CONTRIBUTION OF ALCOHOL USE IN HIV/HCV CO-INFECTION TO ALL-CAUSE MORTALITY

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BACKGROUND

- Among persons with HIV (PWH), both alcohol use and having hepatitis C virus (HCV) are separately associated with increased morbidity and mortality
- The effects of high alcohol use may alter after HCV cure as alcohol can exacerbate HCV infection by causing oxidative stress and promoting fibrosis, thereby accelerating disease progression to cirrhosis
- We aimed to investigate :
  - a) Whether the association between alcohol use and mortality among PWH differed by HCV status
  - b) Whether the interaction between alcohol use and HCV status on mortality differed after HCV cure

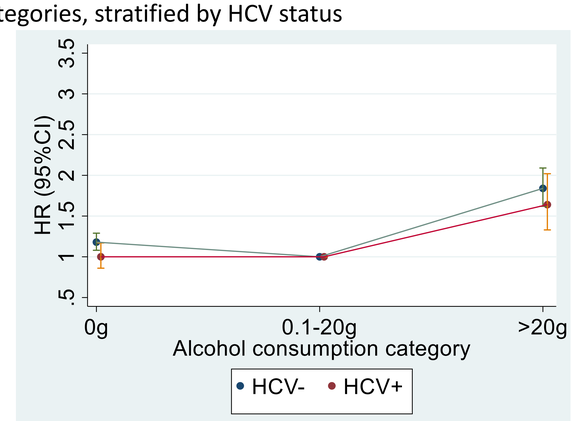
TABLE: Characteristics at start of ART stratified by HCV status and daily alcohol use category

	HCV negative			HCV positive		
	0g	0.1-20g	>20g	0g	0.1-20g	>20g
Overall	**27202 (50%)**	**22336 (41%)**	**4432 (8%)**	**2509 (52%)**	**1638 (34%)**	**4432 (8%)**
16-29 years	5555 (53%)	4163 (40%)	667 (6%)	152 (48%)	116 (36%)	667 (6%)
30-39 years	8693 (52%)	6994 (41%)	1178 (7%)	561 (53%)	321 (30%)	1178 (7%)
40-49 years	7136 (48%)	6228 (42%)	1390 (9%)	916 (52%)	575 (33%)	1390 (9%)
≥50 years	5818 (49%)	4951 (41%)	1197 (10%)	880 (53%)	626 (37%)	1197 (10%)
Male	18939 (45%)	19362 (46%)	4089 (10%)	1953 (50%)	1411 (36%)	4089 (10%)
Female	8263 (71%)	2974 (26%)	343 (3%)	556 (64%)	227 (26%)	343 (3%)
2001-2013 ART start	21036 (50%)	17615 (42%)	3322 (8%)	2191 (52%)	1462 (35%)	3322 (8%)
2014-2017 ART start	6166 (51%)	4721 (39%)	1110 (9%)	318 (53%)	176 (29%)	1110 (9%)
0-49 CD4 count (cells/µL)	3643 (56%)	2304 (36%)	512 (8%)	324 (57%)	185 (33%)	512 (8%)
50-99	2184 (55%)	1452 (37%)	331 (8%)	187 (47%)	144 (36%)	331 (8%)
100-199	4305 (51%)	3383 (40%)	690 (8%)	483 (50%)	332 (35%)	690 (8%)
200-349	8118 (49%)	6971 (42%)	1389 (8%)	804 (51%)	532 (34%)	1389 (8%)
≥350 CD4	8952 (48%)	8226 (44%)	1501 (8%)	711 (55%)	445 (34%)	1501 (8%)
0-9999 VL (copies/mL)	4581 (52%)	3705 (42%)	597 (7%)	536 (54%)	347 (35%)	597 (7%)
10000-99999	10640 (50%)	8944 (42%)	1768 (8%)	1019 (53%)	644 (33%)	1768 (8%)
≥100000 VL	11981 (50%)	9687 (41%)	2067 (9%)	954 (51%)	647 (35%)	2067 (9%)
HIV acquisition route:						
Sex between men	9406 (43%)	10389 (47%)	2286 (10%)	231 (47%)	205 (41%)	59 (12%)
IDU	377 (43%)	342 (39%)	156 (18%)	853 (52%)	433 (27%)	341 (21%)
Heterosexual sex	12463 (63%)	5926 (30%)	1348 (7%)	440 (59%)	212 (28%)	98 (13%)
Other/unknown	4956 (44%)	5679 (50%)	642 (6%)	985 (51%)	788 (41%)	154 (8%)
No prior AIDS	21872 (50%)	18382 (42%)	3488 (8%)	1906 (52%)	1253 (34%)	484 (13%)
Prior AIDS	5330 (52%)	3954 (39%)	944 (9%)	603 (52%)	385 (33%)	168 (15%)
HCV negative	27202 (50%)	22336 (41%)	4432 (8%)	0 (0%)	0 (0%)	0 (0%)
HCV positive	0 (0%)	0 (0%)	0 (0%)	2509 (52%)	1638 (34%)	652 (14%)

