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The impact of past and current alcohol consumption patterns on progression of carotid intima media thickness among women and men living with HIV-infection

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Abstract

Background: The relationship between alcohol consumption and atherosclerosis has not been sufficiently examined among people living with HIV (PLWH).

Methods: We analyzed data from PLWH in the Women's Interagency HIV Study (WIHS; n=1164) and the Multicenter AIDS Cohort Study (MACS; n=387) with no history of cardiovascular disease (CVD). Repeated measures of intima-media thickness of the right common carotid artery (CCA-IMT) were assessed using B-mode ultrasound from 2004–2013. Current alcohol consumption was collected at time of CCA-IMT measurement and was categorized according to gender-specific weekly limits. Group-based trajectory models categorized participants into past 10-year consumption patterns (1994–2004). Multivariate generalized estimating equations were conducted to assess the association of past and current alcohol use patterns on change in CCA-IMT by cohort, controlling for age, race, cigarette and illicit drug use, probable depression, HIV RNA viral load, antiretroviral therapy exposure, and Hepatitis C co-infection.

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The authors declare that they have no conflicts of interest.

Results: Among the WIHS, past heavy alcohol consumption was associated with increased CCA-IMT level over time (β 8.08, CI 0.35, 15.8, p=0.04), compared to abstinence. Among the MACS, compared to abstinence all past consumption patterns were associated with increased CCA-IMT over time (past low: β 15.3, 95% CI 6.46, 24.2, p<0.001; past moderate: β 14.3, CI 1.36, 27.2, p= 0.03; past heavy: β 21.8, CI 4.63, 38.9, p=0.01). Current heavy consumption was associated with decreased CCA-IMT among the WIHS (β −11.4, 95% CI −20.2, −2.63, p=0.01) and MACS (β −15.4, 95% CI −30.7, −0.13, p=0.04). No statistically significant time by consumption pattern effects were found.

Conclusion: In both cohorts, 10-year heavy consumption was associated with statistically significant increases in carotid artery thickness, compared to abstinence. Long-term patterns of drinking at any level above abstinence was particularly significant for increases in IMT among men, with heavy consumption presenting with the greatest increase. Our results suggest a potentially different window of risk among past and current heavy drinkers. Further studies are needed to determine whether alcohol consumption level is associated with intermediate measures of atherosclerosis. Alcohol screening and interventions to reduce heavy consumption may benefit PLWH who are at risk for CVD.

Keywords

HIV; cardiovascular disease; atherosclerosis; alcohol; carotid intima media thickness

INTRODUCTION

Persons living with HIV (PLWH) have higher odds for subclinical atherosclerosis, compared to uninfected controls after adjusting for standard metabolic and HIV-related risk factors (Grunfeld et al., 2009, Hsue et al., 2012, Hanna et al., 2015). This suggests that there are important indicators of cardiovascular health outside of the traditional risk factor framework, such as alcohol consumption. Epidemiological studies in the general population have found a J-shaped curve relationship between level of alcohol use and cardiovascular disease (CVD) morbidity and mortality (Fernández-Solá 2015; Gonçalves et al., 2015; Bell et al., 2017). Hazardous drinking among PLWH is associated with a 43% increased risk for CVD including coronary heart disease, acute myocardial infarction, stroke, or heart failure compared to low-moderate drinking (Freiberg et al., 2010). In this population, history of alcohol abuse/dependence is associated with 55% increased risk of CVD (Freiberg et al., 2010), including heart failure (Butt et al., 2011), compared to those without abuse/dependence.

Different levels of alcohol consumption tend to have a differential effect on important cardiovascular risk factors and biomarkers. For example, compared to non-drinkers, moderate alcohol consumption (1 drink per day for women or up to 2 drinks per day for men) is associated with a 10% increase in HDL cholesterol (Brinton, 2012). Heavy alcohol consumption is associated with an even greater increase in HDL, but is paradoxically associated with increases in triglyceride, LDL, and total cholesterol levels (Brinton, 2012). Further, compared to never drinkers, moderate drinkers were less likely to have increases in damaging cardiac biomarkers (i.e., high sensitivity cardiac troponin T and N-terminal pro B-type natriuretic peptide); however, heavy drinkers were more likely to have incident

increases in these same biomarkers (Lazo et al., 2016). While the evidence of such differential risk of specific alcohol levels is substantial, there is uncertainty of a true relationship. For example, those reporting cross-sectional 'abstinence' may include some who were previously heavy drinkers who may have stopped due to alcohol-related illness, termed 'sick-quitters' (Poli et al, 2013). When this is the case, abstainers will present as a risky and inappropriate reference group. Further, there may be important lifestyle and dietary differences by alcohol use level that may be driving differences in risk. For example, moderate drinkers are more likely to be physically active, have a lower BMI, and be of higher socioeconomic status (Mukamal et al., 2006)

