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Non-alcoholic beverage and caffeine consumption and mortality: the Leisure World Cohort Study

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Abstract

Objective— To examine the effects of non-alcoholic beverage and caffeine consumption on all-cause mortality in older adults.

Methods— The Leisure World Cohort Study is a prospective study of residents of a California retirement community. A baseline postal health survey included details on coffee, tea, milk, soft drink, and chocolate consumption. Participants were followed for 23 years (1981–2004). Risk ratios (RRs) of death were calculated using Cox regression for 8644 women and 4980 men (median age at entry, 74 years) and adjusted for age, gender and multiple potential confounders.

Results— Caffeine consumption exhibited a U-shaped mortality curve. Moderate caffeine consumers had a significantly reduced risk of death (multivariable-adjusted RR=0.94, 95% CI: 0.90, 0.99 for 100–199 mg/day and RR=0.90, 95% CI: 0.85, 0.94 for 200–399 mg/day compared with those consuming <50 mg/day). Individuals who drank more than 1 can/week of artificially sweetened (but not sugar-sweetened) soft drink (cola and other) had a 8% increased risk (95% CI: 1.01–1.16). Neither milk nor tea had a significant effect on mortality after multivariable adjustment.

Conclusions— Moderate caffeine consumption appeared beneficial in reducing risk of death. Attenuation in the observed associations between mortality and intake of tea and milk with adjustment for potential confounders suggests that such consumption identifies those with other mortality-associated lifestyle and health risks. The increased death risk with consumption of artificially sweetened, but not sugar-sweetened, soft drinks suggests an effect of the sweetener rather than other components of the soft drinks, although residual confounding remains a possibility.

Keywords

mortality; longevity; caffeine; coffee; tea; milk; carbonated beverages; risk factors

INTRODUCTION

Coffee, tea and soft drinks are the major sources of caffeine in the diets of US adults, with coffee being the primary and most potent source [Knight 2004, Frary 2005]. In cohort studies of younger (< 60 years old) adults, coffee has shown a reduced risk of death with moderate

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(1–4 cups/day) drinking [Woodward 1999, Kleemola 2000, Jazbec 2003]. However, studies in older adults and those including other sources of caffeine are limited.

Coffee and tea contain many different chemical compounds and no certainty exists as to which ones may be associated with disease risk. In addition to caffeine, coffee contains chlorogenic and caffeic acids that may have antioxidant properties [Kleemola 2000]. Likewise, tea contains antioxidant flavonoids [Mukamal 2002]. Antioxidants may reduce mortality by decreasing the incidence of cardiovascular disease [Steinberg 2002], cancer [van Poppel 1997] and dementia [Deschamps 2001].

In 1981 we undertook a prospective cohort study of nearly 14000 elderly men and women with the aim of studying factors, especially modifiable lifestyle practices, associated with longevity and successful aging. We report here the results of non-alcoholic beverage consumption intake on all-cause mortality.

METHODS

The Leisure World Cohort Study was established in the early 1980s when 13978 (8877 female and 5101 male) residents of a California retirement community (Leisure World Laguna Hills) completed a postal health survey. The population and the cohort are mostly Caucasian, well-educated, and upper-middle class. The baseline health survey asked demographic information (birth date, sex, height, weight); brief medical history (high blood pressure, angina, heart attack, stroke, diabetes, rheumatoid arthritis, fractures after age 40, cancer, gallbladder surgery, glaucoma, cataract surgery); medication use (hypertensive medication, digitalis, nonprescription pain medication); personal habits (cigarette smoking, exercise, alcohol); food and beverage intake (chocolate, coffee, tea, milk, soft drinks).

