Neurocognitively-Acting Potentially Inappropriate Medications, Alcohol, and Community-Acquired Pneumonia among Patients with and without HIV

Christopher T. Rentsch, MPH, Janet P. Tate, MPH, ScD, Kirsha S. Gordon, PhD, Alice Tseng, PharmD, Kristina M. Niehoff, PharmD, E. Jennifer Edelman, MD, MHS, and Amy C. Justice, MD, PhD for the Veterans Aging Cohort Study Project Team

Background

Alcohol interactions with neurocognitively-acting potentially inappropriate medications (NC-PIMs) may be more common, more harmful, and associated with lower levels of alcohol use among people living with HIV compared to those without HIV

Objective

To evaluate the potentially additive effects of alcohol and NC-PIMS on risk of community acquired pneumonia (CAP)

Methods

Subjects and Study Period

- Veterans Aging Cohort Study (VACS), a national study of >50,000 HIV-infected and 1:2 matched uninfected individuals receiving care in the US Department of Veterans Affairs (VA)
- Study period: 1 Oct 2007 to 30 Sep 2015
- Baseline: First AUDIT-C with concurrent non-ART outpatient prescription fill that occurred >12 months after enrollment
- Baseline period: 12-month window prior to baseline, used to define adjusting covariates
- Excluded: if received chemotherapy/immunosuppressive medication during baseline period, or no VA visit after baseline
- Cases: First CAP requiring hospitalization, after baseline
- Controls: Cases matched to up to 5 controls by age, sex, race, HIV status, baseline year, and duration of observation
- Index date: CAP date for cases; matched date for controls

Exposure groups

- NC-PIM: Dispensed at least one NC-PIM of any duration in the year prior to index date for anticonvulsants, sedatives (including benzodiazepines), prescription opioids, antidepressants, antipsychotics, and muscle relaxants; and additionally among HIV+: ritonavir (RTV) and efavirenz (EFV)
- Alcohol use categories: Defined by AUDIT-C assessed in the year prior to index date
  - Abstinent/"sick quitter": AUDIT-C 0
  - Lower-risk drinking: AUDIT-C 1-3
  - At-risk drinking: AUDIT-C 4-7
  - Hazardous/binge drinking: AUDIT-C ≥8
- HIV status: ICD-9 diagnosis (two outpatient or one inpatient of 042, 044, or V08)

Statistical analysis

- Conditional logistic regression models were used to estimate interactions between NC-PIMs (any and by class) and alcohol on the risk for CAP, stratified by HIV status
- Models were adjusted for smoking status, VACS Index, steroids, vaccination status (influenza and pneumonia), hepatitis C, previous CAP, and various comorbidities (e.g., chronic obstructive pulmonary disorder, asthma, congestive heart failure, coronary artery disease, ischemic stroke, diabetes)

Contact: Christopher.Rentsch@va.gov

Results

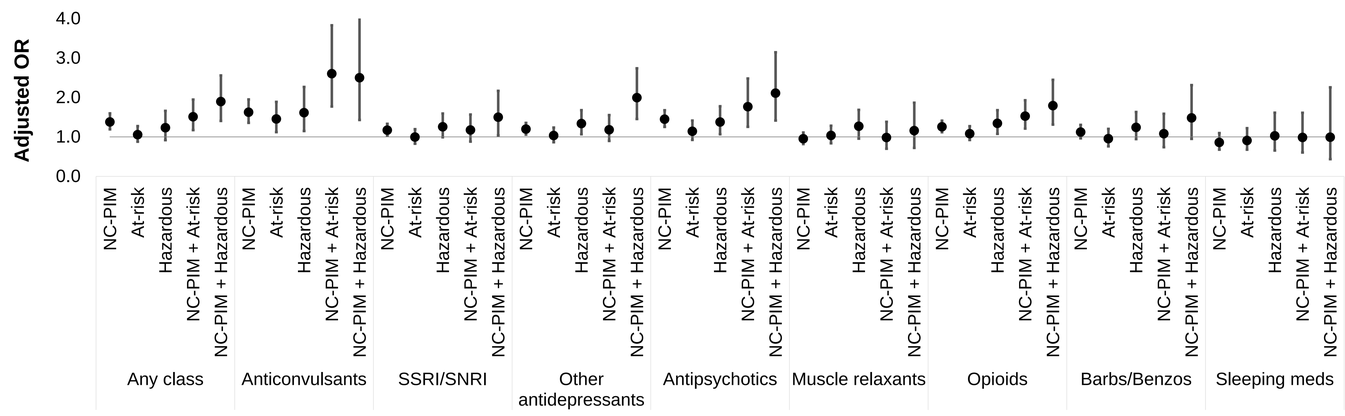
Among 37,193 patients (6,250 cases; 30,943 controls), 98% were male and median age was 58 years.