While the exact mechanisms underlying CVD risk is unclear, new evidence suggests alcohol-associated alterations in the gastrointestinal microbiota (also known as dysbiosis). Dysbiosis is the main driver of microbial translocation, the breakdown of the endothelial walls of the gastrointestinal tract, allowing bacterial product into the bloodstream, and the alcohol-associated pro-inflammatory state (Bull-Otterson et al., 2013; Leung et al., 2016). Inflammation and microbial translocation, in turn, are major drivers of atherosclerosis and subsequent CVD (Brenchley and Douek, 2012; Golia et al., 2014; Libby 2012; Maniar et al., 2013; Pant et al., 2014; Salisbury and Bronas, 2014). Because HIV infection alone increases systemic inflammation (Shrestha et al., 2014; Bahrami et al., 2016) and immune activation (Strategies for Management of Antiretroviral Therapy Study Group et al., 2006; Hsue et al., 2009; Neuhaus et al., 2010; Maniar et al., 2013), PLWH who drink (particularly heavy drinkers) may be in 'double jeopardy' for atherosclerosis development.

Literature on the effect of alcohol on intermediate measures of CVD development or subclinical atherosclerosis among PLWH is scant (Kelly et al., 2016; Kelso-Chichetto et al., 2017). To our knowledge, there are no publications investigating the effects of past longitudinal and current alcohol consumption patterns on progression of carotid intima-media thickness (cIMT). We aimed to assess the association of past (10-year) and current (6-month) alcohol consumption patterns with change in cIMT over time. We hypothesized that past alcohol consumption patterns would be more significantly associated with changes in cIMT over time versus current alcohol consumption. Specifically, we expected that 10-year patterns of moderate consumption would be associated with a protective effect and heavy consumption would be associated with a harmful effect on cIMT progression over time.

MATERIALS AND METHODS

Study Setting, Selection, and Inclusion Criteria

The Multicenter AIDS Cohort Study (MACS; Kaslow et al., 1987, Detels et al., 1992, Dudley et al., 1995) and Women's Interagency HIV Study (WIHS; Barkan et al., 1998, Bacon et al., 2005) are well-documented, ongoing multicenter observational cohorts of men who have sex with men (MSM) and of women, respectively. Each cohort include HIV-infected and demographically similar uninfected individuals. Participants from MACS were recruited from the following metropolitan areas: Baltimore, MD, Washington, DC, Chicago, IL, Pittsburgh, PA, Los Angeles, CA. Participants from WIHS were recruited from the following metropolitan areas: Brooklyn and Bronx, NY, Washington, DC, Chicago, IL, Los Angeles and San Francisco, CA. The MACS recruited MSM across three waves, in 1984–

1985 (n=4954), 1987–1991 (n=668), and 2001–2003 (n=1350). Women were recruited in the WIHS across two waves, in 1994–1995 (n=2625) and 2001–2002 (n=1141). The data were collected through structured interviews and standardized physical and laboratory assessments. HIV status was assessed by enzyme-linked immunosorbent assay (ELISA) with confirmatory testing at baseline for HIV-infected participants. The questionnaires are available online for the MACS at http://aidscohortstudy.org and for the WIHS at https://statepi.jhsph.edu/wihs/wordpress/.

