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Unhealthy alcohol use and risk of coronary heart disease among young and middle-aged adults

Jamal S. Rana [a,b,*], Felicia W. Chi [b], Isaac Acquah [c], Stacy A. Sterling [b]

[a] Department of Cardiology, The Permanente Medical Group. Oakland CA, USA
[b] Division of Research, Kaiser Permanente Northern California, Oakland CA, USA
[c] Department of Medicine, MedStar Union Memorial Hospital, Baltimore MD, USA

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ABSTRACT

Objective: To examine the associations between unhealthy alcohol use and risk of coronary heart disease (CHD) among women and men aged 18–65 years.
Methods: An observational study in an integrated healthcare system with systematic alcohol screening. We identified 432,265 primary care patients aged 18–65 years who, in 2014–2015, reported weekly alcohol intake levels. Weekly alcohol intake, categorized into below (≤14/week men; ≤7/week women) and above limits (≥15/week men; ≥ 8/week women) per U.S. guidelines, and heavy episodic drinking (HED, ≥5/≥4 drinks any day in past 3 months for men/women, respectively). Main outcome was CHD during 4-year follow-up, based on inpatient ICD diagnoses of myocardial infarction and CHD. Cox proportional hazards models adjusted for age, sex, race/ethnicity, body mass index, physical activity, smoking, hypertension, diabetes, and hyperlipidemia.
Results: The cohort comprised 44 % women, mean age (standard deviation) of 43.5 years (±13.1). Weekly alcohol intake above limits was associated with higher prevalence of cardiovascular risk factors, and a 26 %, 19 % and 43 % higher risk on the overall, men- and women-specific risk of CHD after adjusting for these risk factors (hazard ratio [95 % confidence interval] = 1.26[1.13 -1.40], 1.19[1.04–1.35] and 1.43[1.20–1.71], respectively).
Conclusions: In a large, real-world, diverse population with a systematic alcohol screening program, having weekly alcohol intake above limits was associated with increased risk of CHD among young and middle-aged men and women. Increased CHD risk due to alcohol intake above limits warrants particular awareness and interventions.

1. Introduction

The previously upward trajectory of life expectancy experienced a slowdown, and even a decline between 2014 and 2017 in the United States, in contrast to the continued rise observed in other high-income countries [1]. This stagnation has been partially linked to a rise in mortality rates in the U.S. among middle-aged and younger adults attributed to causes such as drug- and alcohol-related incidents and suicide [2]. Unhealthy alcohol use is a significant public health challenge: in the U.S., roughly 140,000 deaths annually and nearly 4 % of global deaths and 5 % of disease burden [3,4] are attributable to unhealthy use [4]. A recent Health and Public Policy Committee of the American College of Physicians called on physicians to increase their knowledge of the health effects of varying patterns of alcohol use and interventions to address excessive alcohol use [5].

US national guidelines recommend no >4 drinks a day or 14 per week for men aged 18 to 64 years and no >3 per day or 7 per week for women [6]. However, 2 in 3 adult U.S. adults who drink report exceeding these guidelines [7]. The widespread intake of alcohol exceeding the weekly recommended guidelines is compounded by a high prevalence of heavy episodic drinking (HED) or "binge" drinking (consuming 5+/4+ drinks per occasion, for men and women, respectively), with approximately 24 % of adults 18 and above reporting HED in the past month [8]. In a study among those reporting alcohol use,

Abbreviations and Acronyms: CHD, coronary heart disease; EHR, electronic health record; HED, heavy episodic drinking.

* Corresponding auhtor at: Department of Cardiology, The Permanente Medical Group, Kaiser Permanente Oakland Medical Centre, 3600 Broadway, Oakland, California 94611, USA.
E-mail address: Jamal.S.Rana@kp.org (J.S. Rana).

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patients with diabetes, hypertension, chronic obstructive pulmonary disease, atrial fibrillation, cancer, chronic liver disease, or injury or poisoning were more likely to report drinking above recommended guidelines [9].

While the adverse effects of alcohol use on many health conditions are well-documented [10,11], research on its impact on coronary heart disease (CHD), the leading cause of US morbidity and mortality, especially for young to middle aged women and men, remains surprisingly sparse [12]. Earlier epidemiologic research reported "cardioprotective" effects, thought to be exerted through increased levels of high-density lipoprotein (HDL) cholesterol and improved platelet function [13]. However, the causality of these associations remains uncertain and biases of reverse causality often affect such studies [14]. Further studies comparing the health outcomes of people who drink moderate levels to people who are lifetime abstainers do not completely account for pre-existing poor health, also known as 'sick quitter' or 'healthy user' phenomenon and may overestimate the better health outcomes from moderate alcohol intake [15]. Additionally, most of these studies have focused on racially/ethnically populations, thereby limiting the generalizability of findings.

