.1%
ADS scale					
≥1	91.5%	15.4%	1.0	0.55	37.2%
≥2	76.6%	90.6%	1.1	0.26	86.6%
≥3	46.8%	100%	8.1	0.53	84.8%
≥4	12.8%	100%	—	0.87	75.0%

ABS, Anticholinergic Burden Scale, ADS, Anticholinergic Drug Scale; ARS, Anticholinergic Risk Scale; CCR, correct classification rate; LR+, positive likelihood ratio; LR–, negative likelihood ratio.



Drugs with ACB Score of 1

Generic Name	Brand Name
Alimemazine	Theralen™
Alverine	Spasmonal™
Alprazolam	Xanax™
Aripiprazole	Abilify™
Asenapine	Saphris™
Atenolol	Tenormin™
Bupropion	Wellbutrin™, Zyban™
Captopril	Capoten™
Cetirizine	Zyrtec™
Chlorthalidone	Diuril™, Hygroton™
Cimetidine	Tagamet™
Clidinium	Librax™
Clorazepate	Tranxene™
Codeine	Contin™
Colchicine	Colcrys™
Desloratadine	Clarinex™
Diazepam	Valium™
Digoxin	Lanoxin™
Dipyridamole	Persantine™
Disopyramide	Norpace™
Fentanyl	Duragesic™, Actiq™
Furosemide	Lasix™
Fluvoxamine	Luvox™
Haloperidol	Haldol™
Hydralazine	Apresoline™
Hydrocortisone	Cortef™, Cortaid™
Iloperidone	Fanapt™
Isosorbide	Isordil™, Ismo™
Levocetirizine	Xyzal™
Loperamide	Immodium™, others
Loratadine	Claritin™
Metoprolol	Lopressor™, Toprol™
Morphine	MS Contin™, Avinza™
Nifedipine	Procardia™, Adalat™
Paliperidone	Invega™
Prednisone	Deltasone™, Sterapred™
Quinidine	Quinaglute™
Ranitidine	Zantac™
Risperidone	Risperdal™
Theophylline	Theodur™, Uniphyl™
Trazodone	Desyrel™
Triamterene	Dyrenium™
Venlafaxine	Effexor™
Warfarin	Coumadin™

Drugs with ACB Score of 2

Generic Name	Brand Name
Amantadine	Symmetrel™
Belladonna	Multiple
Carbamazepine	Tegretol™
Cyclobenzaprine	Flexeril™
Cyproheptadine	Periactin™
Loxapine	Loxitane™
Meperidine	Demerol™
Methotrimeprazine	Levoprome™
Molindone	Moban™
Nefopam	Nefogesic™
Oxcarbazepine	Trileptal™
Pimozide	Orap™

Categorical Scoring:

- Possible anticholinergics include those listed with a score of 1; Definite anticholinergics include those listed with a score of 2 or 3

Numerical Scoring:

- Add the score contributed to each selected medication in each scoring category
- Add the number of possible or definite Anticholinergic medications

Notes:

- Each definite anticholinergic may increase the risk of cognitive impairment by 46% over 6 years. [3]
- For each on point increase in the ACB total score, a decline in MMSE score of 0.33 points over 2 years has been suggested. [4]
- Additionally, each one point increase in the ACB total score has been correlated with a 26% increase in the risk of death. [4]