The WIHS cardiovascular (CVD) sub-study recruited women aged 25 to 60 years, with no history of heart surgery or coronary angioplasty/stent placement; The MACS CVD sub-study recruited men over 40 years of age and under 300 lbs, with no history of heart surgery or coronary angioplasty/stent placement. The current study focused on those with sero-prevalent HIV at baseline and excluded those with less than 4 semi-annual alcohol use assessments prior to the first atherosclerosis assessment (WIHS: n=21; MACS: n=187) to ensure accurate modeling of nonlinear patterns of change (quadratic or cubic) if present. Further, those in the 10-year abstinent consumption pattern, who reported heavy drinking at enrollment were excluded from the analysis to reduce bias (MACS: n = 4; WIHS: n = 10). The final sample sizes were n=1164 in the WIHS and n=387 in the MACS. The mean person-years of follow-up from 1994–2014 were 17.2 years (interquartile range [IQR]: 16.5–19.0 years) for the WIHS participants and 13.8 years (IQR: 10.5–18.0 years) for the MACS participants. All of the MACS and WIHS participants provided written informed consent after institutional approval for both the core and CVD protocols. The Institutional Review Board at the University of Florida approved this analysis.

Data Collection

In addition to the standard data collection for the MACS and WIHS, participants in the cardiovascular sub-studies without detectable plaque/lesions in the right carotid artery underwent high-resolution B-mode carotid artery ultrasounds of six locations (the near and far walls of the common carotid artery [CCA], carotid bifurcation, and internal carotid artery [ICA]; Hodis et al., 2001) by automated computerized edge detection (Prowin, Patent, 2005, 2006; Selzer et al., 2001) using a standardized protocol across all study sites (Kaplan et al., 2008). Ultrasound machine models were not uniform by site. However, quality control and reliability of the carotid artery ultrasound measurement was performed among a subset of the WIHS and MACS participants and was found to have high intraclass correlations (ICC) in both the WIHS (variation coefficient = 1.8%; ICC = 0.98) and MACS (variation coefficient = 1.0%; ICC=0.99; Kaplan et al., 2008).

Main Outcome Measure.—Non-plaque carotid intima media thickness at the far right CCA (CCA-IMT) was measured up to 4 times in the WIHS and up to 3 times in the MACS from 2004–2013. The outcome of interest was change in CCA-IMT from the baseline to subsequent assessments.

Independent Variable.—Alcohol consumption frequency (number of days per week) and quantity (number of drinks per drinking day) were self-reported semi-annually. Participants were asked about the average number of standard drinks they consumed per day on days that

they drank alcohol, defined as “one can, bottle or glass of beer, a 4-ounce glass of wine, a 1 ½ ounce shot of liquor, or a mixed drink with that amount of liquor”. In the MACS, the response options were 0 drinks, 1–2 drinks, 3–4, 5–6, or 7 or more. In the WIHS, open-ended responses were elicited during 1996–2004 and categorized choices for 2005 onward with the same categories as used in the MACS. Open-ended responses such as “a pint of vodka” were converted to number of standard drinks. Next, participants were asked about the average number of days per week that they consumed alcohol. Response option were every day, 5–6 days a week, 3–4 days a week, 1–2 days a week, less than once a week, and none. We multiplied the frequency by the quantity to yield the average number of drinks per week at baseline and at all follow-up assessments. To establish past 10-year drinking patterns, group-based trajectory models (GBTM; Nagin, 1999; Nagin, 2005) were fit; for proper model convergence, we capped the maximum number of drinks per week at 14 for women and 21 for men in accordance with the definition of hazardous alcohol use (Reid et al., 1999). The 10-year alcohol consumption patterns were modeled using the number of drinks per week (continuous), without imposing categories of consumption prior to modeling. Repeated measures for current alcohol consumption from the baseline CCA-IMT to follow-up measurements were categorized as abstinent (<1 per week), moderate (1–7 drinks per week for women or 1–14 drinks per week for men), and heavy (>7 drinks per week for women or >14 drinks per week for men).

