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Association of coffee consumption with all-cause and cardiovascular disease mortality

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Abstract

Objective—To evaluate the association between coffee consumption and mortality from all causes and cardiovascular disease (CVD).

Patients and Methods—Data from the Aerobics Center Longitudinal Study (ACLS) representing a total of 43,727 participants contributing to 699,632 person-years of follow-up time, were included. Baseline data were collected by an in-person interview based on standardized questionnaires and a medical examination, including fasting blood chemistry analysis, anthropometry, blood pressure, electrocardiography, and a maximal graded exercise test, between February 3, 1971 and December 30, 2002. Cox regression analysis was used to quantify the association between coffee consumption and all-cause and cause-specific mortality.

Results—During the 17-year median follow-up period, 2512 deaths occurred (32% due to CVD). In multivariate analyses, coffee intake was positively associated with all-cause mortality in men. Men who drank >28 cups coffee per week had higher all-cause mortality (hazard ratio (HR): 1.21; 95% confidence interval (CI): 1.04–1.40). However, after stratification based on age, both younger (<55 years) men and women showed a statistically significant association between high coffee consumption (>28 cups/week) and all-cause mortality, after adjusting for potential confounders and fitness level (HR: 1.56; 95% CI: 1.30–1.87 for men and HR: 2.13; 95% CI: 1.26–3.59 for women, respectively).

Conclusion—In this large cohort, a positive association between coffee consumption and all-cause mortality was observed among men and both men and women <55 years of age. Based on our findings, it seems appropriate to suggest that younger people avoid heavy coffee consumption

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Disclosures
None.

(ie, averaging >4 cups/day). However, this finding should be assessed in future studies from other populations.

Introduction

Drinking coffee has become a normal daily routine for more than half of Americans and large numbers of people worldwide. According to the latest National Coffee Drinking Study from the National Coffee Association, approximately 64% of American adults drink coffee each day, and among coffee drinkers, the average coffee consumption in the United States is 3.1 cups per day.[1] Nevertheless, coffee has long been suspected to contribute to a variety of chronic health conditions. Over the last four decades, the association between coffee consumption and chronic health outcomes has been investigated in relation to conditions such as obesity[2–6], hypertension [7,8], and coronary heart disease [9,10]. However, studies on coffee consumption in relation to all-cause and cause-specific mortality are limited, and the results are often controversial. Several studies have found a positive association between higher levels of coffee consumption and all-cause and cardiovascular disease (CVD) mortality [11–13], while others have found an inverse association with all-cause mortality in both men and women [14–16], only in women [17,18], or only in men[19–21], with some evidence suggesting that there may be a U- shape or J- shape relationship between coffee drinking and health outcomes. Still, other researchers suggest that the association may not exist at all [22–24]. The objective of the current study was to investigate the effect of coffee consumption on all-cause and CVD mortality in the Aerobics Center Longitudinal Study (ACLS) cohort, with an average follow-up period of 16 years and a relatively large sample size of men and women.

Patients and Methods

Patients

The ACLS is a prospective observational study and has been described in detail previously[24,25]. Between 1979 and 1998, 44,963 individuals aged 20–87 years participated and returned a medical history questionnaire assessing lifestyle habits (including coffee intake) and personal and family medical history. We examined a total of 43,727 participants (33,900 men and 9,827 women) in our final analysis, after excluding those with a prior history of myocardial infarction (MI) (n=54), stroke (n=11), or cancer (n=141), those with abnormal resting or exercise electrocardiogram (ECG; n=319), those who did not achieve 85% age-predicted maximal heart rate (n=122), those who were underweight (body mass index (BMI) <18.5 kg/m^2) (n=501), and those with less than 1 year mortality follow-up (n=88). All of the study participants provided written informed consent. The Cooper Clinic Institutional Review Board reviewed and approved the study protocol annually.

Measurement of Exposure

Regular coffee consumption, expressed as number of cups per week, was assessed by a standardized questionnaire. Consumption of regular coffee was grouped as 0, 1–7, 8–14, 15–21, 22–28, and >28 cups per week for primary analysis.

Measurement of outcome

All participants were followed for mortality from the baseline examination to the date of death or December 31, 2003. All-cause mortality and CVD mortality were identified through the National Death Index or by accessing the death certificates in the decedents' states of residence. CVD mortality was determined using the International Classification of Diseases ninth version, codes 390–449.9 before 1999, and tenth version, codes 100–178 from 1999–2003.

