The Relationship of Coffee Consumption with Mortality

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Background: Coffee consumption has been linked to various beneficial and detrimental health effects, but data on its relation with mortality are sparse.

Objective: To assess the association between coffee consumption and mortality from cardiovascular disease (CVD), cancer, and all causes during 18 years of follow-up in men and 24 years of follow-up in women.

Design: Sex-specific Cox proportional hazard models were used to investigate the association between coffee consumption and incidence of all-cause and disease-specific mortality in a prospective cohort study.

Setting: Health Professionals Follow-up Study and Nurses' Health Study.

Participants: 41 736 men and 86 214 women with no history of CVD or cancer at baseline.

Measurements: Coffee consumption was assessed first in 1986 for men and in 1980 for women and then every 2 to 4 years through 2004. Investigators documented 6888 deaths (2049 due to CVD and 2491 due to cancer) among men and 11 095 deaths (2368 due to CVD and 5011 due to cancer) among women.

Results: After adjustment for age, smoking, and other CVD and cancer risk factors, the relative risks for all-cause mortality in men across categories of coffee consumption (<1 cup per month, 1 cup per month to 4 cups per week, 5 to 7 cups per week, 2 to 3 cups per day, 4 to 5 cups per day, and ≥6 cups per day) were 1.0, 1.07 (95% CI, 0.99 to 1.16), 1.02 (CI, 0.95 to 1.11), 0.97 (CI, 0.89 to 1.05), 0.93 (CI, 0.81 to 1.07), and 0.80 (CI, 0.62 to 1.04), respectively (P for trend = 0.008). For women, the relative risks were 1.0, 0.98 (CI, 0.91 to 1.05), 0.93 (CI, 0.87 to 0.98), 0.82 (CI, 0.77 to 0.87), 0.74 (CI, 0.68 to 0.81), and 0.83 (CI, 0.73 to 0.95), respectively (P for trend < 0.001). This inverse association was mainly due to a moderately reduced risk for CVD mortality and was independent of caffeine intake. By contrast, coffee consumption was not statistically significantly associated with risk for cancer death after adjustment for potential confounders. Decaffeinated coffee consumption was associated with a small reduction in all-cause and CVD mortality.

Limitation: Coffee consumption was estimated from self-report; thus, some measurement error is inevitable.

Conclusion: Regular coffee consumption was not associated with an increased mortality rate in either men or women. The possibility of a modest benefit of coffee consumption on all-cause and CVD mortality needs to be further investigated.

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Several epidemiologic studies have examined coffee consumption and risk for coronary heart disease and other chronic diseases, but data on coffee consumption in relation to all-cause and disease-specific mortality are sparse. Some studies found that those who drank coffee were the healthiest cohort members (1–5), an inverse association that has been attributed to a possible confounding effect by morbidity. However, it has recently been suggested that the inverse association between coffee and all-cause mortality is attributable to the beneficial effect of coffee consumption on inflammation (6). The **Appendix Table** (available at www.annals.org) lists the previous studies that have examined coffee consumption and the risk for mortality by different causes.

In support of this hypothesis, we found in a previous study an inverse association between coffee consumption and several markers of inflammation and endothelial dysfunction (7). In addition, in the NHS (Nurses' Health Study) and HPFS (Health Professionals Follow-up Study), consumption of 6 or more cups of coffee per day was associated with a slightly lower risk for fatal coronary heart disease versus nonconsumers in both men and women (8). Moreover, epidemiologic studies have consistently found an association between higher coffee consumption and lower risk for type 2 diabetes (9). Finally, several studies have suggested that coffee might decrease the risk for some types of cancer, such as liver, colon, oral, pharyngeal, and esophageal (10–12).

The objective of this study was to assess the association of coffee consumption with all-cause, cardiovascular disease (CVD), and cancer mortality. The long follow-up and the use of repeated dietary measurements allowed us to assess long-term coffee consumption. In addition, information about incident diseases during the follow-up and updated measurements of main risk factors for CVD and cancer allowed us to control for potential confounders in detail.

See also:

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Summary for Patients I-40

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Appendix Table
Conversion of graphics into slides

METHODS

Study Population

The HPFS was established in 1986 and the NHS in 1976. Information (excluding diet) on the cohort members

has been updated every 2 years. Further details have been published elsewhere (13). We used 1980 as baseline for the NHS because this was the first year in which dietary information was collected in this cohort. After excluding participants with CVD or cancer at baseline or those with no information about coffee consumption at baseline (1183 persons in the HPFS and 879 in the NHS), we included 41 736 men and 86 214 women who were followed until 2004. The Harvard School of Public Health and Brigham and Women's Hospital Human Subjects Committee Review Board approved the study protocol.