Estimation of Intake

Participants were asked “How many cups or glasses per DAY do you drink of the following – milk, decaffeinated coffee, coffee, black or green tea?” and “How many cans or glasses per WEEK do you drink of the following – cola beverages with sugar, other soft drinks with sugar, cola beverages artificially sweetened, other soft drinks artificially sweetened?” Response choices were none, less than 1, 1, 2–3, 4–5, ≥ 6 . Also asked was intake of “CHOCOLATE (milk chocolate, fudge, M & M’s, Tootsie Rolls, chocolate covered centers, chocolate topping, chocolate cake, chocolate pie, hot chocolate, chocolate milk)”. Response choices were rarely or never, a few times per year, about monthly, a few times a month, a few times per week, daily or almost daily.

We estimated the caffeine content (mg/standard unit) of each beverage category and chocolate as 115, 3, 50, 50, 6 for regular coffee, decaffeinated coffee, tea, cola soft drinks, chocolate, respectively [Brown 2001]. Daily cola soft drink intake was derived by dividing the weekly intake by 7. Total daily intake of caffeine was calculated by multiplying the servings/day of each caffeine source by its estimated caffeine content and then summing for all sources.

Determination of Outcome

Cohort members have been followed by periodic resurvey, review of local hospital discharge data, and determination of vital status by search of death indexes and ascertainment of death certificates. Participants were followed to death or December, 31, 2004, whichever came first. Forty-two cohort members were lost to follow-up. Previous reports present details of data collection [Paganini-Hill 1986, 1991, 1993b, 2001].

Statistical Analysis

Age- and sex-adjusted risk ratios (RRs) and 95% confidence intervals (CIs) for each beverage, chocolate and caffeine were obtained using Cox regression analysis [Cox 1972]. For these Cox models, chronological age was used as the fundamental time scale, age at death was the event of interest, and delayed entry was used with baseline age as the age of entry. To control for potential confounding factors previously found to be related to mortality in this cohort, we adjusted in the regression analyses for age at entry (continuous), sex, smoking (never, past, current), alcohol intake (0, ≤ 1 , 2–3, 4+ drinks/day), exercise (0, $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$ –1 $\frac{3}{4}$, 2+ hour/day), body mass index (<18.5 (underweight), 18.5–24.9 (normal), 25–29.9 (overweight), 30+ kg/m² (obese)), and seven separate histories (no, yes) of hypertension, angina, heart attack, stroke, diabetes, rheumatoid arthritis, and cancer. Statistical analyses were performed using SAS® version 9.1 (SAS Institute Inc., Cary, NC). No adjustment in the p-values was made for multiple comparisons.

Several additional analyses were performed. To account for the possibility that recent disease development may have altered beverage intakes as well as be related to mortality, we repeated the analyses excluding the first five years of follow-up. We also repeated the analyses excluding persons with major disease (hypertension, angina, heart attack, stroke, diabetes, rheumatoid arthritis, cancer) at baseline. Since caffeine consumption was related to age, we checked for a cohort effect by stratifying on age (<75 and 75+ years). In addition, we examined risk of death among tea drinkers in cohort members reporting cardiovascular disease at baseline.

This study was approved by the Institutional Review Boards of the University of Southern California and the University of California, Irvine.

RESULTS

After excluding 233 women and 121 men with missing information on the variables of interest or potential confounding variables, data on 8644 women and 4980 men were analyzed. At study entry, the participants ranged in age from 44 to 101 years (median, 74 years). By December 31, 2004, 11386 had died at ages 59 to 110 years (median, 87 years).

Table 1 presents selected characteristics of the participants by sex, coffee and tea consumption. About 90% of the cohort drank coffee (60% regular, 62% decaffeinated coffee) and 50% drank tea. Over two-thirds of the cohort drank less than one can of soft drink per week or not at all. Just over 15% ate chocolate a few times a week or more frequently. Caffeine consumption was significantly related to age and sex in our cohort. Median age decreased with increasing caffeine consumption: 75, 74, 74, 73, and 71 years for <50, 50–99, 100–199, 200–399, 400+ mg/day. A greater proportion of men than women consumed caffeine (62% vs 58%).