Covariates.—Covariates of interest were chosen based on prior literature on potential factors that influence alcohol consumption and changes in early atherosclerosis development (Qu and Qu, 2015). Age was assessed in years, using participants’ self-reported date of birth. Race/ethnicity was self-reported and categorized as non-Hispanic White, non-Hispanic Black, and other races (i.e. Hispanic, Asian/Pacific Islander or Native American/Alaskan). Self-reported smoking was assessed in number of packs smoked using standardized categories: less than half a pack per day; at least half a pack but less than one pack per day; at least one but less than two packs per day; two or more packs per day. Cumulative pack-years were calculated by multiplying the number of reported packs consumed at each visit by 0.5 to reflect semi-annual visits and summed across follow-up assessments. Self-reported illicit drug use was dichotomous and measured by asking if participants used any of the following: crack or any form of cocaine; uppers (including crystal, methamphetamines, speed, ice); heroin or other opiates. Depressive symptoms were assessed at each semi-annual visit with the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977). Some research has found that utilizing the score of 16 or greater may inflate the rate of depression among PLWH, due to the overlapping somatic symptoms that may be present due to HIV-infection (Kalichman et al., 2000). Therefore, a score of 23 or greater was considered probable depression (Choi et al., 2015). Plasma HIV RNA viral load was measured using standard laboratory techniques and was categorized as <200 copies/mL or ≥ 200 copies/mL. Cumulative years of exposure to the three main classes of antiretroviral medications (i.e., nucleoside reverse transcriptase inhibitors; non-nucleoside reverse transcriptase inhibitors; protease inhibitors) were included. Hepatitis C co-infection (HCV) status was based on HCV viral RNA or antibody and was dichotomized as having ever had HCV or not. Cardiovascular-related factors that mediate the relationship between alcohol consumption

and atherosclerosis were not included as confounding factors (i.e., cholesterol, blood pressure, and triglyceride, body mass index, diabetes) (Brinton, 2012; Vu et al., 2016).

Data Analyses.—To describe patterns of alcohol consumption over time, we conducted group-based trajectory models (GBTM) as previously described (Kelso-Chichetto et al., 2018). Age, probable depression, pack-years, illicit drug use, HIV RNA viral load, and current alcohol consumption were included as repeated measures at each CCA-IMT assessment (Figure 1). Of note, two distinct alcohol predictors were modeled, 1) a past 10-year alcohol consumption pattern, modeled as a fixed pattern spanning from 1994–2004 (just before baseline CCA-IMT measurement) and 2) repeated measures of 6-month alcohol use that is assessed at each CCA-IMT measurement. This is the time-varying alcohol predictor that served as a proxy for current/proximal alcohol use.

Univariate analyses were conducted to assess frequencies and proportions of alcohol consumption patterns and distribution of CCA-IMT at baseline and follow-up. Crude and adjusted associations of past and current alcohol consumption patterns on CCA-IMT were conducted using generalized estimating equations (GEE), by cohort. Prior to constructing GEE change models, outliers in CCA-IMT change values greater than two standard deviations from the mean were excluded to reduce type I error (WIHS = 22; MACS = 65). We developed the models in a stepwise fashion by 1) assessing the effect of time on CCA-IMT, 2) assessing time, past alcohol consumption, and current alcohol consumption, 3) adjusting for aforementioned covariates, 4) assessing the best fitting covariance structure (i.e, independent - responses are uncorrelated; exchangeable - responses are equally correlated; autoregressive – correlation between responses decrease over time; unstructured – correlations are allowed to be complex) (Ye & Pan, 2006). We used the quasi-information criterion (QIC) to compare model fit between covariance structures and chose the model with the smallest QIC. Finally, we 5) included interactions between past alcohol consumption and time and current alcohol consumption and time to test rate of change by consumption. Past and current alcohol consumption patterns were considered statistically significantly associated with change in CCA-IMT at p-value <.05 level.

Missing Data.—Missing longitudinal data were assessed and variables associated with missing data were identified. In order to address the potential for bias, we conducted Multiple Imputation, averaged across 10 imputations by cohort. The final averaged dataset was used for the current analyses. All of the WIHS and MACS participants in the final sample completed the baseline CCA-IMT measurement. Of the final WIHS sample, 41% completed only one CCA-IMT measurement, 6% completed two, 19% completed three, and 34% completed all four measurements. Measurements of CCA-IMT were about 2 years apart for those that completed all four measurements [baseline to FU1 mean 2.5 years (SD 0.17), FU1 to FU2 mean 2.1 years (SD 0.26), FU2 to FU3 mean 2.2 years (SD 0.31)]. Among the MACS participants, 32% completed one CCA-IMT measurement, 23% completed two, and 45% completed all three measurements. Of those that completed all three assessments, measurements were about 3 years apart from baseline to FU1 [mean 2.9 years (SD 0.34)], with 4.5 years between FU1 and FU2 [mean 4.5 years (SD 0.46)]. All statistical analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