METHODS

- Data were combined from European and North American cohorts contributing to the Antiretroviral Therapy Cohort Collaboration (ART-CC) of adult PWH who started antiretroviral therapy (ART) between 2001-2017
- Baseline was date of ART initiation and PWH were followed for mortality
- Data on daily alcohol use were based on self-report
- Alcohol use data, collected in diverse ways between cohorts, were harmonised to give a value of grams alcohol/day
- HCV antibody and/or HCV RNA tests when available were used to define HCV status at baseline
- Effect modification by baseline alcohol use (0, 0.1-20.0, >20.0 grams/day) and HCV status was assessed using interaction terms in multivariable Cox models
- These models adjusted for ART start year category, HIV acquisition group, gender, prior AIDS status, age, CD4 count cells/µL, and log HIV-1 RNA copies/mL
- In additional analyses, we stratified follow-up into multiple periods per person based on time-updated HCV status (negative, positive, and cured/cleared)

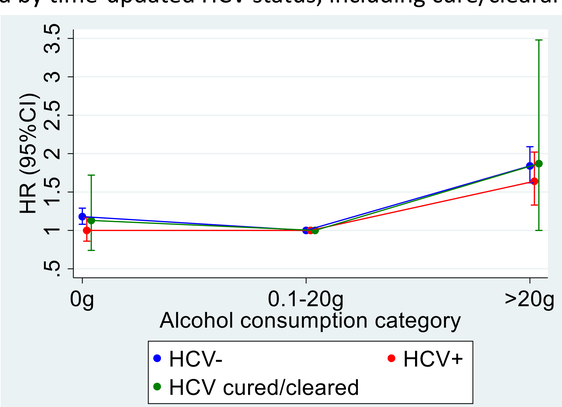
FIGURE 1: Adjusted mortality hazard ratios for alcohol use categories, stratified by HCV status



RESULTS

- Of 58,769 PWH, 21% were women and the median age at ART initiation was 40 years (interquartile range: 32-49)
- 29,711 (51%) self-reported alcohol use of 0g/day, 23,974 (41%) 0.1-20.0g/day, and 5,084 (9%) >20.0g/day, and 4,799 (8%) had HCV at baseline
- There were 3,599 deaths in 480,849 person-years
- The mortality rate per 1000 person-years was higher among PWH with HCV (21.6) than without HCV (6.2)
- Among PWH without HCV, there was a J-shaped relationship between mortality and alcohol use with adjusted hazard ratios (aHRs) of 1.21 (95%CI: 1.11-1.32) for 0.0g/day and 1.87 (1.65-2.12) for >20.0g/day compared with 0.1-20.0g/day (Figure 1)
- The J-shaped pattern was not seen for those with HCV (interaction p-value<0.001), with aHRs 0.99 (0.85-1.15) for 0.0g/day and 1.71 (1.39-2.10) for >20.0g/day compared with 0.1-20.0g/day
- In the analyses stratifying follow-up by HCV status including having cured/cleared HCV, the J-shaped pattern was seen among both those HCV negative and those who had been cured/cleared of HCV, but not for those with HCV (Figure 2)

FIGURE 2: Adjusted mortality hazard ratios for alcohol use category, stratified by time-updated HCV status, including cure/clearance



CONCLUSIONS

- In PWH followed from ART initiation, the association between alcohol consumption and all-cause mortality was modified by HCV co-infection
- Among those HCV-negative, mortality was higher in both non-drinkers and heavy drinkers compared with moderate drinkers
- Among those HCV-positive, mortality was higher in heavy drinkers but not non-drinkers
- This is potentially due to differences between those HCV-negative and positive in reasons for not drinking (e.g., previous alcohol use or comorbidities), or higher mortality among HCV-positive moderate drinkers

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