Tables 2 shows the age- and sex-adjusted and multivariable-adjusted RRs of mortality for beverages, chocolate and caffeine intake. In the age- and sex-adjusted models, individuals who drank a moderate amount (<1 to 3 cups/day) of regular coffee had 5–10% lower risk of death compared with nondrinkers of regular coffee. Similarly, those who drank 1 or less than 1 cup/day of decaffeinated coffee or of tea had a 6–9% reduced risk of death compared with nondrinkers. Those who drank 1 or less than 1 can/week of cola with sugar had an 8% lower risk of death compared with nondrinkers, while those who drank more than 1 can/week of artificially sweetened (cola or other soft drink) had a 11–24% higher risk. Infrequent chocolate consumers (a few times/month or less frequently) also had a decreased death risk. Total caffeine consumption exhibited a U-shaped mortality curve. Moderate caffeine consumers (100–399 mg/day) had significantly reduced risks of all-cause mortality compared with those consuming <50 mg/day. Those drinking some but less than 1 glass/day of milk also exhibited decreased mortality.

Adjustment for potential confounders had little effect on the observed RRs for caffeine consumption but reduced any significant effect on mortality observed for milk, black or green tea. Those who drank 4+ cups of decaffeinated coffee had significantly reduced mortality compared with nondrinkers. However, intake of regular coffee and decaffeinated coffee were inversely related ($r=-0.31$). Among nondrinkers of regular coffee, intake of decaffeinated coffee was unrelated to risk of death. Individuals who drank more than 1 can/week of artificially sweetened soft drink (cola or other) had a 8% increased risk (95% CI: 1.01–1.16).

Neither exclusion of the first five years of follow-up (including 1864 early deaths) nor exclusion of 8013 individuals with histories of hypertension, angina, heart attack, stroke, diabetes, rheumatoid arthritis, or cancer substantially changed the findings for caffeine consumption or artificially sweetened soft drinks (Table 3). The multivariable-adjusted risk estimates changed by less than 4% and remained statistically significant.

Analyses stratified by age showed RRs similar to those for the cohort as a whole. For 50–99, 100–199, 200–399 and 400 mg/day of caffeine compared with <50 mg/day, the multivariable-RRs (95% CI) were 1.03 (0.94–1.12), 0.94 (0.87–1.02), 0.92 (0.85–0.99), and 0.96 (0.86–1.06) for those less than 75 years old at baseline and 0.96 (0.88–1.04), 0.93 (0.87–1.00), 0.89 (0.82–0.95), and 0.96 (0.86–1.08) for those 75 or older.

Analyses limited to 6946 subjects with cardiovascular disease (hypertension, angina, heart attack, stroke, or diabetes) showed a small reduction in risk of death among tea drinkers. RRs (95% CI) were 0.94 (0.89–1.01), 0.92 (0.86–0.99), and 0.96 (0.88–1.04) for <1, 1 and 2+ cups/day compared with nondrinkers. After multivariable-adjustment, the RR for 1 cup/day was no longer significantly decreased (RR=0.93, 95% CI: 0.87–1.00)

DISCUSSION

Among adults aged 65 years and older, over 90% consume caffeine, with females consuming an average of 188 mg/day and males 217 mg/day [Frary 2005]. In our cohort, the average daily caffeine intake was 168 mg in females and 176 mg in males. We observed a clear U-shaped mortality curve for total caffeine consumption with moderate consumers (100–399 mg/day) having a significantly reduced risk and heavy drinkers (400+ mg/day) having the same risk compared with those consuming <50 mg/day.