Assessment of Coffee Consumption

Dietary questionnaires were sent to the HPFS participants in 1986, 1990, 1994, and 1998 and to the NHS participants in 1980, 1984, 1986, 1990, 1994, and 1998. In each questionnaire, participants were asked how often on average during the previous year they had consumed coffee and tea. The participants could choose from 9 responses. Decaffeinated coffee and different types of caffeinated soft drinks were first assessed in 1986 in the HPFS and in 1984 in the NHS. We also inquired at baseline about whether the participant's consumption for each beverage had greatly increased or decreased during the preceding 10 years. Using the U.S. Department of Agriculture food composition sources supplemented with other sources, we estimated that the caffeine content was 137 mg per cup of coffee, 47 mg per cup of tea, 46 mg per can or 12-ounce bottle of a soft drink, and 7 mg per 1-ounce serving of chocolate candy. We assessed the total intake of caffeine by summing the caffeine content for a unit of each food during the previous year multiplied by a weight proportional to the frequency of its consumption. In our validation study, we obtained high correlations between consumption of coffee and other caffeinated beverages estimated from the food frequency questionnaire and consumption estimated from repeated 1-week diet records (coffee, $r = 0.78$; tea, $r = 0.93$; and caffeinated soft drinks, $r = 0.85$) (14).

Ascertainment of Mortality

Deaths were reported by the next of kin or the postal authorities or were ascertained through the National Death Index. We estimated that follow-up for deaths was more than 98% complete (15). For all deaths, we sought death certificates and, when appropriate, requested permission from the next of kin to review medical records. The underlying cause of death was assigned according to the International Classification of Diseases, Eighth Revision (ICD-8). The primary end point in this analysis was death from any cause. We also conducted analyses according to the main causes of deaths in the cohorts, which were CVD (ICD-8 codes 390.0 through 458.9 and 795.0 to 795.9) and cancer (ICD-8 codes 140.0 through 207.9), and according to secondary causes of death, such as chronic liver disease and cirrhosis (ICD-8 code 571.0), chronic obstructive pulmonary disease (ICD-8 codes 492.0, 496.0, and 519.0), diabetes (ICD-8 codes 250.0, 250.1, and 250.9), neurodegenerative diseases (ICD-8 codes 331.0 and 332.0), and sudden death (ICD-8 code 798.0).

Context

Previous studies have examined the association between coffee consumption and a variety of specific diseases, such as type 2 diabetes, different types of cancer, and cardiovascular disease. However, the relationship between coffee consumption and all-cause mortality remains unclear.

Contribution

This study followed 2 large cohorts of men and women who provided data on coffee consumption, other behaviors, and health outcomes every 2 to 4 years over 2 decades. High coffee consumption was not related to increased mortality and may even be associated with lower total and cardiovascular mortality.

Caution

Misclassification of coffee consumption or confounding by other behavioral factors may account for these observations.

—The Editors

Assessment of Medical History, Anthropometric Data, and Lifestyle Factors

In the baseline questionnaires, we requested information about age; weight and height; smoking status; parental history with respect to myocardial infarction; menopausal status and use of hormone therapy in women; and history of hypertension, hypercholesterolemia, and type 2 diabetes mellitus. We updated this information, with the exception of height and parental history, in the biennial follow-up questionnaires. We assessed perceived health in 2000 by asking the participants to describe their health as excellent, very good, good, fair, or poor. We calculated body mass index, and we also assessed physical activity biennially. In the HPFS, participants were queried about the average time spent per week during the preceding year in specific activities (for example, walking outdoors, jogging, and bicycling) (16). The time spent in each activity in hours per week was multiplied by its typical energy expenditure, expressed in metabolic equivalent tasks and then summed over all activities to yield a metabolic equivalent task or hour score. In the NHS, physical activity was reported in hours per week of moderate (for example, brisk walking) and vigorous exercise (for example, strenuous sports and jogging) (17). Standard portion sizes for alcoholic drinks were specified as a can, bottle, or glass for beer; 4-oz glass for wine; and 1 drink or shot for liquor. Detailed information on the validity and reproducibility of the information from the questionnaires about self-reported weight, physical activity, and alcohol consumption has been reported elsewhere (18–20).

Table 1. **Baseline Characteristics, by Caffeinated Coffee Consumption Levels, among Participants in the Health Professionals Follow-up Study and the Nurses' Health Study***