Measurement of covariates

All participants underwent a baseline clinical examination at the Cooper Clinic in Dallas, Texas. The medical examination was performed after an overnight fast (>12 hours) including fasting blood chemistry analysis, personal and family health history, anthropometry, blood pressure, electrocardiography, and a maximal graded exercise test. BMI was calculated as weight in kilograms divided by the square of height in meters. Responses to a standardized questionnaire were used to assess smoking status, alcohol drinking, regular tea (cups/week), regular and decaffeinated coffee (cups/week), decaffeinated or herbal tea (cups/week), physical activity, and parental history of CVD. Medical conditions, including hypertension, hypercholesterolemia, diabetes, cancer, MI and stroke, were evaluated using a standardized questionnaire.

Cardiorespiratory fitness (CRF) was quantified by the total time of the treadmill test using a modified Balke protocol [26]. Participants were encouraged to reach their maximal effort and the test was terminated once the participant requested to stop because of exhaustion or when the physician stopped the test due to medical reasons. Maximal metabolic equivalents (METs; 1 MET = 3.5 ml of oxygen uptake per kilogram/minute) were estimated from the final treadmill speed and grade [27].

Statistical Analysis

Baseline characteristics of the population were estimated by baseline coffee consumption categories and gender status. Hazard ratios and 95% confidence intervals for mortality associated with coffee consumption were estimated using Cox proportional-hazards regression models, with person-years as the underlying time metric; models also were stratified by age and BMI using the same underlying time metric. The proportional-hazards assumption was tested by Martingale-based residuals and the observed results satisfied the assumption. Analyses were conducted with the use of SAS® software, version 9.3. Statistical tests were two-sided, and the significant level was set at $\alpha = 0.05$.

Risk estimates are presented separately for men and women. Multivariate models were adjusted for age, baseline examination year, decaffeinated coffee use, regular tea use, decaffeinated or herbal tea use, physical inactivity, BMI, smoking, alcohol drinking, diabetes, hypertension, hypercholesterolemia, parental history of CVD and CRF. Hazard ratios for death associated with categories of coffee consumption (1–7, 8–14, 15–21, 22–28, >28 cups per week), was compared with no coffee consumption. In stratified analysis, we categorized age and BMI into two groups (age<55 and age ≥55) and (BMI<25 and BMI 25), respectively. The covariates were the same as the main analysis.

Results

During the 17-year median follow-up period, 2512 deaths occurred (men: 87.5%; women: 12.5%) and 32% were caused by CVD. Tables 1 and 2 show the association between coffee consumption and participants' characteristics at baseline. Both men and women who consumed higher amounts of coffee were more likely to smoke and had lower levels of CRF.

Coffee consumption and all-cause mortality

The hazard ratios for all-cause mortality among coffee consumption groups are shown in Table 3 (top portion). In the age-adjusted analyses, compared to men who did not drink coffee, men who drank coffee at a rate of 8–14 cups/week, 15–21 cups/week and ≥28 cups/week had a higher risk of all-cause mortality. In the multivariable-adjusted model, men who consumed >28 cups coffee per week had the highest risk of all-cause mortality. This

association persisted in the final model, which further adjusted for CRF level. However, coffee consumption was not associated with all-cause mortality risk among women. Kaplan-Meier survival curves indicate that both women (Figure 1a) and men (Figure 1b) with higher coffee consumption had lower mortality-free time as compared with those did not drink coffee.

Coffee consumption and CVD-related mortality

The hazard ratios of CVD-related mortality among coffee consumption groups are shown in Table 3 (lower portion). In the age-adjusted analyses, compared to men who did not drink coffee, men who drank coffee at a rate of >28 cups/week had a 36% higher risk of CVD mortality. However, this association disappeared in the final model, which adjusted for potential confounders and CRF level. For women, coffee consumption was not associated with CVD mortality risk in any model.

Coffee consumption and all-cause mortality by age group

The associations between coffee consumption and all-cause mortality for younger and older age groups are depicted in Figure 2. Figure 2a shows that younger men who consumed coffee at a rate of 8–14 cups/week, 15–21 cups/week and >28 cups/week had higher risks of all-cause mortality than did those who did not drink coffee, after adjusting for the potential confounders and CRF level. The final model indicated that younger women who consumed >28 cups of coffee per week had a higher risk of all-cause mortality than those who did not drink coffee. However, coffee consumption was not associated with all-cause mortality among older men and women (Figure 2b).

Coffee consumption and all-cause mortality by BMI group (data not shown)

The only marginally significant association of coffee consumption and all-cause mortality was observed among men with BMI≥25 who consumed >28 cups of coffee per week, indicating that overweight/obese men who consumed >28 cups of coffee per week had slightly higher all-cause mortality risk than those who did not drink coffee. Because of sample size limitations, we could not further investigate this association based on additional age stratification.