Like studies in younger subjects in which coffee exhibited a beneficial trend on mortality with moderate drinking [Woodward 1999, Kleemola 2000, Jazbec 2003] but an increased risk with high (5+ cups/day) intake [Woodward 1999, Kleemola 2000], we observed a U-shaped mortality response with regular coffee consumption in our older cohort. In another cohort which included older individuals (40–79 years), Japanese men who consumed 2+ cups/day of coffee had a lower mortality risk (RR=0.43) compared with those who consumed less than ½ cup/day; for those who consumed ½-1 cup/day risk was 0.70 [Iwai 2002]. No statistically significant effect was seen in women. In contrast, other studies have found no association of coffee consumption and mortality [Dawber 1974, Yano 1977, Heyden 1978, Klatsky 1993, Jazbec 2003, Mukamal 2004] or a small increased risk [Lindsted 1992].

While some prospective cohort studies have found lower mortality among moderate and heavy tea drinkers than among those who drank no tea [Mukamal 2002, Nakachi 2003], others have seen no significant effect [Klatsky 1993, Woodward 1999, Iwai 2002, Stensvold 1992]. In a Japanese cohort of 8852 individuals followed for 13 years, increased consumption of green tea was associated with higher ages at death [Nakachi 2003]. Tea consumption may have the strongest benefit in persons with cardiovascular disease. In individuals without baseline disease in the Kaiser Permanente cohort, risk of mortality was reduced 2% for each cup of tea ($p=.04$) [Klatsky 1993]. In the male Health Professionals Follow-up Study, the inverse association

between flavonoid intake (main source being tea) and risk of death from coronary heart disease was limited to men who had previously had cardiovascular disease but was not statistically significant [Rimm 1996]. In a cohort of 1900 US patients hospitalized with acute myocardial infarction, tea consumption was associated with lower mortality (RR=0.69 for moderate (<14 cups/week) drinkers and RR=0.61 for heavy drinkers (14+ cups/week) compared with nondrinkers) [Mukamal 2002]. We found that the significantly decreased association between tea and mortality in our cohort was attenuated and no longer significant after multivariable adjustment. The perception of tea as a healthful beverage might cause some health conscious persons to choose tea or for some ill persons to switch from coffee to tea.

Few studies have reported on the relationship of soft drink intake and mortality. Caffeinated cola consumption was not associated with death among 1902 patients hospitalized for acute myocardial infarction and followed for 3.8 years [Mukamal 2004]. In the Nurses' Health Studies sugared and diet cola beverages were associated with increased risks of hypertension [Winkelmayr 2005] and diabetes [Schulze 2004]. While the consumption of caffeine from soft drinks is increasing [Frary 2005], in our elderly population this was a minor source of caffeine. We found mortality was increased in consumers of artificially sweetened soft drinks (colas and others) but not with sugar-sweetened drinks. Although artificially-sweetened soft drinks may be consumed by more diabetics and overweight individuals and thereby indirectly related to mortality, the association remained significant after adjusting for these and other confounding factors. The increased death risk with consumption of artificially sweetened, but not sugar-sweetened, soft drinks suggests an effect of the sweetener rather than other components of the soft drinks. However, residual confounding remains an alternative explanation.

Coffee, tea and soft drink intake habits might be identifying groups of people with different lifestyles. In our study, non-coffee drinking subjects had higher prevalences of several diseases than coffee drinkers (Table 1). Some may have stopped drinking coffee because of their underlying diseases. We did not ask about history of coffee drinking and, therefore, cannot answer this question. However, exclusion of the first five years of follow-up did not appreciably change the mortality and caffeine association. In two studies [Murray 1981, Jacobsen 1986] and in women in a third [Iwai 2002], the increased mortality among those with no or low coffee consumption was limited to the first few years of follow-up. A study of potential confounders contributing to the reported associations of caffeine with disease found that of 32 risk factors only sex and cigarette smoking were important confounders [Schreiber 1988b]. Others have found coffee and tea consumption related to each other and to smoking, alcohol, body mass index, exercise, high blood pressure, diabetes mellitus, heart attack, and soft drink consumption [Murray 1981, Jacobsen 1986, Lindsted 1992, Stensvold 1992, Klatsky 1993, Woodward 1999, Iwai 2002, Kleemola 2002, Mukamal 2002, Mukamal 2004]. In our study, neither adjustment for these and other confounders including age and sex nor stratification by age materially changed the lower risk seen for coffee or caffeine drinkers.

