

Supplementary Materials

Association of cannabis use with risk of subsequent falls among adults aging with HIV

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Supplementary Methods

Inverse Probability Weighting

In order to assess cannabis use and falls at multiple time points while controlling for time-varying confounders and cohort drop-out, inverse probability weighting (IPW) was employed in the final models. IPW assigns a weight for each participant at each time interval that is equal to the inverse probability of being in their cannabis use group for inverse probability of treatment weights (IPTWs), or remaining on study for inverse probability of censoring weights (IPCWs), based on covariates and past outcomes and exposures.

Stabilized IPTWs for time k were calculated as:

$$\text{IPTW} = \prod_{t=0}^k \frac{p(\text{trt}|\text{trt}_{k-1}, \text{baseline covariates})}{p(\text{trt}|\text{trt}_{k-1}, \text{falls}_{k-1}, \text{covariates})}$$

Since age, sex and race were controlled for as covariates in the weighted model, they were included in the numerator and denominator, resulting in their effects cancelling out.

For all models, probability of treatment (cannabis use group) was modeled via logistic models using the confounders (identified as described in the main manuscript), cannabis use and falls at the previous visits as predictors. For the baseline visits, treatment history and falls history were omitted from the models.

For the IPCWs, probability of remaining on study at visit k was estimated using cannabis use, falls, and the covariates selected for the IPTW models from visit $k-1$. For the baseline visit, probability of being on study was set to 1 for all participants.

$$\text{IPCW} = \prod_{t=1}^k \frac{p(\text{on study})}{p(\text{on study}|\text{trt}_{k-1}, \text{falls}_{k-1}, \text{covariates}_{k-1})}$$

The overall IPWs are the product of the IPTWs and IPCWs.

The IPW were evaluated by checking their distributions by visit (Supplementary Table 1 **Error! Reference source not found.**), and by comparing the distributions of time-updated variables before and after weighting. IPW means ranged from 1.00 at visits 1-3 to 1.13 at visit 7. The maximum and minimum weights occurred at visit 4 with max=9.48 and visit 6 with min=0.05.

The IPW slightly over adjusted smoking use, with never smokers going from 21% among current users and 48% among non-users in the unweighted data to 46% among current users and 41% among non-users in the IP weighted data. Current smokers were well matched at 22% of current users and 23% of non-users after weighting. Among remaining IPW variables, all categories were matched to within 5 percentage points after weighting (Supplementary Table 2).

Sensitivity Models

Sensitivity models (Supplementary Table 3) were run to explore the effects of the following:

S1: Use in past year (instead of month): Cannabis use within the past year was modeled by combining intermittent users (use >1 month ago but within the past year) with current users (use within the past month). Intermittent users made up 5.8% of the cohort across all visits. From baseline to the next visit, only 29% of intermittent users remained intermittent, while 37% became current users, and 35% became non-users. In comparison, 82% of current (use within the last month) and 94% of non-users (no use within the last year) remained in their respective categories from baseline to the next visit. Due to this group's small size and

transitory nature, intermittent users were combined with non-users in the main model. To test the impact of this decision, intermittent users were instead combined with current users in model S1.

S2: Inclusion of cannabis history: The short-term effect of cannabis use was assessed by including cannabis at the prior visit as covariates in the model.

S3: Removal of fall at prior visit from IPW: the fully adjusted model was run with IPW that did not control for falls at the prior visit.

S4: Exclusion of FOCB imputed data: Exclusion of data imputed via First observation Carried Backward (FOCB) from the IPW. Three covariates had missing baseline data: heavy alcohol use, non-prescribed psychoactive substance use, and smoking status. This resulted in dropping 31 observations and three participants that were included in the main model.

The remaining sensitivity models were run to explore how the inclusion of covariates changed the main effect.

S5a: Effect of substance use: substance use was removed from the IPW models and included instead as a covariate in the partially and fully adjusted models.

S5b: Removal of substance use from IPW: substance use was excluded from the IPW models for the partially and fully adjusted models.

S6a: Effect of medication use: medication use was removed from the IPW models and included instead as a covariate in the partially and fully adjusted models.

S6b: Removal of medication use from IPW: medication use was excluded from the IPW models for the partially and fully adjusted models.