Sample characteristics by cohort are presented in Table 1. Median age (years) at CCA-IMT baseline was 35.2 in the WIHS (n=1164) and 69.6 in the MACS (n=387). The WIHS participants were more likely to be of black race than the MACS participants (60% vs. 31%). Among the WIHS, the mean CCA-IMT (μm) was 729.8 (standard deviation [SD] 114.7) at baseline, 733.7 (SD 114.0) at follow-up 1, 732.4 (SD 115.3) at follow-up 2, and 750.8 (SD 124.3) at follow-up 3. Among the MACS, the mean CCA-IMT (μm) was 742.6 (SD 125.6) at baseline, 756.7 (SD 125.9) at follow-up 1, and 791.1 (SD 127.2) at follow-up 2.

A four-group trajectory model emerged as the best fitting model for WIHS (Figure 2, Panel A; model entropy 0.88) and MACS (Figure 2, Panel B; model entropy 0.92). Qualitative descriptions of the patterns are as follow: “Abstinent” (WIHS 35%; MACS 13%, <1 drink/week throughout 10-years), “Low” (WIHS 30%; MACS 61%, low to moderate [1–2 (3) drinks/week for women (men)] throughout 10-years), “Moderate” (WIHS 29%; MACS 18% [3–4 (6–8) drinks/week for women (men)] and “Heavy” (WIHS 6%; MACS 8% [> 7 (14) drinks/week for women (men)] consumption throughout 10-years). Current alcohol consumption at baseline was comparable by cohort (Abstinence: WIHS 55%, MACS 58%; Moderate WIHS 38%, MACS 37%; Heavy: WIHS 8%, MACS 5%). Crude associations between past and current alcohol consumption patterns and mean CCA-IMT at baseline are presented in Table 2. At baseline past alcohol consumption patterns were not statistically significantly associated with baseline CCA-IMT in the WIHS or MACS cohorts. In WIHS, current moderate alcohol consumption was associated with a statistically significantly lower baseline CCA-IMT (β −21.9, CI −34.6, −9.31, p<.001) compared to abstinence. In MACS current heavy alcohol consumption was associated with a significantly lower baseline CCA-IMT (β −67.5, CI −126.−8.36, p<.05). Adjusted associations between past and current alcohol consumption patterns and baseline CCA-IMT are shown in Table 3.

Past alcohol consumption and CCA-IMT change.

In the WIHS, past heavy alcohol consumption was associated with a statistically significant increase in CCA-IMT over time, compared to abstinence (β 8.08, CI 0.35, 15.8, p<.05). Past low and moderate alcohol consumption patterns were not statistically significantly associated with CCA-IMT change (Low: β 3.39, CI −2.36, 9.14; Moderate: β 3.06, CI −2.32, 8.43). In the MACS, past low (Table 3; β 15.3, CI 6.46, 24.2, p<.001) moderate (β 14.3, CI 1.36, 27.2, p<.05) and heavy (β 21.8, CI 4.63, 38.9, p<.05) alcohol consumption patterns were statistically significantly associated with increased CCA-IMT over time, compared to abstinence. No time by past alcohol consumption pattern interactions were found in either cohorts.

Current alcohol consumption and CCA-IMT change.

In the WIHS, while current moderate consumption was not statistically significantly associated with CCA-IMT change (β 2–0.95, CI −5.82, 3.93), current heavy consumption was associated with decreased CCA-IMT over time (β −11.4, CI −20.2, −2.63, p<.05). In the MACS, current moderate consumption was not statistically significantly associated with CCA-IMT change (β 0.26, CI −9.99, 10.5); However, heavy alcohol consumption was

significantly associated with decreased CCA-IMT over time, compared to abstinence (β −15.4, CI −30.7, −0.13, p<.05). No time by current alcohol consumption pattern interactions were found in either cohorts.

DISCUSSION

We aimed to assess the association between past (10-year) and current (6-month) patterns of alcohol consumption and change in non-plaque right CCA-IMT over time, as measured by B-mode carotid artery ultrasound. Specifically, we tested the effect of heavy and moderate alcohol consumption on early atherosclerosis development among PLWH. Those in the 10-year heavy alcohol consumption group tended to have the highest baseline CCA-IMT. Membership in this group was statistically significantly associated with increased CCA-IMT in both the WIHS and MACS cohorts, compared to the abstinence group.