Measurement error may explain some of the discrepancies in studies of caffeine and mortality [Schreiber 1988a, Schreiber 1988b, Brown 2001]. Some studies are limited to coffee intake and do not include caffeine from tea and soft drinks. Others have not separated caffeinated from decaffeinated coffee. We, like many others, did not ask consumption on weekdays separately from weekends, the size of the containers, the methods of brewing coffee, or variations with the season or over time. As we asked subjects to report their consumption of black or green tea, we may have misclassified subjects who predominantly drank decaffeinated teas. Although we included soft drinks in our questionnaire, we did not ask about other beverage sources of caffeine including caffeinated fruit juices/drinks and bottled water or caffeine-containing medications, such as analgesics. The combined caffeine contribution from these other sources in the general population is small: <1% for the beverages in Americans [Knight 2004] and

1.7% and 3.2% for medications in Canadian males and females aged 60–75 years [Brown 2001].

The beneficial effect of coffee and caffeine on mortality may be due to the antioxidant properties of chlorogenic and caffeic acids in coffee [Kleemola 2000]. Antioxidants may prevent oxidation of low density lipoproteins which occur in atherosclerotic plaques in the cardiovascular system. Caffeine may also increase an individual's awareness of hypoglycemia and thus may be useful for the early identification of diabetes [Watson 1999]. This increased sensitivity to hyperglycemia may be mediated through the combined effects of reducing substrate delivery to the brain via constriction of the cerebral arteries and increasing brain glucose metabolism and augmenting catecholamine production. In addition, coffee consumption has been inversely related with blood pressure and indices of liver enzymes [Iwai 2002].

Our investigation is an observational study, not a randomized trial, with the possibility that unrecognized confounders or bias account for the observed results. In general populations, health-promoting habits often cluster resulting in two extreme groups. For example, individuals who drink coffee may differ from those who do not drink coffee in their smoking, exercise habits and medical history. They may also differ from nondrinkers in unmeasured ways that influence longevity. Although differences between drinkers and nondrinkers of coffee, tea, soft drinks, and milk in this study are not great and adjusting for other risk and potentially confounding factors did not change the observed RRs for caffeine, uncontrolled confounding cannot be ruled out.

Our data on beverage consumption and potential confounders were self-reported using a mailed questionnaire. Previous studies in our population and others support the reliability of recall medical history of major chronic disease. In the Leisure World community agreement between self-report and physician/hospital record was 96% for diabetes, 90% for hypertension, 80% for cancer [Paganini-Hill 1982,1993]. The self-reports of heart attack were less accurate; however, the false positives generally included other cardiovascular disease. Although we assigned one caffeine value to each category of beverage and chocolate, the true caffeine content varies within a category due to both manufacturer and preparation method. The subjects in our study were also healthier and better educated than the general population. In addition, changes over time in all potential risk factors may affect our outcomes.

CONCLUSIONS

Results in this large elderly cohort with long follow-up showing a U-shaped association of caffeine Intake (from coffee, tea, soft drinks, and chocolate) suggest a beneficial effect of moderate consumption. Individuals drinking 100–399 mg/day had the lowest risk. Those consuming more than 1 can/week of artificially-sweetened soft drinks had a small increased risk of death.