Aging Brain Care

www.agingbraincare.org

Drugs with ACB Score of 3

Generic Name	Brand Name
Amitriptyline	Elavil™
Amoxapine	Asendin™
Atropine	Sal-Tropine™
Benztropine	Cogentin™
Brompheniramine	Dimetapp™
Carbinoxamine	Histex™, Carbihist™
Chlorpheniramine	Chlor-Trimeton™
Chlorpromazine	Thorazine™
Clemastine	Tavist™
Clomipramine	Anafranil™
Clozapine	Clozaril™
Darifenacin	Enablex™
Desipramine	Norpramin™
Dicyclomine	Bentyl™
Dimenhydrinate	Dramamine™, others
Diphenhydramine	Benadryl™, others
Doxepin	Sinequan™
Doxylamine	Unisom™, others
Fesoterodine	Toviaz™
Flavoxate	Urispas™
Hydroxyzine	Atarax™, Vistaril™
Hyoscyamine	Anaspaz™, Levsin™
Imipramine	Tofranil™
Meclizine	Antivert™
Methocarbamol	Robaxin™
Nortriptyline	Pamelor™
Olanzapine	Zyprexa™
Orphenadrine	Norflex™
Oxybutynin	Ditropan™
Paroxetine	Paxil™
Perphenazine	Trilafon™
Promethazine	Phenergan™
Propantheline	Pro-Banthine™
Propiverine	Detrunorm™
Quetiapine	Seroquel™
Scopolamine	Transderm Scop™
Solifenacin	Vesicare™
Thioridazine	Mellaril™
Tolterodine	Detrol™
Trifluoperazine	Stelazine™
Trihexyphenidyl	Artane™
Trimipramine	Surmontil™
Trospium	Sanctura™

OXFORD UNIVERSITY PRESS | Journal of Antimicrobial Chemotherapy

Polypharmacy, anticholinergic burden, and drug-drug interaction assessment in people with 4-class resistant HIV: data from the PRESTIGIO Registry

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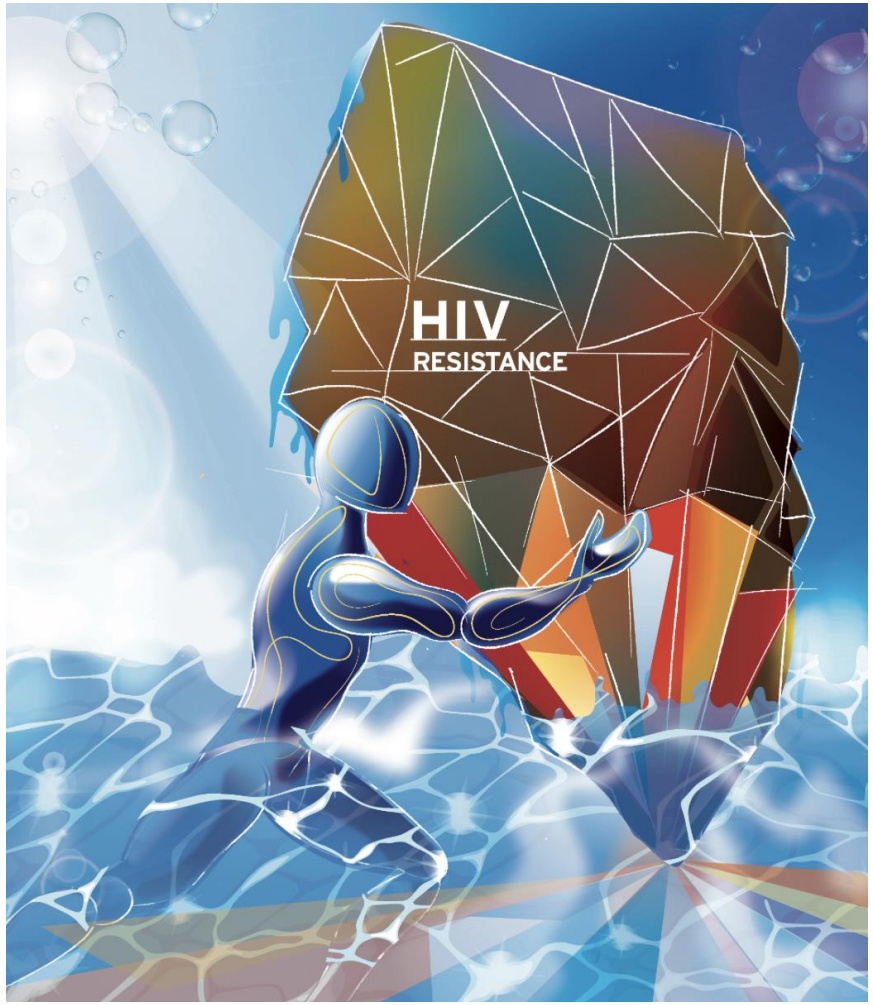