Discussion

Key findings

We found that coffee intake was positively associated with higher all-cause mortality in men, but found only a suggestion of an effect in women. In men, those who drank more than 28 cups of coffee weekly had a 21% higher risk of dying compared to their non-coffee consuming peers. Neither men nor women showed significant associations between CVD mortality and coffee consumption. The results from the stratified analysis showed that both younger men and women who consumed >28 cups of coffee/week had a higher risk of all-cause mortality than those who did not drink coffee, after adjusting for the potential confounders and CRF level. For people, particularly men, who were overweight or obese, coffee consumption trended positively, although not significantly, on all-cause mortality. We did not conduct stratified analysis based on CVD mortality because of the null findings between coffee consumption and CVD death.

Comparison with other studies

Our findings for all-cause mortality are consistent with earlier studies [11,13,20,21], but the results among recent studies have been highly variable [15,16, 17,23,28]. The majority of inverse associations between coffee consumption and mortality were observed from studies based

on middle-aged or older populations. Freedman et al found an inverse association between coffee consumption and all-cause mortality after adjusting for potential confounders [16]. Lopez-Garcia et al also found an inverse association in men [23]. However, Kleemola et al found this inverse association only in women [18]. One possible explanation for this inverse association between coffee consumption and all-cause mortality might be survival selection, because the results of the majority of the previous studies are based on older or middle-aged populations. Our study, however, had a very wide age range, from 20 to 87 years, so the survival selection might be smaller. Our stratified analyses also support this explanation. Figure 2 shows that younger men and women had an increased risk of mortality for heavy coffee drinking (>28 cups/wk) compared to non-coffee drinkers. Additionally, the non-coffee-drinking group may have had a higher mortality risk not related to the consumption of coffee; however, those unknown factors maybe exert an inverse effect on the association between coffee consumption and mortality. No statistically significant association was found between coffee consumption and CVD mortality in our study. Some cohort studies also have examined the effect of coffee consumption on CVD mortality, and the results have been variable, somewhat similar to the situation with all-cause mortality.

Possible mechanism

Coffee is a complex mixture of chemicals consisting of thousands of components [29]. Recent research has found that coffee is one of the major sources of antioxidants in the diet [30,31], and has potential beneficial effects on inflammation [32,33]. However, it is also well-known that coffee has potential adverse effects because of caffeine's potential to stimulate the release of epinephrine [34], inhibit insulin activity[35], and increase blood pressure and homocysteine levels [36]. Thus, all of these mechanisms could counterbalance one another. Research also suggests that heavy coffee drinkers may experience additional risk through potential genetic mechanisms [37] or because of confounding through the deleterious effects of other risk factors with which coffee drinking is associated. Genetic factors may partly explain why moderate coffee consumption is not as likely to be associated with increased mortality, whereas heavy coffee consumption could lead to increased mortality, as was especially noted in the men in our study. Therefore, we hypothesize that the positive association between coffee and mortality may be due to the interaction of age and coffee consumption, combined with a component of genetic coffee addiction.

Strengths

There are several strengths of this study. First, it examined a large cohort, including a total of 43,727 participants of both genders and with a wide age range from 20 to almost 90 years. Although the majority of the study population was white, highly educated, and from middle-to-upper social economic status, the homogeneity of the study population enhanced our internal validity. Second, we were able to control for potential confounders, including physical activity and CRF. Third, subclinical disease is unlikely to be a major problem in this study, because we excluded people who had baseline CVD, cancer, underweight, and abnormal ECG and also controlled for major chronic diseases, such as hypertension, diabetes, and hypercholesterolemia in the analysis. Fourth, the possibility that reverse causality may bias our results is small because the study population is homogenous.

Limitations

On the other hand, our study does have certain limitations. First, our study did not have repeated measures of coffee consumption over time, which prevents our ability to analyze long-term coffee consumption patterns and changes in coffee consumption over time. However, several studies have examined long-term habitual coffee intake and found that coffee drinking, besides being easy to measure, tends to be stable in adulthood [23,38] and that a single point measurement of coffee consumption is a valid indicator for long-term coffee

consumption [39]. Still, future studies with repeated measures of coffee consumption are warranted to elucidate the effect of change in coffee consumption on longevity. Second, we did not have data on coffee preparation methods, and the constituents of coffee may differ, which might also impact its potential association with CVD risk factors based on the different preparation methods. Third, data on marital status and total energy consumption were not included in the current study. Although educational level is not available for the analysis, we stated previously that the ACLS population is highly educated and homogeneous, which in fact increases the study's internal validity. Fourth, residual confounding may still exist even though we adjusted for all the potential confounders available in the current study. Finally, a cohort effect might exist. A recent ACLS paper from Willis et al,[40] examining the secular change across different decades when participants entered the ACLS study, from 1970s, 1980s, 1990s and 2000s, reported that there was little change on participants' characteristics such as age, BMI, blood profile and chronic disease over time. However, to remove or control the possible cohort effect, we included the baseline examination year as a covariate, which is a general approach that we have applied in most of our ACLS analyses.