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Table 1
Characteristics of the Leisure World Cohort at baseline

	Sex		Regular coffee drinker	
	Male	Female	No	Yes
Number	4980	8644	5502	8122
	Mean \pm Standard deviation			
Age at baseline (years)	74.3 \pm 7.2	73.2 \pm 7.4	74.2 \pm 7.3	73.2 \pm 7.3
Age at last follow-up (years)	85.6 \pm 6.9	87.5 \pm 7.0	86.9 \pm 7.0	86.7 \pm 7.0
Follow-up years	11.2 \pm 6.8	14.3 \pm 6.8	12.7 \pm 6.9	13.5 \pm 6.9
Body mass index (kg/m ²)	24.2 \pm 2.9	23.1 \pm 3.5	23.3 \pm 3.3	23.6 \pm 3.3
Exercise (hrs/day)	1.1 \pm 1.3	0.9 \pm 1.1	1.0 \pm 1.1	1.0 \pm 1.2
Caffeine (mg/day)	177 \pm 172	168 \pm 165	42 \pm 58	259 \pm 162
	Per cent			
Alive	11	20	14	18
Female sex	0	100	66	62
History of disease				
High blood pressure	36	41	41	38
Angina	15	9.5	13	9.9
Heart attack	16	6.6	12	8.9
Stroke	7.1	3.7	5.7	4.4
Cancer	9.3	13	12	11
Diabetes	8.2	4.9	6.4	6.0
Rheumatoid arthritis	4.4	6.7	6.0	5.9
Cigarette use				
Never	33	55	52	44
Past	58	33	41	43
Current	9	12	7	13
Alcohol drinker	78	72	67	80
Regular coffee drinker	63	58	0	100
Decaffeinated coffee drinker	61	62	72	55
Black or green tea drinker	46	53	49	51
Soft drinks (\geq 1/week)	37	28	29	33
Chocolate (\geq few times/week)	17	16	16	17

Table 2
 Non-alcoholic Beverage and Chocolate Consumption and Risk Ratio (RR) of Death: the Leisure World Cohort Study, 1981–2004

	Number of subjects	Number of deaths	Model 1: RR (95% CI)	Model 2: RR (95% CI)
Regular coffee (cups/day)				
None	5502	4733	1.00 (reference)	1.00 (reference)
< 1	1476	1207	0.90 (0.84–0.96)	0.90 (0.85–0.96)
1	2473	2087	0.95 (0.90–1.00)	0.96 (0.91–1.01)
2–3	3301	2674	0.90 (0.86–0.94)	0.89 (0.85–0.94)
4+	872	685	1.01 (0.93–1.09)	0.94 (0.87–1.02)
Decaffeinated coffee (cups/day)				
None	5238	4382	1.00 (reference)	1.00 (reference)
< 1	1697	1387	0.91 (0.85–0.96)	0.94 (0.89–1.00)
1	3040	2583	0.94 (0.89–0.99)	0.95 (0.91–1.00)
2–3	3000	2505	0.97 (0.92–1.02)	0.97 (0.93–1.02)
4+	649	529	0.93 (0.85–1.02)	0.90 (0.82–0.99)
Black or green tea (cups/day)				
None	6777	5720	1.00 (reference)	1.00 (reference)
< 1	3023	2473	0.94 (0.90–0.99)	0.97 (0.93–1.02)
1	2273	1906	0.94 (0.89–0.99)	0.96 (0.91–1.01)
2+	1551	1287	0.98 (0.92–1.04)	0.98 (0.92–1.04)
Cola with sugar (cans/week)				
None	11552	9712	1.00 (reference)	1.00 (reference)
≤ 1	1599	1289	0.92 (0.86–0.97)	0.95 (0.89–1.01)
> 1	473	385	1.00 (0.90–1.11)	1.02 (0.92–1.13)
Cola artificially sweetened (cans/week)				
None	10968	9343	1.00 (reference)	1.00 (reference)
≤ 1	2067	1595	1.01 (0.95–1.06)	0.98 (0.93–1.03)
> 1	589	448	1.24 (1.12–1.36)	1.18 (1.07–1.30)
Other soft drinks with sugar (cans/week)				
None	11122	9302	1.00 (reference)	1.00 (reference)
≤ 1	2129	1780	0.97 (0.92–1.03)	1.00 (0.95–1.05)
> 1	373	304	1.00 (0.89–1.12)	1.03 (0.92–1.16)
Other soft drinks artificially sweetened (cans/week)				
None	10583	9014	1.00 (reference)	1.00 (reference)
≤ 1	2478	1942	0.98 (0.93–1.03)	0.96 (0.92–1.02)
> 1	563	430	1.11 (1.01–1.23)	1.07 (0.97–1.19)
Chocolate				
None	4034	3473	1.00 (reference)	1.00 (reference)
Few times/ year to few times/ month	7338	6033	0.91 (0.87–0.95)	0.94 (0.90–0.98)
Few times/ week to daily	2252	1880	0.97 (0.92–1.03)	0.98 (0.93–1.04)
Caffeine (mg/day)				
< 50	3756	3237	1.00 (reference)	1.00 (reference)
50–99	1943	1649	0.98 (0.92–1.04)	0.99 (0.93–1.05)
100–199	3328	2782	0.94 (0.89–0.99)	0.94 (0.89–0.99)
200–399	3390	2760	0.91 (0.86–0.96)	0.90 (0.85–0.94)
400+	1207	958	1.00 (0.93–1.08)	0.96 (0.89–1.03)
Milk (glasses/day)				
None	3320	2773	1.00 (reference)	1.00 (reference)
< 1	3445	2818	0.92 (0.87–0.97)	0.95 (0.90–1.00)
1	4342	3649	0.97 (0.92–1.02)	1.01 (0.96–1.06)
2+	2517	2146	1.03 (0.97–1.09)	1.04 (0.98–1.10)