Kaiser Permanente Northern California (KPNC), a large integrated health care delivery system, has integrated alcohol screening and brief intervention (ASBI) into adult primary care workflows, through its "Alcohol as a Vital Sign" initiative, which has yielded over 19 million screenings since 2013, across >150 clinics, achieving an 87 % average screening rate. To address these critical gaps and leveraging electronic health record (EHR) data collected during routine clinical encounters, our study analyzes data from a large integrated healthcare system with a robust and systematic, primary care-based ASBI program, to explore the association between unhealthy alcohol use and CHD.

2. Methods

2.1. Setting and study design

Kaiser Permanente Northern California (KPNC) serves a diverse community of over 4.6 million members, representing roughly one-third of the population in Northern California. These individuals access healthcare through various insurance options, including employer-sponsored plans, Medicare, Medicaid, and health insurance exchanges. Notably, the demographics of KPNC members closely mirror the insured population in the US, with 53 % women and significant representation of diverse racial and ethnic groups, including 20 % Asian, 7.5 % Black, and 17 % Hispanic individuals [16].

2.2. Systematic alcohol screening in adult primary care

KPNC's ASBI initiative was implemented in adult primary care beginning in June 2013. Medical assistants screen all patients while collecting vital sign information, using the National Institute on Alcohol Abuse and Alcoholism (NIAAA) evidence-based screening questions, embedded in the EHR. The instrument consists of a modified single-item screening question, automatically tailored to patient age and gender ("How many times in the past three months have you had 5 or more drinks in a day" for men 18–65 years old, or " 4 or more drinks" for women, and men 66+), followed by questions on typical drinking days per week and typical number of drinks per day [6], from which an average number of drinks consumed per week is calculated as the product of two. A detailed description of the protocol for the System-wide ASBI at KPNC Adult Primary Care is included in **Supplementary Methods**.

2.3. Study population

We identified 1885,989 KPNC adult members aged 18–65 with a complete alcohol screening 1/1/2014–12/31/2015; the first screening was selected as the index screening. We restricted our study population to adults ≤65 years to reduce the risk of life course bias, as the risk of CHD in older adults is likely to be driven by stronger determinants such as traditional cardiovascular risk factors. "Complete" was defined as having completed all the alcohol screening items. Among them, we excluded 1300,380 who reported no typical weekly alcohol intake, 144,936 who were members for <50 % of the 2 years before the index date, and 8408 who had cardiovascular disease diagnoses during the 2 years before the index date, resulting in a cohort of 432,265 eligible individuals (Fig. 1). Similar to Wood et al., we focused on individuals who reported recent alcohol intake to limit the biases associated with observational studies such as this [17].

2.4. Research ethics

The KPNC Institutional Review Board (IRB) reviewed the study protocol and granted a waiver of informed consent for accessing EHR data. This report adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

2.5. Alcohol use

Alcohol intake for each individual in the sample was based on results of his/her index screening. Consistent with the NIAAA daily and weekly drinking guidelines [6], we examined two measures of alcohol intake – any HED and weekly intake level above or below recommended limits – defined based on individual's age and sex. Any HED was defined as reporting ≥1 days drinking ≥5 drinks (for men) or ≥4 drinks (for women) in the past 3 months. Based on number of drinks per week, weekly intake levels were categorized into below (1–14/week men; 1–7/week women) and above recommended limits (≥15/week men; ≥ 8/week women).

2.6. Coronary heart disease and clinical risk factors

CHD during 4-year follow-up after the index screening were defined based on inpatient ICD-9 and ICD-10 diagnoses of coronary heart disease (CHD, ICD-9: 410, 411–414; 429.2; ICD-10: I20, I21, I22, I23-I25) [12, 18] We used the most recent record of body mass index in the prior year and created four groups: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), and obese (≥30.0) [19]. Smoking status was determined based on the most recent tobacco screening in the year before the index screening. We used the most recent record of self-reported physical activity in the prior year and classified individuals into 3 groups: inactive (0 min/week), insufficient activity (>0 but <149 min/week), and sufficient activity (≥150 min/week) [20]. Limited missing data were coded as a separate category.

To adjust for medical comorbidity burden, we also identified diagnoses of diabetes using KPNC Diabetes Registry [21], and hypertension and hyperlipidemia in the 2 years prior to the index screening, based on ICD-9 and ICD-10 codes (**Supplement** Table 1).

2.7. Statistical analyses

All statistical analyses were conducted using SAS software, Version 9.4 (SAS Institute Inc., Cary, NC). We described the baseline characteristics of participants, overall and by levels of self-reported alcohol intake. The distribution of categorical variables was summarized using number and proportions (%), and continuous variables were described using the mean (standard deviation). Each eligible individual contributed person-time from the date after index screening until the date of the first inpatient CHD diagnosis, death, disenrollment from the health plan, or end of 4-year follow-up.