Conclusion

In this large U.S. cohort study, the positive association between heavy coffee consumption (>28 cups/week) and all-cause mortality was observed among our total population of men and among both men and women younger than 55 years of age. However, for people older than 55, this association was not statistically significant for either gender. Hence, it may be appropriate to recommend that younger people, in particular, avoid heavy coffee consumption (>28 cups/week or > 4 cups in a typical day). Further studies are needed to assess details regarding the effects of long-term coffee consumption and changes in coffee consumption over time on all-cause and CVD mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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List of abbreviations

ACLS	Aerobics Center Longitudinal Study
BMI	body mass index
CRF	cardiorespiratory fitness

CVD	cardiovascular disease
ECG	electrocardiogram
MI	myocardial infarction

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Figure1a.

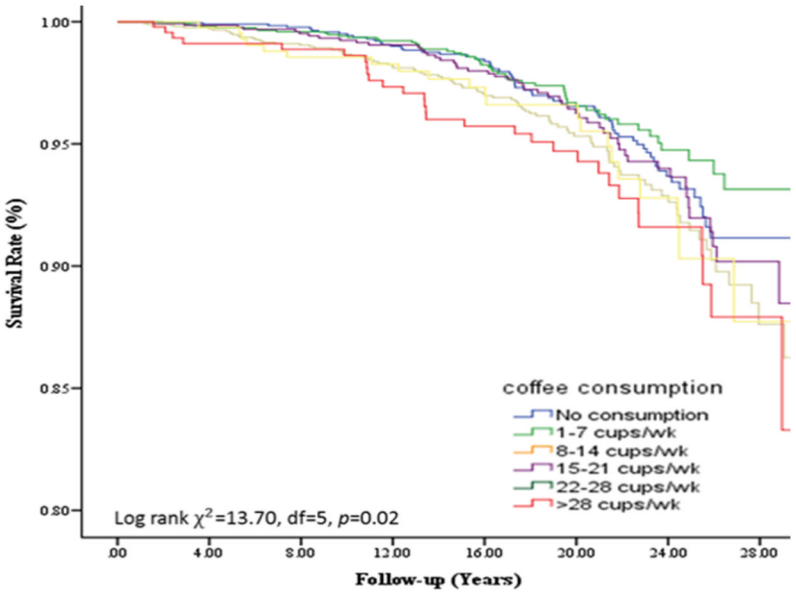

Figure1b.

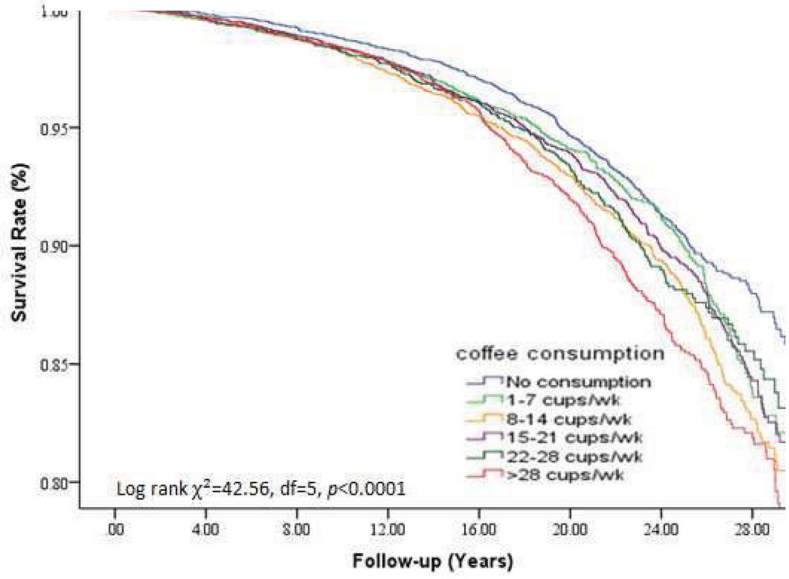

Figure 1.

Kaplan-Meier plots for all-cause mortality due to coffee consumption, ACLS, Dallas, TX, 1979–2003 among women (Figure 1a) and men (Figure 1b).

Figure2a.