Characteristic	Coffee Consumption among Men in HPFS (1986 baseline)						Coffee Consumption among Women in NHS (1980 baseline)					
	<1 cup/mo	1 cup/mo to 4 cups/wk	5 to 7 cups/wk	2 to 3 cups/d	4 to 5 cups/d	≥6 cups/d	<1 cup/mo	1 cup/mo to 4 cups/wk	5 to 7 cups/wk	2 to 3 cups/d	4 to 5 cups/d	≥6 cups/d
Participants, *n*	12 168	7353	7564	9968	3468	1215	19 276	5264	11 672	28 375	14 465	7162
Age, *y*	52	52	53	52	52	52	45	45	46	46	46	46
Current smoker, %	5	7	8	11	18	29	19	20	19	27	40	56
BMI, kg/m^2	24.7	24.8	24.9	25.1	25.3	25.2	24.7	24.5	24.4	24.2	24.1	24.2
Physical activity, *h/wk*	–	–	–	–	–	–	4.0	4.0	3.9	3.9	3.8	3.7
Physical activity in metabolic equivalent tasks, *h/wk*	27.5	25.8	27.2	24.7	24.1	20.0	–	–	–	–	–	–
Alcohol consumption, *g/d*	7.7	10.3	11.5	14.5	14.5	15.9	4.4	5.2	5.7	7.5	7.4	6.7
Parental history of MI, %	32	32	32	31	32	30	20	20	19	20	20	21
Postmenopausal hormone use, %	–	–	–	–	–	–	9	8	8	8	7	7
Multivitamin use, %	12	12	12	12	11	10	36	38	36	33	31	29
Vitamin E supplement use, %	10	11	10	9	8	7	14	15	14	12	11	11
Polyunsaturated fat intake, *% energy*	5.9	5.9	5.9	6.0	6.0	5.9	5.3	5.3	5.2	5.2	5.3	5.4
Saturated fat intake, *% energy*	10.6	10.8	11.0	11.3	11.9	12.4	15.3	15.4	15.4	15.6	15.9	16.3
Fish n-3 fatty acids intake, *% energy*	0.14	0.15	0.15	0.13	0.12	0.11	0.55	0.55	0.55	0.55	0.56	0.56
Trans fat intake, *% energy*	1.2	1.2	1.3	1.3	1.4	1.4	2.2	2.2	2.2	2.2	2.3	2.3
Glycemic load	131	126	124	119	115	111	91	88	88	84	81	79
Folate intake, *μg/d*	506	501	479	450	432	417	387	391	378	358	345	325
Caffeine intake, *mg/d*	51	91	194	418	692	885	117	134	218	418	751	881

* Values are means unless otherwise indicated. Data, except age, were directly standardized to the age distributions of the entire cohorts. BMI = body mass index; HPFS = Health Professionals Follow-up Study; MI = myocardial infarction; NHS = Nurses' Health Study.

Statistical Analysis

We classified participants according to levels of coffee consumption. We calculated person-years of exposure from the date of return of the baseline questionnaire to the date of death or 1 June 2004, whichever came first. To reduce within-participant variation and best represent long-term diet, we used the cumulative average of coffee consumption from all available dietary questionnaires up to the start of each 2-year follow-up interval (21); for example, in the HPFS, the average of the 1986 and 1990 intake was used for the follow-up between 1990 and 1994; and the average of the 1986, 1990, and 1994 intake was used for the follow-up between 1994 and 1998. When a food frequency questionnaire had a missing value for coffee, we used the value from the previous questionnaire.

We used sex-specific Cox proportional hazard models to investigate the association between coffee consumption and incidence of all-cause and disease-specific mortality. To control as finely as possible for confounding by age and calendar time, we stratified the analysis jointly by age in months at start of follow-up and calendar year of the current questionnaire cycle. We used hazard ratios to estimate relative risks in each category in comparison with participants in the lower category of coffee consumption. We adjusted multivariable models for smoking status, body mass index, physical activity, alcohol intake, use of hormone therapy for women, parental history of myocardial infarction, and dietary factors (total energy intake; use of multivitamin and vitamin E supplements; polyunsaturated, saturated, n-3, and trans fat intake; glycemic load; and folic acid intake) by using categorical variables. To test for linear trends across categories, we modeled coffee consumption as a continuous variable by using the median value of each level of coffee consumption. In addition, we calculated pooled relative risks for all-cause mortality in men and women combined across categories of coffee consumption by using a random-effects method. We also examined a possible nonlinear relation between coffee consumption and total and cardiovascular mortality nonparametrically with restricted cubic splines (22).

We conducted stratified analyses according to smoking status, alcohol consumption, and body mass index. We examined interactions between coffee and the categories of the stratification variables with mortality by using likelihood ratio tests, which compared the nested models with and without cross-product terms. We also analyzed the independent effect of total coffee consumption compared with

Table 2. **Relative Risks for All-Cause and Disease-Specific Mortality, by Levels of Caffeinated Coffee Consumption***