Associations between alcohol use and CHD during 4-year follow-up were examined by Cox proportional hazard models adjusted for socio-demographic and clinical characteristics. We first fit a model

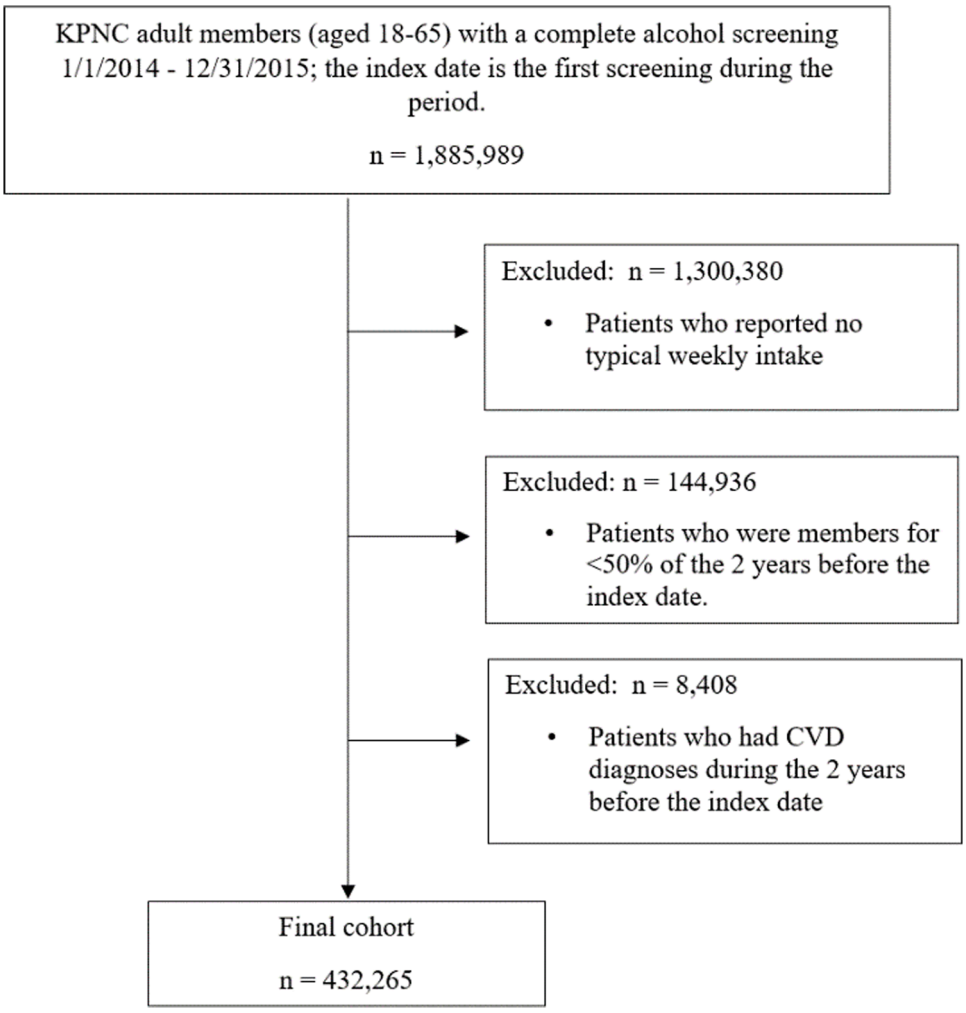

Fig. 1. STROBE diagram of study cohort.
Abbreviations: STROBE, strengthening the reporting of observational studies in epidemiology.

examining both alcohol use measures—any HED and weekly intake level, adjusting for sex, age (analyzed both categorically with groupings of 18–24/25–34/35–44/45–54/55+, and continuously for sensitivity analyses), race and ethnicity (Hispanic, and non-Hispanic Asian, Black, White, and Other), physical activity, smoking, body mass index, and comorbidities of hypertension, diabetes, and hyperlipidemia. We next examined whether the associations between levels of alcohol intake and CHD outcome differ between men and women, and between men and women with and without HED, by re-fitting the models including interactions of levels of alcohol intake with sex and HED. We also conducted a post hoc exploratory analysis re-fitting the multivariable Cox proportional hazard models among those aged 45–65 years (middle aged), a subgroup with elevated CHD risk. Further we conducted comprehensive sensitivity analyses examining age as a continuous variable. A p-value <0.05 was considered statistically significant.