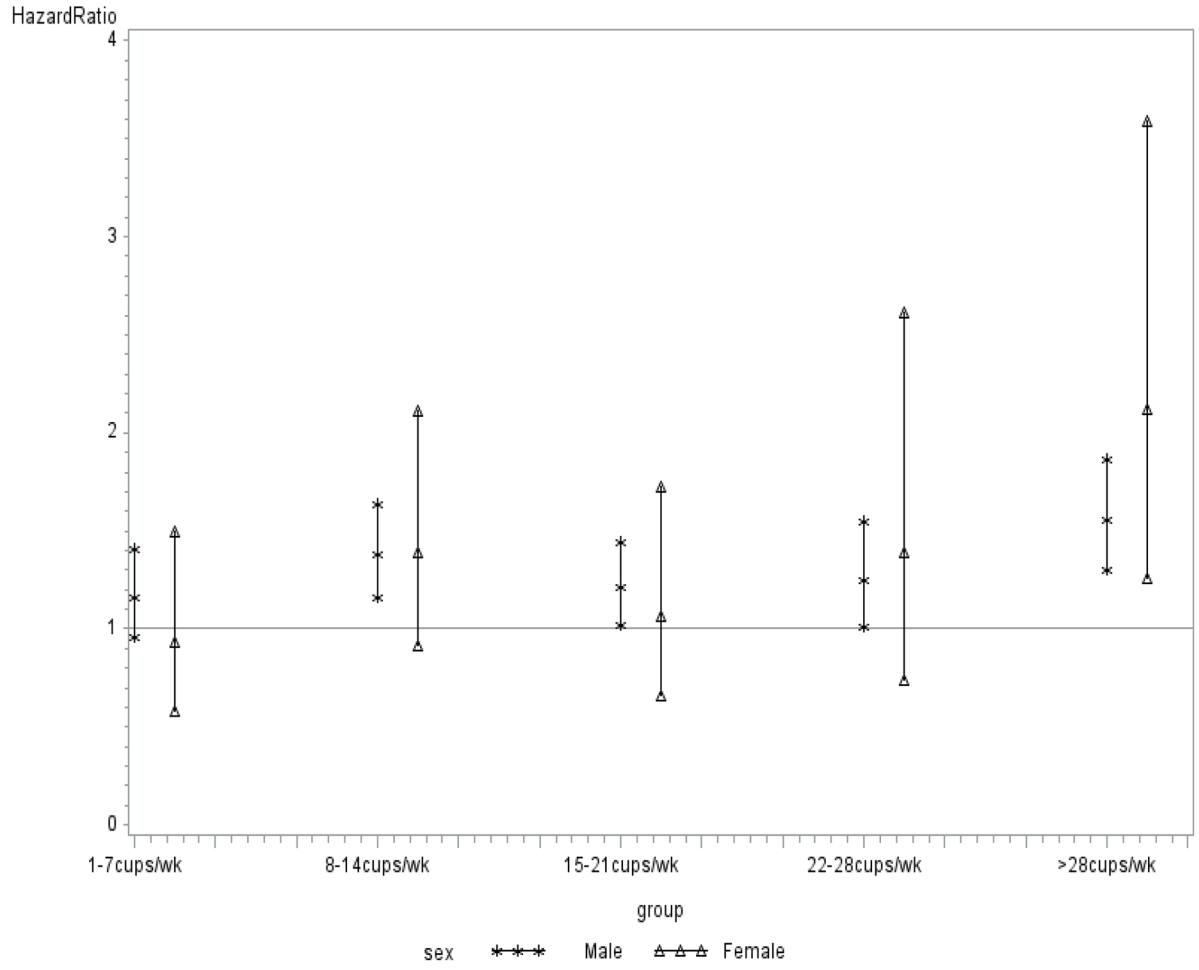

Figure2b.