Participants of the WIHS and MACS had varied results regarding the effect of 10-year moderate and low alcohol use, with low and moderate drinking being associated with significantly increased CCA-IMT in the MACS, but not the WIHS. The difference in effect found between the WIHS and MACS cohorts could be due to important differences in confounding factors, in alcohol consumption level, and/or sex specific processes associated with risk. There are significant demographic differences between the WIHS and MACS cohorts (i.e., age, socioeconomic status, race/ethnicity, and substance use), making direct comparisons of stratified analyses difficult. Because of these differences, we carefully controlled for confounding variables related to socio-demographic status and CVD risk, however it is likely that confounding effects remain. Further, the higher risk seen in the MACS (male participants) may be due to the increased age of this group, whereas the WIHS (female participants) were still of pre or peri-menopausal age and thus could be benefiting from this time-frame of low risk. Other studies have found inconsistent effects of alcohol on subclinical atherosclerosis between women and men (Schminke et al., 2005; Lee et al., 2009; Zyriax et al., 2010) that may be due to gender differences in risk factors and clinical presentation of atherosclerosis and CVD.

Current heavy alcohol use was associated with statistically significant decreases in CCA-IMT in both the WIHS and MACS cohorts. While this finding is inconsistent with research in HIV-uninfected populations that found heavy alcohol use to significantly increase CCA-IMT (Zyriax et al., 2010) and carotid artery stiffness (Hougaku et al., 2005), our results control for past heavy consumption and may be indicative of sporadic or infrequent heavy drinking events. Our results do not support a protective effect of long-term or current moderate alcohol consumption on CVD-related outcomes among PLWH, which is inconsistent with a J-curved association found in previous literature (Fernández-Solá, et al., 2015; Gonçalves et al., 2017; Bell et al., 2017).

Limitations

The readers should consider some limitations of the current study. First, alcohol consumption quantity and frequency were assessed via self-report and is subject to recall and social desirability biases. These potential biases likely result in underestimation of alcohol consumption. However, this method has been established as a reliable and valid

approach to alcohol use assessment (Del Boca & Darkes, 2003). Second, because we used unilateral carotid artery ultrasound to measure non-plaque CCA-IMT, these results can only be generalized to the early developmental stages of atherosclerosis in the carotid artery. However, CCA-IMT is highly correlated to subclinical disease in other vascular territories when compared to other methods that detect low to no disease (Davis et al., 1999; Lester et al., 2009). As previously mentioned, significant demographic differences between the WIHS and MACS cohorts limit the ability to compare the effect of alcohol consumption by cohort. Fourth, GBTM is a semi-parametric and probabilistic model that estimates grouped trajectories of the most similar individual patterns. Therefore, each trajectory group does not fully describe the individual-level patterns contained within them and should not be considered absolute.

Future research should continue to investigate the effect of alcohol consumption on the early development of atherosclerosis and interactions with other significant factors, paying particular focus to the manifestation of atherosclerosis in men and women, in order to accurately depict incremental risk of different alcohol use phenotypes. Future research should also consider past and current alcohol consumption as indicators of potential critical windows of exposure that may be predictive of future atherosclerosis or clinical CVD. Lastly, validation of the association between alcohol consumption and atherosclerosis could focus on the proposed risk mechanisms between alcohol consumption and increased CCA-IMT, including pro-inflammatory (i.e., interleukin-6, tumor necrosis factor alpha) and anti-inflammatory cytokines (interleukin-10) (Autieri, 2012) and cardiac biomarkers (i.e., C-reactive protein, creatine kinase, myoglobin, cardiac troponins).