PRESTIGIO Registry

Characteristic	Overall (N=172)	ACB score ≥3 (n=11)	ACB score = 1-2 (n=33)	ACB score = 0 (n=128)	P-value
3	55 (32)	6 (54.5)	7 (21.2)	42 (32.8)	
4	54 (31.4)	3 (27.3)	13 (39.4)	38 (29.7)	
5	14 (8.1)	0 (0)	4 (12.1)	10 (7.8)	
6	3 (1.7)	0 (0)	0 (0)	3 (2.3)	
7	1 (0.6)	0 (0)	0 (0)	1 (0.8)	
N antiretroviral/person, median (IQR)	3 (2-4)	3 (3-4)	4 (2-4)	3 (2-4)	0.705
NRTI-containing regimens, n (%)	96 (55.8)	6 (54.5)	17 (51.5)	73 (57.0)	0.982
NNRTI-containing regimens, n (%)	53 (30.8)	4 (36.4)	12 (36.4)	37 (28.9)	0.652
PI-containing regimens, n (%)	126 (73.3)	8 (72.7)	24 (72.7)	94 (73.4)	0.996
INSTI-containing regimens, n (%)	148 (86.0)	10 (90.9)	30 (90.9)	108 (84.4)	0.559
Number of drug/person, median (IQR)	3 (2-6)	5 (2-10)	5 (3-7)	3 (2-5)	0.0001
Comorbidities, n (%)					
CKD[a]	28 (16.3)	1 (9.1)	7 (21.2)	20 (15.6)	0.593
COPD	5 (2.9)	1 (9.1)	1 (3)	3 (2.3)	0.441
Diabetes	8 (4.7)	0 (0)	3 (9.1)	5 (3.9)	0.339
Dyslipidaemia	48 (27.9)	3 (27.3)	10 (30.3)	35 (27.3)	0.943
Hypertension	35 (20.3)	2 (18.2)	7 (21.2)	26 (20.3)	0.977
Liver cirrhosis	4 (2.3)	0 (0)	1 (3)	3 (2.3)	0.846
≥1 MACE[b]	22 (12.8)	1 (9.1)	10 (30.3)	11 (8.5)	0.114
≥1 non-AIDS malignancy[c]	20 (11.6)	3 (27.3)	5 (15.2)	12 (9.4)	**0.003**
≥1 musculoskeletal diseases[d]	32 (18.6)	3 (27.3)	3 (9.1)	26 (20.3)	0.553
≥1 neuropsychiatric diseases[e]	39 (22.7)	9 (81.8)	7 (21.2)	23 (18)	0.0008

Characteristic	Overall (N=172)	ACB score ≥3 (n=11)	ACB score = 1-2 (n=33)	ACB score = 0 (n=128)	P-value
Age, years, median (IQR)	49.9 (45.6 – 56)	51.25 (45.3 – 55.2)	49.87 (46.3– 56)	49.82 (45.5 – 54)	0.73
Gender, n (%)					0.39
Female	42 (24.4)	1 (9.1)	7 (21.2)	34 (26.6)	
Male	130 (75.6)	10 (90.9)	26 (78.8)	94 (73.4)	
Ethnicity, n (%)					**0.01**
Asiatic	1 (0.6)	0 (0)	0 (0)	1 (0.8)	
Caucasian	163 (94.8)	10 (90.9)	31 (93.9)	122 (95.3)	
Hispanic	1 (0.6)	1 (9.1)	0 (0)	0 (0)	
Black	7 (4.1)	0 (0)	2 (6.1)	5 (3.9)	
HIV-1 risk factor, n (%)					0.90
Hetero	40 (23.8)	2 (18.2)	7 (21.9)	31 (24.8)	
MSM	48 (28.6)	2 (18.2)	10 (31.3)	36 (28.8)	
Other	35 (20.8)	4 (36.4)	6 (18.8)	25 (20)	
IVDU	45 (26.8)	3 (27.3)	9 (28.1)	33 (26.4)	
Years since HIV diagnosis, median (IQR)	29.9 (25.7 – 33.2)	32.3 (31.1 – 35)	28.2 (24.1 – 33.4)	29.5 (25.7 – 33.6)	**0.049**
ART duration, years, median (IQR)	25.8 (22.3 – 28.7)	26.2 (19.4 – 29)	26.2 (22.3 – 29)	25.7 (22.3 – 28.4)	0.744
Nadir CD4+ T cells/µL, median (IQR)	73 (16 - 182)	50 (6 - 182)	59.5 (21 - 140)	82 (16 - 194)	0.77
Previous AIDS events, n (%)	13 (7.5)	0 (0)	4 (12)	9 (7)	0.629
HIV-RNA (copies/mL), n (%)					0.19
<50	121 (70.3)	9 (81.8)	25 (75.8)	87 (68)	
>50 to<200	23 (13.4)	2 (18.2)	2 (6.1)	19 (14.8)	
>200 to<1000	10 (5.8)	0 (0)	0 (0)	10 (7.8)	
>1000	18 (10.5)	0 (0)	6 (18.2)	12 (9.4)	
CD4+ T cells/µL, median (IQR)	537 (331.5 – 818)	574 (372 - 628)	414 (326 - 740)	537 (338.5 – 843)	0.66
CD4/CD8 ratio, median (IQR)	0.63 (0.3 - 0.9)	0.81 (0.6 - 0.9)	0.7 (0.4 - 1)	0.6 (0.31 - 0.8)	0.25
Antiretroviral drugs, n (%)					0.832
2	45 (26.2)	2 (18.2)	9 (27.3)	34 (26.6)	