3. Results

The study included a total of 432,265 adult participants. Details on the characteristics of the study population by alcohol intake levels are summarized in Table 1. The mean age (standard deviation [SD]) of the cohort was 43.5 years (±13.1), and 44 % were female. Regarding race/ethnicity, 62 % identified as non-Hispanic White, 6 % were non-Hispanic Black, 16 % were Hispanic, and 11 % were Asian. With respect to alcohol intake, approximately 22 % reported any HED in past 3 months and 10 % reported having weekly alcohol intake above the guideline recommended limits. When comparing the prevalence of drinking above guideline-recommended limits by socio-demographic and clinical characteristics, females, older adults, participants identifying as White, smokers, underweight individuals, inactive adults and those with hypertension, hyperlipidemia and any HED were more likely to drink above guideline-recommended limits (not shown).

After a median follow-up of 4 years (1456,753 person-years), 3108 participants experienced CHD. Overall, the incidence of CHD increased with increasing levels of self-reported weekly alcohol intake, irrespective of gender (Table 2). Furthermore, the incidence rate of CHD events was higher among men compared to women. The lowest incidence of events (0.6 per 1000 person-years) was experienced among women who reported HED and weekly intake below limits, while the highest incidence rate was noted among men without HED who reported weekly intake above limits (4.7 per 1000 person-years).

Results from multivariable Cox proportional hazard model indicated a higher hazard of CHD among males compared to females, older adults, non-Hispanic Black individuals compared to White individuals, smokers, underweight and obese compared to normal weight patients, and those with diabetes, hypertension, or hyperlipidemia (Table 3). After adjusting for socio-demographic and clinical characteristics, reporting any HED at baseline was not significantly associated with risk of CHD, but reporting weekly intake above limits was associated with a 26 % higher risk of CHD compared to reporting weekly intake below limits (hazard ratio [HR] and 95 % confidence interval [CI] = 1.26 [1.13–1.40]).

Table 1
Patient characteristics, adult members aged 18–65 who reported weekly alcohol intake.

		Weekly Alcohol Intake, Above or Below Limits		
	Overall (N = 432,265)	Below (*n* = 387,345, [89.6 %])	Above (*n* = 44,920, [10.4 %])	P value
Sex, N (%)				<0.001
Female	189,425 (43.8)	164,506 (42.5)	24,919 (55.5)	
Male	242,840 (56.2)	222,839 (57.5)	20,001 (44.5)	
Age, Mean (SD)	43.5 (13.1)	43.3 (13.1)	45.5 (13.2)	<0.001
Age Group, N (%)				<0.001
18–24	41,260 (9.6)	37,481 (9.7)	3779 (8.4)	
25–34	86,844 (20.1)	79,531 (20.5)	7313 (16.3)	
35–44	90,332 (20.9)	82,113 (21.2)	8219 (18.3)	
45–54	102,773 (23.8)	91,332 (23.6)	11,441 (25.5)	
≥55	111,056 (25.7)	96,888 (25.0)	14,168 (31.5)	
Race and Ethnicity, N (%)				<0.001
Hispanic (Non-Hispanic)	68,247 (15.8)	61,308 (15.8)	6939 (15.5)	
Asian	45,322 (10.5)	42,817 (11.1)	2505 (5.6)	
Black	26,384 (6.1)	24,178 (6.2)	2206 (4.9)	
White	268,715 (62.2)	237,630 (61.4)	31,085 (69.2)	
Other	23,597 (5.5)	21,412 (5.5)	2185 (4.9)	
Smoking Status, N (%)				<0.001
Smoker	53,275 (12.3)	42,629 (11.0)	10,646 (23.7)	
Non-smoker	371,228 (85.9)	337,692 (87.2)	33,536 (74.7)	
Unknown	7762 (1.8)	7024 (1.8)	738 (1.6)	
Body Mass Index, N (%)				<0.001
Underweight	3545 (0.8)	3131 (0.8)	414 (0.9)	
Normal	132,738 (30.7)	118,975 (30.7)	13,763 (30.6)	
Overweight	151,448 (35.0)	136,428 (35.2)	15,020 (33.4)	
Obese	120,789 (27.9)	107,598 (27.8)	13,191 (29.4)	
Unknown	23,745 (5.5)	21,213 (5.5)	2532 (5.6)	
Physical Activity, N (%)				<0.001
Inactive	109,354 (25.3)	94,699 (24.5)	14,655 (32.6)	
Insufficient	112,783 (26.1)	102,356 (26.4)	10,427 (23.2)	
Sufficient	203,689 (47.1)	184,654 (47.7)	19,035 (42.4)	
Unknown	6439 (1.5)	5636 (1.5)	803 (1.8)	
Comorbidity, N (%)				
Diabetes	20,325 (4.7)	18,243 (4.7)	2082 (4.6)	0.478
Hypertension	77,220 (17.9)	66,190 (17.1)	11,030 (24.6)	<0.001
Hyperlipidemia	90,508 (20.9)	80,402 (20.8)	10,106 (22.5)	<0.001
Any HED, N (%)	96,243 (22.3)	76,016 (19.6)	20,227 (45.0)	<0.001

HED= heavy episodic drinking, SD= standard deviation.