Model 1: adjusted for age and sex.

Model 2: adjusted for age, sex, smoking, exercise, body mass index, alcohol intake and histories of hypertension, angina, heart attack, stroke, diabetes, rheumatoid arthritis, and cancer.

Table 3

Caffeine and Artificially-sweetened Soft Drink Consumption and Risk Ratio (RR) of Death: the Leisure World Cohort Study, 1981–2004

	Number of subjects	Number of deaths	Model 1: RR (95% CI)	Model 2: RR (95% CI)
<i>Excluding first five years of follow-up</i>				
Caffeine (mg/day)				
< 50	3195	2676	1.00 (reference)	1.00 (reference)
50–99	1649	1355	0.96 (0.90–1.03)	0.97 (0.90–1.03)
100–199	2852	2306	0.92 (0.87–0.98)	0.92 (0.87–0.97)
200–399	2996	2366	0.92 (0.87–0.97)	0.90 (0.85–0.95)
400+	1068	819	1.00 (0.92–1.08)	0.95 (0.88–1.03)
Artificially sweetened soft drinks (cans/weeks)				
None	8417	6999	1.00 (reference)	1.00 (reference)
≤ 1	2130	1618	0.98 (0.93–1.04)	0.96 (0.91–1.01)
> 1	1213	905	1.16 (1.08–1.24)	1.11 (1.03–1.19)
<i>Excluding those reporting major chronic disease at baseline</i>				
Caffeine (mg/day)				
< 50	1459	1165	1.00 (reference)	1.00 (reference)
50–99	767	611	1.00 (0.90–1.10)	1.01 (0.92–1.12)
100–199	1298	1000	0.92 (0.84–1.00)	0.92 (0.85–1.00)
200–399	1480	1097	0.91 (0.84–0.99)	0.88 (0.81–0.96)
400+	607	441	1.08 (0.97–1.21)	0.99 (0.89–1.11)
Artificially sweetened soft drinks (cans/weeks)				
None	4180	3304	1.00 (reference)	1.00 (reference)
≤ 1	937	663	0.99 (0.91–1.07)	0.97 (0.89–1.06)
> 1	494	347	1.12 (1.00–1.25)	1.12 (1.00–1.25)

Model 1: adjusted for age and sex.

Model 2: adjusted for age, sex, smoking, exercise, body mass index, alcohol intake and, in analyses excluding first five years of follow-up, histories of hypertension, angina, heart attack, stroke, diabetes, rheumatoid arthritis, and cancer.