Table 1. Exposure frequencies by HIV and CAP status

	Uninfected (n=20,838)			HIV+ (n=16,355)		
	CAP	No CAP		CAP	No CAP	
Proximal exposure	**n=3,494**	**n=17,344**	**p**	**n=2,756**	**n=13,599**	**p**
Any non-ART NC-PIM	2,789 (80)	11,654 (67)	<0.0001	2,068 (75)	8,726 (64)	<0.0001
Anticonvulsants	475 (14)	1,356 (8)	<0.0001	215 (8)	700 (5)	<0.0001
SSRI/SNRI	1,130 (32)	4,191 (24)	<0.0001	805 (29)	3,251 (24)	<0.0001
Other antidepressants	1,118 (32)	4,311 (25)	<0.0001	870 (32)	3,473 (26)	<0.0001
Antipsychotics	804 (23)	2,588 (15)	<0.0001	460 (17)	1,630 (12)	<0.0001
Muscle relaxants	669 (19)	2,841 (16)	<0.0001	421 (15)	1,695 (12)	<0.0001
Opioids	1,881 (54)	6,971 (40)	<0.0001	1,413 (51)	4,944 (36)	<0.0001
Barbiturates/Benzodiazepines	795 (23)	2,701 (16)	<0.0001	512 (19)	1,847 (14)	<0.0001
Other sedatives/hypnotics	357 (10)	1,293 (7)	<0.0001	298 (11)	1,047 (8)	<0.0001
Any ART NC-PIM	-	-		1,846 (67)	9,351 (69)	0.0665
Efavirenz				643 (23)	4,335 (32)	<0.0001
Ritonavir				1,282 (47)	5,340 (39)	<0.0001
Alcohol use category						
Abstinent/'sick quitter'	2,125 (61)	8,627 (50)	<0.0001	1,415 (51)	6,079 (45)	<0.0001
Lower-risk	535 (15)	3,838 (22)		614 (22)	3,598 (26)	
At-risk	292 (8)	2,020 (12)		272 (10)	1,496 (11)	
Hazardous	135 (4)	596 (3)		109 (4)	408 (3)	
Missing	407 (12)	2,263 (13)		346 (13)	2,018 (15)	

Abbreviations: ART, antiretroviral therapy; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitors

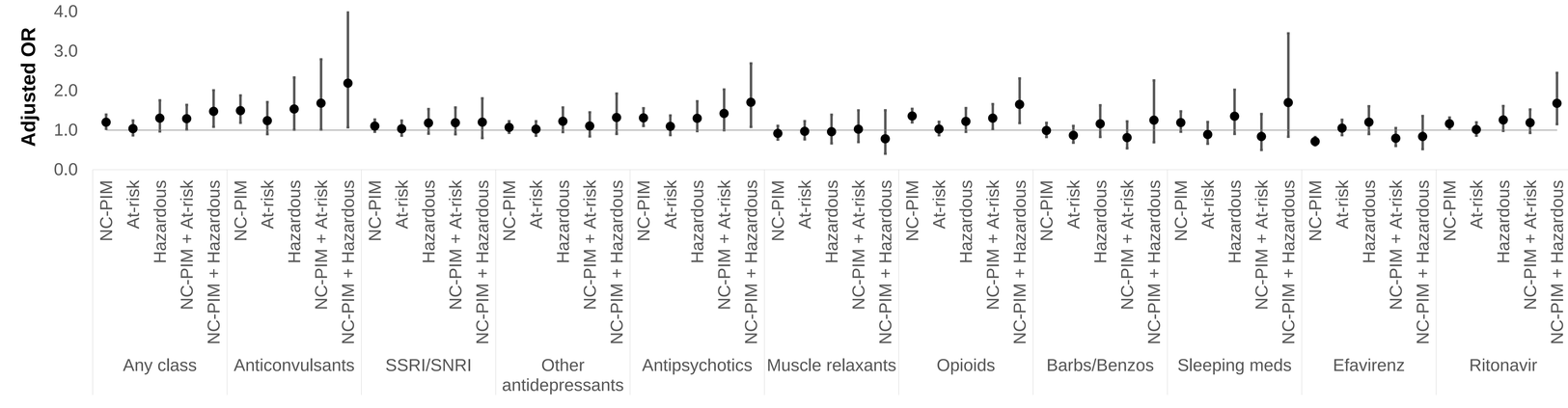
Fig 1. Among uninfected, interactions between alcohol and NC-PIM



Comparisons

Group	Referent group
NC-PIM	No NC-PIM
At-risk	Lower-risk
Hazardous	Lower-risk
NC-PIM + At-risk	No NC-PIM + Lower-risk
NC-PIM + Hazardous	No NC-PIM + Lower-risk

Fig 2. Among HIV+, interactions between alcohol and NC-PIM



Conclusions

NC-PIMs, especially with concurrent at-risk or hazardous alcohol consumption, are associated with increased CAP risk.

In general, patterns were similar among those living with and without HIV

Funding sources

National Institute on Alcohol Abuse and Alcoholism (RO1 AA023733; U24 AA020794; U01 AA020790) and the Veterans Health Administration.
The views are of the authors' and not necessarily those of the Department of Veterans Affairs or the US Government