In multivariable analyses of the associations between weekly alcohol use and CHD, stratified by sex (Fig. 2**A, Central Illustration**), we found that men with above limit intake had 19 % higher hazard of CHD (HR 1.19, 95 % CI = 1.04–1.35). In contrast, women had a 43 % higher hazard of CHD (HR=1.43, 95 % CI = 1.20–1.71) for weekly intake above vs below limits. The p value for the interaction term of sex and weekly intake was however 0.091, suggesting a lack of differential association by sex.

We further examined the associations between weekly intake and CHD by sex and HED and found that, among men with no recent HED, weekly intake above limit was not significantly associated with CHD hazard, while among men with HED in the past 3 months, there was a 30 % higher hazard of CHD (HR 1.30, 95 % CI = 1.09–1.54) for intake reported above compared with below the weekly limit (Fig. 2**B, Central Illustration**). Among women without recent HED, alcohol intake above the limit weekly was associated with 38 % higher hazard of CHD, while for women *with* HED, alcohol intake above the weekly limit was associated with a 61 % higher hazard of CHD, when compared to below weekly limit intake (HR 1.38, 95 % CI = 1.14–1.66 and HR 1.61, 95 % CI = 1.26–2.05, respectively). The p value for the interaction term of sex and weekly intake was 0.054 (**Supplement** Table 2) .

Table 2
Incidence rates of CHD, by sex, HED and weekly alcohol intake levels.

	Person Year	Number of Cases	Incidence Rates (per 1000 person-years)
Men			
No HED			
Weekly Intake Below Limits	576,709.8	1761	3.1
Weekly Intake Above Limits	28,307.1	134	4.7
Any HED			
Weekly Intake Below Limits	171,594.9	354	2.1
Weekly Intake Above Limits	37,014.4	157	4.2
Women			
No HED			
Weekly Intake Below Limits	483,407.6	498	1.0
Weekly Intake Above Limits	55,168.7	106	1.9
Any HED			
Weekly Intake Below Limits	75,826.6	46	0.6
Weekly Intake Above Limits	28,724.2	52	1.8

CHD= coronary heart disease, HED= heavy episodic drinking.

Results from post hoc exploratory analysis among those aged 45+ were consistent with full sample analyses, with significant p values suggesting that the associations between weekly intake level and CHD differ by sex. For men aged 45+, weekly intake above the limit was associated with 15 % higher hazard of CHD (HR 1.15, 95 % CI = 1.00–1.32); among women aged 45+, the hazard ratio of CHD was 1.47 (95 % CI = 1.21–1.77) for weekly intake above vs below limits (**Supplement** Table 3). When further examining the associations between weekly intake and CHD by sex and HED, we found that for men aged 45+, above limit weekly intake was associated with null and 23 % higher hazard of CHD among those without and with HED (HR 1.09, 95 % CI = 0.92–1.29 and HR 1.23, 95 % CI = 1.02–1.48) (**Supplement Table 4**). For women aged 45+, above limit weekly alcohol intake was associated with 42 % and 61 % higher hazard of CHD among those without and with HED (HR 1.42, 95 % CI = 1.17–1.73 and HR 1.61, 95 % CI = 1.24–2.08, respectively).

Sensitivity analyses examining age as a continuous variable demonstrated no substantial differences in the results (**Supplement Tables 5–7**).

4. Discussion

In a large, diverse, real-world clinical population, in the context of a systematic primary care-based ASBI program, among young and middle-aged men and women, unhealthy weekly alcohol intake but not HED was associated with increased risk of CHD. Our results further show a higher risk of CHD among middle aged women compared to their male counterparts for weekly intake above guideline-recommended limits.

Our results are consistent with prior studies of the association

Table 3
Associations of patient characteristics and alcohol intake with CHD during 4-year follow-up (N = 432,265).