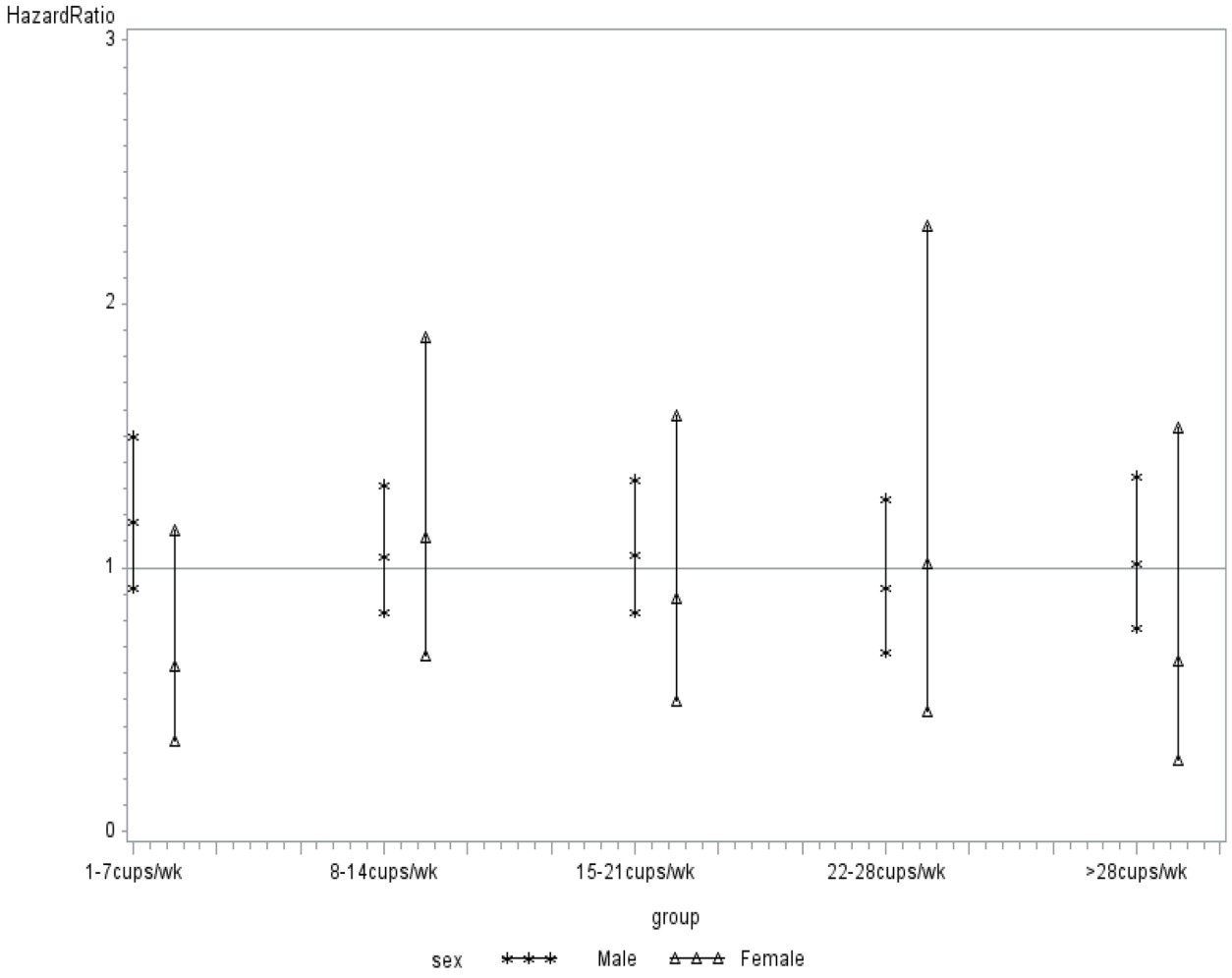

Figure 2.
Multivariate-adjusted hazard ratios and 95% confidence intervals between coffee consumption and all-cause mortality for men and women across age groups (Figure 2a. <55 years and Figure 2b. ≥55 years).

Table 1

Baseline characteristics of the study participants by weekly coffee consumption, mean (standard deviation) or percent for men[a,b]

Characteristics	Overall (N=33,900)	Coffee consumption (cups/week)						
		0 (N=6387)	1–7 (N=6772)	8–14 (N=7045)	15–21 (N=1766)	22–28 (N=7559)	>28 (N=4371)	P-value
Age (year)	43.37 (9.25)	41.43 (9.76)	43.03 (9.98)	43.97 (9.19)	43.88 (8.67)	44.29 (8.27)	44.58 (8.17)	<.0001
Body mass index (kg/m^2)	26.40 (3.70)	26.00 (3.90)	26.32 (3.93)	26.47 (3.62)	26.56 (3.55)	26.58 (3.43)	26.70 (3.47)	<.0001
Total Cholesterol (mg/dL)	208.48 (39.40)	201.90 (37.97)	205.16 (39.97)	209.37 (39.23)	211.89 (39.17)	213.10 (39.51)	214.53 (39.36)	<.0001
Fasting glucose (mg/dL)	99.95 (16.10)	98.85 (16.50)	99.61 (15.60)	100.22 (15.40)	100.29 (16.73)	100.24 (13.97)	101.10 (17.74)	<.0001
Systolic blood pressure (mmHg)	121 (13)	121 (13)	122 (13)	122 (13)	121 (13)	121 (13)	121 (13)	<.0001
Diastolic blood pressure (mmHg)	81 (9)	81 (9)	81 (10)	81 (10)	81 (9)	81 (9)	81 (9)	0.004
Cardiorespiratory fitness (Maximal Mets)	11.74 (2.40)	12.08 (2.54)	11.98 (2.47)	11.75 (2.33)	11.57 (2.33)	11.44 (2.25)	11.15 (2.17)	<.0001
Maximal treadmill time (minutes)	18.10 (4.89)	18.78 (5.08)	18.61 (4.99)	18.16 (4.79)	17.77 (4.78)	17.51 (4.69)	16.91 (4.58)	<.0001
Drink decaffeinated coffee, %	9.26	5.71	17.90	10.82	6.77	5.01	3.86	<.0001
Drink regular tea drinker, %	57.01	50.27	60.56	57.70	59.83	56.15	55.93	<.0001
Drink decaffeinated/herbal tea, %	4.53	6.89	7.15	4.03	2.82	2.28	1.37	<.0001
Alcohol heavy drinker[c], %	7.62	4.43	6.67	7.66	9.30	10.47	9.68	<.0001
Current smoker, %	18.18	10.71	13.50	17.73	23.75	25.53	31.85	<.0001
Physical inactivity[d], %	29.47	28.60	24.31	26.91	31.26	35.24	38.65	<.0001
Diabetes[e], %	5.26	4.78	5.38	5.70	5.18	4.86	5.46	0.20
Hypercholesterolemia[f], %	26.61	22.25	26.11	27.99	28.08	28.34	28.31	<.0001
Hypertension[g], %	30.36	29.12	31.08	31.26	30.21	29.10	30.53	<.0001
Parental history of CVD, %	26.52	23.56	25.10	26.27	27.75	28.91	30.93	0.045