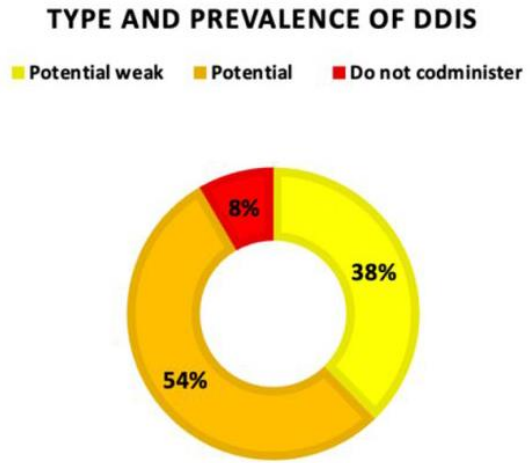
Figure 1. Summary and features of DDIs in the PRESTIGIO cohort

A

Number and proportion of DDIs/person

N DDIs	N PWH	% PWH
0	57	33,1
1	51	29,7
2	31	18,0
3	16	9,3
4	3	1,7
5	7	4,1
6	4	2,3
7	2	1,2
9	1	0,6

B



C

Antiretroviral causing DDIs and type of interactions

	Overall		Potential weak		Potential		Do not coadminister	
Drug	N DDIs= 258	100%	n	%	n	%	n	%
Ritonavir	115	44,6	42	16,5	65	25,2	8	3,1
Cobicistat	80	31,0	28	11,0	47	18,2	5	1,9
Etravirine	27	10,5	14	5,5	13	5,0	0	0,0
TAF/FTC or TDF/FTC	7	2,7	6	2,4	1	0,4	0	0,0
Dolutegravir	8	3,1	2	0,8	6	2,3	0	0,0
Bictegravir	3	1,2	0	0,0	3	1,2	0	0,0
Fostemsavir	7	2,7	2	0,8	5	1,9	0	0,0
Doravirine	1	0,4	1	0,4	0	0,0	0	0,0
Rilpivirine	4	1,6	2	0,8	2	0,8	0	0,0
Lamivudine	2	0,8	2	0,8	0	0,0	0	0,0
Atazanavir	2	0,8	0	0,0	1	0,4	1	0,4
Maraviroc	1	0,4	0	0,0	1	0,4	0	0,0
Zidovudina	1	0,4	0	0,0	1	0,4	0	0,0

Future Perspective and Research Ideas

- Impact of deprescribing on symptoms
- Correlation between AC and SD
- Correlation between bPIs and AC symptoms
- **Open up to collaborations!**

Acknowledgments

L A R I C O N O S C E N Z A I N F I N I T A
M A G R I T T E