	CHD HR (95 % CI)
Sex	
Male vs. Female	**2.39 (2.19–2.61)**
Age Group	
25–34 vs. 18–24	**2.21 (1.24–3.93)**
35–44 vs. 18–24	**5.97 (3.49–10.24)**
45–54 vs. 18–24	**13.35 (7.85–22.70)**
≥55 vs. 18–24	**24.11 (14.20–40.96)**
Race and Ethnicity	
Hispanic vs. White	**0.82 (0.74–0.92)**
(Non-Hispanic)	
Asian vs. White	0.95 (0.83–1.08)
Black vs. White	**1.27 (1.12–1.43)**
Other vs. White	**0.76 (0.63–0.91)**
Smoking Status	
Smoker vs. Non-smoker	**1.86 (1.70–2.04)**
Unknown vs. Non-smoker	1.01 (0.80–1.27)
Body Mass Index	
Underweight vs. Normal	**2.78 (1.89–4.10)**
Overweight vs. Normal	1.08 (0.97–1.21)
Obese vs. Normal	**1.35 (1.21–1.51)**
Unknown vs. Normal	**1.20 (1.00–1.42)**
Physical Activity	
Inactive vs. Sufficient	**1.35 (1.24–1.47)**
Insufficient vs. Sufficient	1.07 (0.97–1.17)
Unknown	1.05 (0.81–1.36)
Comorbidity, Yes vs No	
Diabetes	**1.77 (1.60–1.95)**
Hypertension	**1.97 (1.82–2.14)**
Hyperlipidemia	**1.20 (1.11–1.29)**
Any HED	
Yes vs. No	0.96 (0.88–1.05)
Weekly Alcohol Intake Level	
Above Limits vs. Below	**1.26 (1.13–1.40)**

Hazard ratios and 95 % confidence intervals were estimated by a Cox Proportional Hazard model that includes sex, age (18–24/25–34/35–44/45–54/55+), race and ethnicity, physical activity, smoking, body mass index, comorbidities of hypertension, diabetes, and hyperlipidemia, any HED/past 3 months, and weekly alcohol intake level (above limits defined as ≥15/week for men and ≥ 8/week for women; below defined as 1–14/week for men and 1–7/week for women). CHD= coronary heart disease, CI= confidence interval, HED= heavy episodic drinking, HR=hazard ratio.

between alcohol intake and heart disease. For instance, in a cohort study using the UK Biobank (2006–2010, follow-up until 2016), genetic evidence supported a nonlinear, consistently increasing risk association between all amounts of alcohol intake and both hypertension and coronary artery disease, with modest increases in risk with light alcohol intake and exponentially greater risk increases at higher levels of intake [22]. Notably, the drinking groups defined in the study, as light (>0–8.4 drinks/week), moderate (>8.4–15.4 drinks/week), and heavy (>15.4–24.5 drinks/week) were much higher than the intake levels used in the current study, categorized into above or below current U.S. weekly low-risk limits (≤14/week men; ≤ 7/week women). Additionally, no distinction was made for differential cut offs for women versus men, and most of the population was of European ancestry. Our results build on this growing evidence in a more racially and ethnically diverse population and with a more nuanced consideration of intake among women and overall, at lesser threshold of alcohol intake.

Alcohol has various metabolic effects on the body. A study among about 6000 Multi-Ethnic Study of Atherosclerosis (MESA) participants showed a link between increased alcohol intake and elevated ectopic fat deposition, known to be associated with increased cardiovascular risk [23]. There is also increasing data on the link between alcohol intake, gut microbiota and the immune system, that in turn can have effect on cardiovascular system [24,25].

A comprehensive meta-analysis by Wood et al. underscored the detrimental effects of alcohol, even at moderate levels, suggesting increased all-cause mortality and a shortened lifespan [26]. Similarly, a recent WHO statement emphasized the lack of a safe drinking threshold for alcohol [27]. The 2025 U.S. Surgeon General's advisory on alcohol and cancer warns that for certain cancers risk may start to increase around one or fewer drinks per day [28], which is also consistent with Canadian guidelines that say even 3–6 dinks per week can increase risk for cancer [29]. Regarding heart disease, Canadian guidelines highlight that research in the last decade is more nuanced, with the most recent and highest quality systematic reviews showing that drinking a little alcohol neither decreases nor increases the risk of ischemic heart disease, but it is a risk factor for most other types of cardiovascular disease, including, hypertension, heart failure, high blood pressure, atrial fibrillation [29].

In our study, middle aged men and women had a 15 % and 47 % higher risk respectively of CHD. These associations were despite the adjustment for confounders (and potential mediators which could attenuate these associations) such as cardiovascular risk factors. Of note, compared to other studies [26,30,31], the follow up period for our study was relatively short (4 years), suggesting that a longer follow up period could have resulted in stronger associations.

Despite established mechanisms linking unhealthy alcohol intake to cardiovascular disease, the precise shape of this association remains an area of debate. Conventional epidemiological research has suggested a J-shaped relationship, where people who drink moderate levels exhibit lower risk compared to people who do not drink and people who drink heavy amounts of alcohol. This cardioprotective effect is thought to be exerted through several mechanisms, including increased levels of high-density lipoprotein (HDL) cholesterol and therefore reduced plaque [13]. Other proposed mechanisms include antioxidant properties of alcohol as well as improved platelet function. However, these studies have faced limitations such as self-report bias, residual confounding, and the "sick quitter" phenomenon, wherein individuals with pre-existing health risks, in some cases alcohol-related, are more likely to abstain from alcohol [32].