[a] CVD=cardiovascular disease.

[b] SI conversion factors: To convert total cholesterol values to mmol/L, multiply by 0.0259; to convert fasting blood glucose levels to mmol/L, multiply by 0.0555.

[c] Alcohol heavy drinker is defined as alcohol drinks >14 per week for men and >7 per week for women.

[d] Physical inactivity is defined as no leisure-time physical activity during past three months.

[e] Diabetes is defined as fasting glucose ≥126 mg/dl or physician diagnosed diabetes, or insulin use.

[f] Hypercholesterolemia is defined as total cholesterol ≥240 mg/dl, or physician diagnosed hypercholesterolemia.

[g] Hypertension is defined as resting BP ≥140/90 mm Hg, or physician diagnosed hypertension.

Table 2

Baseline characteristics of the study participants by weekly coffee consumption, mean (standard deviation) or percent for women[a,b]

Characteristics	Overall (N=9827)	Coffee consumption (cups/week)						
		0 (N=2025)	1–7 (N=2823)	8–14 (N=1440)	15–21 (N=249)	22–28 (N=2602)	>28 (N=688)	P-value
Age (year)	42.97 (10.10)	40.35 (10.32)	42.65 (10.74)	44.07 (9.70)	44.40 (9.00)	44.91 (9.45)	43.77 (8.67)	<.0001
Body mass index (kg/m^2)	23.15 (3.86)	23.02 (4.09)	23.21 (3.94)	23.29 (3.97)	22.98 (3.44)	23.05 (3.27)	23.10 (3.51)	0.08
Total Cholesterol (mg/dL)	198.34 (40.56)	193.77 (36.10)	197.39 (46.83)	199.50 (38.48)	202.14 (37.32)	202.77 (38.26)	201.11 (38.68)	<.0001
Fasting glucose (mg/dL)	94.60 (96.43)	92.73 (15.06)	97.00 (178.00)	93.79 (12.07)	93.75 (12.41)	95.80 (20.73)	93.84 (10.59)	0.75
Systolic blood pressure (mmHg)	112 (14)	112 (14)	112 (14)	113 (14)	112 (14)	112 (14)	110 (14)	0.02
Diastolic blood pressure (mmHg)	75 (9)	75 (9)	75 (9)	76 (9)	76 (9)	75 (9)	75 (9)	0.03
Cardiorespiratory fitness (Maximal Mets)	9.61 (2.14)	9.90 (2.16)	9.81 (2.16)	9.57 (2.16)	9.44 (2.09)	9.30 (2.05)	9.18 (1.93)	<.0001
Maximal treadmill time (minutes)	13.60 (4.60)	13.76 (4.63)	14.03 (4.61)	13.51 (4.63)	13.21 (4.51)	12.93 (4.44)	12.67 (4.2)	<.0001
Drink decaffeinated coffee, %	12.77	10.42	21.68	10.95	7.36	6.09	2.60	<.0001
Drink regular tea drinker, %	53.15	48.40	57.21	54.07	52.50	49.58	49.67	<.0001
Drink decaffeinated/herbal tea, %	12.83	17.88	16.08	11.18	7.08	7.56	3.47	<.0001
Alcohol heavy drinker[c], %	19.56	6.07	9.07	11.91	11.60	10.08	7.59	<.0001
Current smoker, %	10.66	7.31	7.93	11.03	13.06	19.12	23.86	<.0001
Physical inactivity[d], %	26.09	26.67	23.84	25.13	27.78	29.83	33.62	<.0001
Diabetes[e], %	3.25	3.46	3.33	3.31	2.71	3.78	2.60	0.79
Hypercholesterolemia[f], %	19.18	16.54	19.06	20.56	20.83	18.28	19.52	0.010
Hypertension[g], %	15.71	15.46	14.84	16.87	16.32	16.18	13.23	<.0001
Parental history of CVD, %	16.20	20.79	26.11	27.98	29.72	28.15	27.55	0.22