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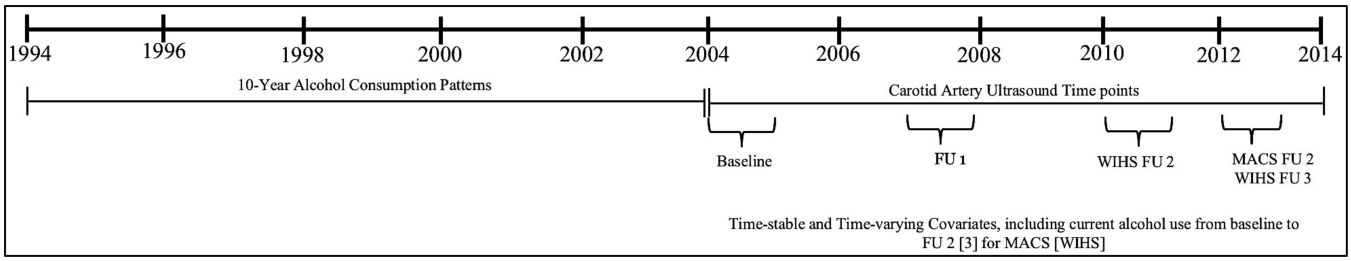

Figure 1.

Timeline for 10-year trajectory models prior to baseline carotid artery ultrasound. FU = follow-up

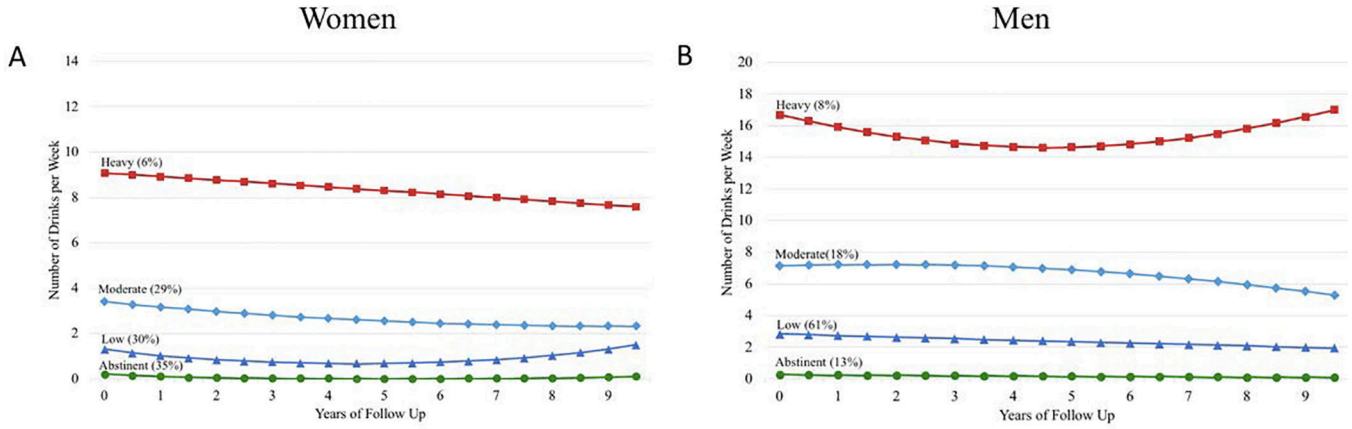

Figure 2.

10-year alcohol consumption trajectories by cohort.

Panel A: Alcohol consumption patterns in women prior to baseline carotid artery ultrasound measurement. Number of drinks per week capped at 14; Panel B: Alcohol consumption patterns in men prior to baseline carotid artery ultrasound measurement. Number of drinks per week capped at 21.

Table 1.