More recent research has therefore questioned this J-shaped relationship [31,33], and effects of alcohol intake, even at modest levels, is a growing area of concern. For instance, in a recent systematic review and meta-analysis of 107 studies by Stockwell et al., the authors found that the exclusion of low-quality studies that included some of the aforementioned lifetime selection bias of comparison with non- drinkers who may have stopped due to ill health or alcohol disorder, resulted a significant reduction in the "protective effect" and subgroups of studies least likely to be biased had no significant reduction of mortality risk among lower-volume drinkers of alcohol on people who drink relatively low volumes [34]. More recent studies have used two main approaches to address these biases, including the use of mendelian randomization [22,35], or excluding individuals reporting no drinking [17]. In our study, we excluded individuals who do not drink and focused on alcohol intake levels among individuals who actively drink [36,37]. This strategy minimizes the potential influence of the "sick quitter" bias and allows for a more nuanced examination of the dose-response relationship.

In our study, we further explored the effect of HED on CHD. While we did not find a significant association between HED and CHD in the overall study population, stratified analyses by HED showed a relatively higher but statistically non-significant risk of CHD among men and women reporting recent HED and weekly intake above limits compared to their non-HED counterparts. A systematic review by Roerecke et al., suggest that HED may modify the relationship between alcohol intake and CVD, leading to elevated risk, and found a 45 % higher risk of ischemic heart disease among participants with irregular heavy drinking compared to those with regular moderate drinking [38]. Our observation of an increased risk of CHD among both sexes reporting HED in this contemporary population is noteworthy. While the stratified analyses showed stronger associations among participants who reported any HED, suggesting a dose-response relationship, the interaction term for

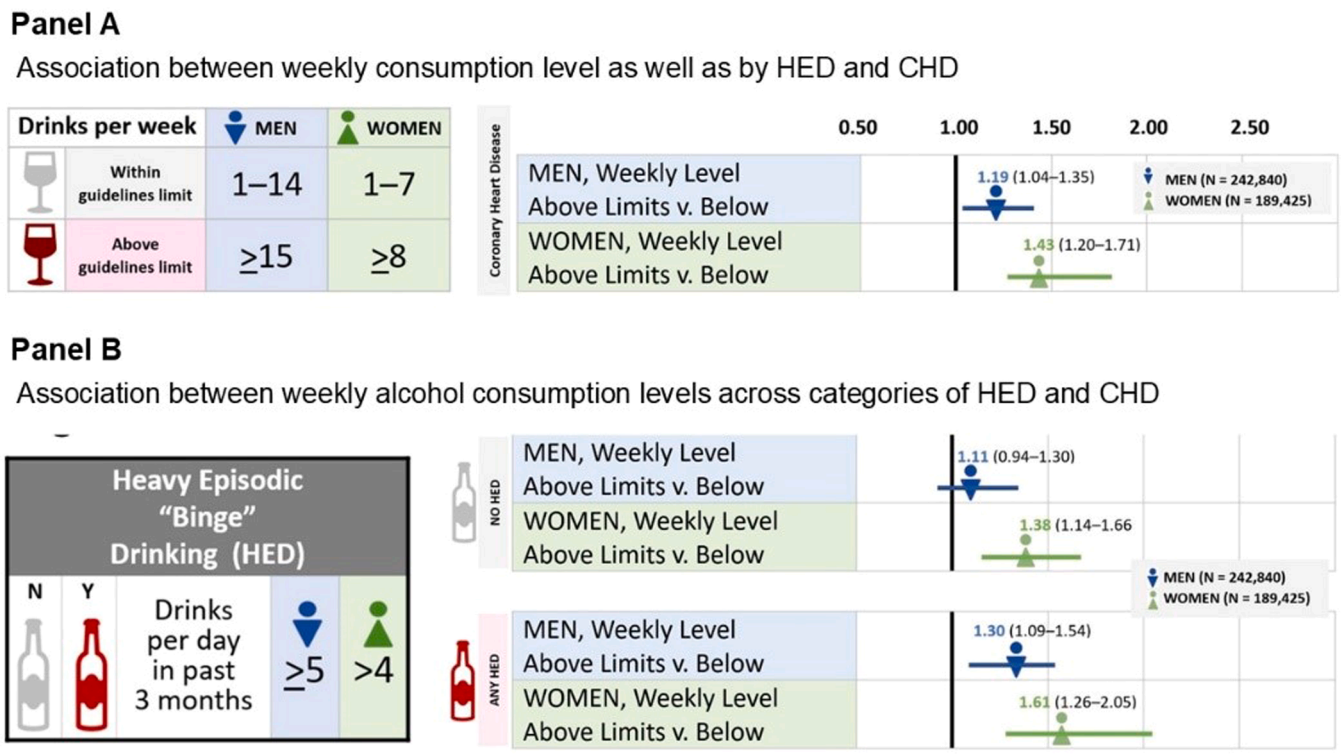

Fig. 2. Association between levels of alcohol consumption and CHD.
Panel A: Association between levels of alcohol consumption and CHD in the overall population
Panel B: Association between levels of alcohol consumption any by levels of HED and CHD
Abbreviations: CHD, coronary heart disease; HED, heavy episodic drinking.