[a] CVD=cardiovascular disease.

[b] SI conversion factors: To convert total cholesterol values to mmol/L, multiply by 0.0259; to convert fasting blood glucose levels to mmol/L, multiply by 0.0555.

[c] Alcohol heavy drinker is defined as alcohol drinks >14 per week for men and >7 per week for women.

[d] Physical inactivity is defined as no leisure-time physical activity during past three months.

[e] Diabetes is defined as fasting glucose ≥126 mg/dl or physician diagnosed diabetes, or insulin use.

[f] Hypercholesterolemia is defined as total cholesterol ≥240 mg/dl, or physician diagnosed hypercholesterolemia.

[g] Hypertension is defined as resting BP ≥140/90 mm Hg, or physician diagnosed hypertension.

Table 3

Association of coffee consumption (cups/week) with all-cause and cardiovascular disease (CVD) mortality.

	Men			Women		
	Model 1[a]	Model 2[b]	Model 3[c]	Model 1[a]	Model 2[b]	Model 3[c]
All-cause mortality						
0	1	1	1	1	1	1
1–7	1.11 (0.96,1.28)	1.09 (0.94–1.27)	1.09 (0.94–1.27)	0.73 (0.51–1.06)	0.73 (0.50–1.05)	0.73 (0.50–1.06)
8–14	1.23 (1.07,1.41)	1.14 (0.99–1.31)	1.14 (0.99–1.31)	1.10 (0.80–1.52)	1.04 (0.75–1.44)	1.05 (0.76–1.46)
15–21	1.16 (1.01,1.33)	1.05 (0.91–1.20)	1.04 (0.91–1.19)	0.88 (0.61–1.26)	0.86 (0.59–1.24)	0.85 (0.58–1.22)
22–28	1.16 (0.97,1.38)	1.04 (0.87–1.24)	1.03 (0.86–1.23)	1.11 (0.68–1.81)	1.03 (0.63–1.69)	1.04 (0.63–1.71)
>28	1.41 (1.22,1.64)	1.22 (1.05–1.42)	1.21 (1.04–1.40)	1.35 (0.88–2.08)	1.22 (0.78–1.89)	1.21 (0.78–1.88)
P for linear trend	<0.0001	0.06	0.09	0.13	0.36	0.37
CVD mortality						
0	1	1	1	1	1	1
1–7	1.05 (0.81,1.35)	1.02 (0.79–1.32)	1.02 (0.79–1.32)	0.83 (0.39–1.79)	0.87 (0.40–1.89)	0.87 (0.40–1.90)
8–14	1.16 (0.92,1.47)	1.03 (0.81–1.31)	1.03 (0.81–1.30)	1.41 (0.73–2.72)	1.27 (0.64–2.49)	1.29 (0.66–2.54)
15–21	1.16 (0.92,1.47)	1.02 (0.80–1.29)	1.01 (0.80–1.28)	0.96 (0.45–2.09)	0.94 (0.43–2.05)	0.92 (0.42–2.01)
22–28	1.14 (0.85,1.54)	1.02 (0.75–1.38)	1.01 (0.75–1.37)	1.06 (0.35–3.24)	0.92 (0.30–2.84)	0.97 (0.31–2.99)
>28	1.36 (1.06,1.76)	1.16 (0.90–1.50)	1.15 (0.89–1.49)	0.89 (0.29–2.71)	0.72 (0.23–2.24)	0.73 (0.23–2.27)
P for linear trend	0.02	0.29	0.93	0.02	0.23	0.19

[a]Model 1: Adjusted for age and baseline examination year

[b]Model 2: Adjusted for age, baseline examination year, decaffeinated coffee, regular tea, decaffeinated or Herbal tea, physical inactivity, body mass index, smoking, alcohol drinking, diabetes, hypertension, hypercholesterolemia, family history of CVD.

[c]Model 3: All covariates in Model 2 and additional for fitness.