S7: Sequential addition of covariates: to further explore the effects of the time-varying covariates, they were added sequentially to the partially adjusted model and retained if their addition lowered the QIC.

Supplementary Table 1: Inverse probability weight distributions by visit

Visit	N	Mean	Min	Max	Q1	Q3
1	957	1.00	0.25	3.60	0.86	1.04
2	806	1.00	0.20	4.15	0.84	1.06
3	701	1.00	0.15	4.93	0.81	1.07
4	658	1.02	0.14	9.13	0.79	1.10
5	503	1.02	0.07	7.01	0.76	1.09
6	516	1.02	0.05	8.25	0.72	1.13
7	234	1.13	0.25	9.78	0.64	1.19

Inverse probably weights (IPW) were evaluated by checking their distributions by visit.

Supplementary Table 2: Unweighted and IP-weighted variables by cannabis use group

Variable	Category	Unweighted Non-Users (%)	Unweighted Current Users (%)	IP Weighted Non-Users (%)	IP Weighted Current Users (%)
Antidepressant, anti-anxiety, or prescription opioid medication use	Yes	35.8	48.0	40.1	35.8
Heavy alcohol use	Yes	15.6	29.3	18.0	19.0
Neuropathy diagnosis	Yes	57.6	55.6	57.7	60.1
Non-prescribed psychoactive substance use	Yes	4.6	15.1	7.1	7.3
Smoking status	Never	48.4	21.8	40.8	45.9
	Prior	33.3	40.8	36.4	31.9
	Current	18.3	37.4	22.8	22.2

Supplementary Table 3: Adjusted association between falls and cannabis use: main and sensitivity models

Model effects	Partially adjusted		Fully adjusted	
	Risk ratio (95% CI)	p-value	Risk ratio (95% CI)	p-value
<u>Main model</u>				
Cannabis use in past month	1.27 (1.02, 1.57)	0.029	1.11 (0.83, 1.49)	0.487
<u>S1: Use in past year (instead of month)</u>				
Cannabis use in past year	1.23 (1.00, 1.52)	0.045	1.09 (0.84, 1.41)	0.516
<u>S2: Inclusion of cannabis history</u>				
Cannabis use in past month	1.07 (0.82, 1.39)	0.623	0.98 (0.71, 1.34)	0.894
<u>S3: Removal of fall at prior visit from IPW</u>				
Cannabis use in past month			1.13 (0.84, 1.52)	0.414
<u>S4: Exclusion of FOCB imputed data</u>				
Cannabis use in past month	1.28 (1.03, 1.59)	0.025	1.11 (0.83, 1.48)	0.467
<u>S5a: Effect of substance use</u>				
Cannabis use in past month	1.22 (0.99, 1.52)	0.065	1.10 (0.83, 1.45)	0.518
Illicit substance use	1.37 (1.06, 1.78)	0.017	1.26 (0.91, 1.74)	0.167
<u>S5b: Removal of substance use from IPW</u>				
Cannabis use in past month			1.12 (0.85, 1.47)	0.437
<u>S6a: Effect of medication use</u>				
Cannabis use in past month	1.19 (0.96, 1.48)	0.116	1.08 (0.81, 1.43)	0.616
Antidepressant, anti-anxiety, or Rx opioid use	1.57 (1.31, 1.89)	<.001	1.51 (1.24, 1.85)	<.001
<u>S6b: Removal of medication use from IPW</u>				
Cannabis use in past month			1.10 (0.83, 1.46)	0.492
<u>S7: Sequential addition of covariates</u>				
Cannabis with age, sex, race & smoking	1.15 (0.93, 1.42)	0.203		
Cannabis with age ... & substance use	1.11 (0.90, 1.38)	0.328		
Cannabis with age ... & medications	1.08 (0.87, 1.34)	0.472		

All models adjusted for age group, sex at birth, and race/ethnicity, and IP-weighted for drop-out. Fully adjusted models also IP-weighted for falls at prior visit (excluding S3) and time-varying confounders: non-prescribed psychoactive substance use (heroin, cocaine, amphetamines, or other non-prescribed drugs), medication use* (antidepressants, anti-anxiety, or opioid pain medications), heavy alcohol use, peripheral neuropathy and smoking status. *Except when included as a covariate.*