any HED for these analyses was not significant. We however believe that the subgroup analyses may have limited our statistical power to detect any differences.

Our study also revealed some sex differences in CHD risk. Specifically, among middle aged (45–65-years) participants, the risk of CHD among individuals with above-limits weekly intake was approximately 30 % higher for women compared to men. Data exploring effect of alcohol and CHD, specifically for women is sparse [39]. Awareness of risk factors is critical in reducing cardiovascular risk in women [40]. Women's awareness that cardiovascular disease is a leading cause of death among women has declined from 64.8 % in 2009 to 43.7 % in 2019 and, of further concern, this decline was greatest among women aged 25–34 years and in those with CVD risk factors [41]. Our observation of higher risk of CHD associated with exceeding alcohol consumption limits among women may be partially explained by the fact that women, on average, tend to have smaller body sizes and lower alcohol tolerance, making them more susceptible to the harmful effects of alcohol at even moderate levels [42]. It is worth noting that our findings are in spite of the lower U.S. threshold for healthy drinking among women compared to men. These findings raise the question as to whether adopting absolute or equivalent limits of intake among women compared to men, a movement occurring in some countries, may confer higher health risks on women, particularly in light of the narrowing gap in alcohol-related deaths among women and men in the U.S. [43]

A major strength of our study is the setting of KPNC, a large integrated health care delivery system that has integrated alcohol screening into adult primary care workflows, through its ASBI initiative, with 19 million screenings achieving an 87 % average screening rate. KPNC has a racially diverse population and reflects the US population with access to care, which allows us to study a large population-based sample of patients. Leveraging EHR data collected during routine clinical encounters, we contribute to the expanding body of knowledge on alcohol's health effects by examining alcohol intake patterns within a diverse, representative sample of primary care patients. Through this analysis, we strove to facilitate a more nuanced understanding of associations between varying levels of alcohol intake and CHD, thereby informing targeted disease management strategies for clinicians and shaping evidence-based policies for policymakers.

4.1. Limitations

The present study has several limitations. First, despite attempting to address potential bias inherent in such studies by excluding the non-consuming group and adjusting for recognized confounders, the possibility of residual confounding remains [44]. Related to this is the categorical nature of most of our variables as well as our inability to adjust for other potential confounders such as diet. Nevertheless, our findings are consistent with prior studies establishing an association between alcohol and CHD. We cannot establish temporality of the associations observed between medical conditions and alcohol intake levels, since patients were asked about intake over the past 3 months at the screening. Additionally, relying on self-reported alcohol intake introduces potential for recall and underreporting bias, which may dampen the true association [35,44]. However, comprehensive reviews have concluded that self-reports are more accurate and reliable when gathered under specific conditions [45], and KPNC designed an alcohol screening workflow to minimize stigma and optimize patient comfort in disclosing alcohol use based on trial findings [46]. Despite this, underreporting among high-level users is likely, which may typically bias the results towards the null, suggesting that the association may be potentially stronger than what was found. Alcohol use was obtained at index screening, and it is possible that individuals changed their use behavior during follow-up. However, our findings align with previous research establishing a relationship between alcohol intake and CHD risk [22]. Furthermore, by using a relatively short follow-up period, we believe that we may underestimate the effect of alcohol intake on CHD, given

that the manifestation of such a phenomenon requires several years. The restriction of our study population to younger age group may potentially limit the generalizability of our findings. Nonetheless, we believe these results likely pertain even to even older populations who may be more susceptible to the effects of alcohol.

5. Conclusions

The study provides evidence for an association between alcohol intake exceeding U.S. guidelines and increased risk of CHD among young to middle-aged women and men. Future research should utilize robust epidemiologic methodologies with the aim of establishing causality. Increased CHD risk due to alcohol intake about limits, warrants awareness and interventions.

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CRediT authorship contribution statement

Jamal S. Rana: Writing – review & editing, Methodology, Conceptualization. **Felicia W. Chi:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Isaac Acquah:** Writing – review & editing, Writing – original draft. **Stacy A. Sterling:** Writing – review & editing, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2025.100947.

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