Baseline characteristics of persons living with HIV by cohort

	WIHS	MACS
Baseline Characteristics	Frequency (Column %) *Mean (Standard Deviation)*	
CCA-IMT μm		
Baseline (WIHS N=1164; MACS N=387)	*729.8 (114.7)*	*742.6 (125.6)*
Follow-up 1 (WIHS N=662; MACS N=321)	*733.7 (114.0)*	*756.7 (125.9)*
Follow-up 2 (WIHS N=492; MACS N=233)	*732.4 (115.3)*	*791.1 (127.2)*
Follow-up 3 (WIHS N=538)	*750.8 (124.3)*	N/A
Race/ethnicity		
White (non-Hispanic)	255 (22)	245 (63)
African American/Black (non-Hispanic)	702 (60)	119 (31)
Other	207 (18)	23 (6)
Age, years	*35.2 (7.6)*	*69.6 (5.5)*
Pack-years	*2.0 (2.9)*	*3.0 (6.5)*
Probable depression		
No	888 (76)	338 (87)
Yes	276 (24)	49 (13)
Illicit drug use		
No	1069 (92)	308 (80)
Yes	95 (8)	79 (20)
HIV RNA Viral Load		
<200 copies/Ml	516 (44)	252 (65)
≥ 200 copies/Ml	648 (56)	135 (35)
Cumulative ART exposure, years		
NRTI	4.93 (3.42)	13.9 (7.87)
NNRTI	1.68 (1.89)	2.48 (2.60)
PI	2.45 (2.63)	4.12 (3.65)
Hepatitis C Co-infection		
No	936 (80)	316 (82)
Yes	228 (20)	71 (18)
10-year alcohol consumption pattern		
Abstinence	409 (35)	51 (13)
Low	347 (30)	235 (61)
Moderate	332 (29)	71 (18)
Heavy	76 (6)	30 (8)
Current alcohol consumption		
Abstinence	635 (55)	226 (58)
Moderate	441 (38)	142 (37)
Heavy	88 (8)	19 (5)

Italicized text represents mean and standard deviations for continuous variables. CCA-IMT μm Common Carotid Artery-Intima Media Thickness in micrometers; WIHS Women's Interagency HIV Study; MACS Multicenter AIDS Cohort Study; SD Standard Deviation

Table 2.

Crude associations between 10-year alcohol consumption patterns, current alcohol consumption, and carotid artery intima-media thickness at baseline, by gender

	WIHS (N=1149)		MACS (N=387)	
	CCA-IMT, μm Mean (95% CI)	**β (95% CI)**	**CCA-IMT, μm Mean (95% CI)**	**β (95% CI)**
10-year Alcohol Consumption Patterns				
Abstinence	736.8 (721.0, 752.6)	REF	734.3 (698.3, 770.3)	REF
Low	727.6 (714.3, 740.8)	−9.20 (−28.8, 10.4)	726.9 (702.7, 751.2)	−7.32 (−38.6, 23.9)
Moderate	735.1 (722.1, 748.2)	−1.67 (−21.9, 18.6)	772.6 (733.8, 811.5)	38.3 (−15.5, 92.2)
Heavy	745.4 (724.9, 765.9)	8.58 (−17.9, 35.1)	787.7 (735.9, 839.5)	53.4 (−18.6, 125.4)
Current Alcohol Consumption				
Abstinence	745.5 (735.3, 755.6)	REF	778.7 (752.0, 805.4)	REF
Moderate	723.5 (712.7, 734.3)	−21.9 (−34.6, −9.31) ***	776.2 (753.8, 798.6)	−2.52 (−30.1, 25.1)
Heavy	739.7 (724.5, 754.9)	−5.72 (−23.5, 12.1)	711.2 (667.5, 754.9)	−67.5 (−126.6, −8.36) *

* p<.05

** p<.01

*** p<.001

CCA-IMT μm Common Carotid Artery-Intima Media Thickness in micrometers; β Beta; CI Confidence Interval; REF Reference Group

Table 3.

Adjusted[†] associations between 10-year alcohol consumption patterns, current alcohol consumption, and carotid artery intima-media thickness, by cohort

	WIHS (N=1149)	MACS (N=387)
	β (95% CI), μm	**β (95% CI), μm**
10-year Alcohol Consumption Patterns		
Abstinence	REF	REF
Low	3.39 (−2.36, 9.14)	15.3 (6.46, 24.2)***
Moderate	3.06 (−2.32, 8.43)	14.3 (1.36, 27.2)*
Heavy	8.08 (0.35, 15.8)*	21.8 (4.63, 38.9)*
Current Alcohol Consumption		
Abstinence	REF	REF
Moderate	−0.95 (−5.82, 3.93)	0.26 (−9.99, 10.5)
Heavy	−11.4 (−20.2, −2.63)*	−15.4 (−30.7, −0.13)*

*p<.05

**p<.01

***p<.001

CCA-IMT Common Carotid Artery-Intima Media Thickness; β Beta; CI Confidence Interval; REF Reference Group

[†]All analyses controlled for time, age, race, pack-years of cigarette use, illicit drug use, probable depression, suppressed HIV RNA viral load, cumulative antiretroviral therapy, Hepatitis C Co-infection.