Mortality Cause	Coffee Consumption						
	<1 cup/mo	1 cup/mo to 4 cups/wk	5 to 7 cups/wk	2 to 3 cups/d	4 to 5 cups/d	≥6 cups/d	*P* Value for Trend
Men							
All causes							
Person-years	170 743	145 607	187 985	148 389	37 639	10 601	–
Deaths, *n*	1553	1570	2117	1289	286	73	–
Age-adjusted RR (95% CI)	1.0	0.99 (0.93–1.07)	0.97 (0.91–1.03)	0.98 (0.91–1.06)	1.11 (0.97–1.25)	1.28 (1.01–1.62)	0.14
Age- and smoking-adjusted RR (95% CI)	1.0	1.02 (0.95–1.10)	1.00 (0.94–1.07)	0.95 (0.89–1.03)	0.97 (0.85–1.10)	0.95 (0.75–1.21)	0.12
Multivariable-adjusted RR (95% CI)†	1.0	1.07 (0.99–1.16)	1.02 (0.95–1.11)	0.97 (0.89–1.05)	0.93 (0.81–1.07)	0.80 (0.62–1.04)	0.008
CVD							
Deaths, *n*	459	488	664	357	66	15	–
Age-adjusted RR (95% CI)	1.0	1.03 (0.91–1.17)	1.01 (0.90–1.14)	0.93 (0.81–1.06)	0.89 (0.69–1.15)	0.93 (0.56–1.56)	0.10
Age- and smoking-adjusted RR (95% CI)	1.0	1.06 (0.93–1.20)	1.04 (0.92–1.17)	0.90 (0.78–1.03)	0.79 (0.61–1.03)	0.72 (0.43–1.20)	0.003
Multivariable-adjusted RR (95% CI)†	1.0	1.05 (0.90–1.21)	1.09 (0.95–1.25)	0.95 (0.81–1.11)	0.85 (0.65–1.13)	0.56 (0.31–1.03)	0.03
Cancer							
Deaths, *n*	537	578	729	491	122	34	–
Age-adjusted RR (95% CI)	1.0	1.06 (0.95–1.20)	0.98 (0.88–1.09)	1.07 (0.95–1.21)	1.33 (1.10–1.63)	1.65 (1.17–2.34)	0.002
Age- and smoking-adjusted RR (95% CI)	1.0	1.08 (0.96–1.22)	0.99 (0.89–1.11)	1.03 (0.91–1.16)	1.17 (0.96–1.42)	1.27 (0.89–1.80)	0.27
Multivariable-adjusted RR (95% CI)†	1.0	1.14 (1.00–1.30)	1.01 (0.89–1.15)	1.01 (0.88–1.16)	1.15 (0.93–1.43)	1.14 (0.79–1.65)	0.82
Other causes							
Deaths, *n*	557	504	724	441	98	24	–
Age-adjusted RR (95% CI)	1.0	0.89 (0.79–1.01)	0.92 (0.83–1.03)	0.94 (0.83–1.06)	1.05 (0.85–1.31)	1.16 (0.77–1.75)	0.41
Age- and smoking-adjusted RR (95% CI)	1.0	0.93 (0.82–1.05)	0.98 (0.88–1.09)	0.92 (0.81–1.05)	0.92 (0.74–1.14)	0.84 (0.55–1.26)	0.30
Multivariable-adjusted RR (95% CI)†	1.0	1.01 (0.88–1.17)	0.98 (0.85–1.12)	0.93 (0.80–1.08)	0.76 (0.59–0.98)	0.65 (0.11–1.04)	0.006
Women							
All causes							
Person-years	319 326	247 470	609 374	563 666	172 583	60 180	–
Deaths, *n*	1665	1610	3946	2876	738	260	–
Age-adjusted RR (95% CI)	1.0	0.90 (0.84–0.96)	0.86 (0.81–0.91)	0.90 (0.84–0.95)	1.01 (0.93–1.10)	1.39 (1.22–1.59)	0.001
Age- and smoking-adjusted RR (95% CI)	1.0	0.89 (0.83–0.95)	0.82 (0.77–0.87)	0.77 (0.73–0.82)	0.76 (0.70–0.83)	0.92 (0.80–1.05)	<0.001
Multivariable-adjusted RR (95% CI)†	1.0	0.98 (0.91–1.05)	0.93 (0.87–0.98)	0.82 (0.77–0.87)	0.74 (0.68–0.81)	0.83 (0.73–0.95)	<0.001
CVD							
Deaths, *n*	362	362	868	563	151	62	–
Age-adjusted RR (95% CI)	1.0	0.91 (0.79–1.06)	0.86 (0.76–0.97)	0.80 (0.70–0.91)	0.95 (0.79–1.15)	1.53 (1.16–2.00)	0.78
Age- and smoking-adjusted RR (95% CI)	1.0	0.91 (0.79–1.05)	0.82 (0.72–0.92)	0.67 (0.58–0.76)	0.67 (0.55–0.81)	0.91 (0.69–1.19)	<0.001
Multivariable-adjusted RR (95% CI)†	1.0	1.06 (0.91–1.22)	0.99 (0.87–1.12)	0.75 (0.66–0.86)	0.66 (0.54–0.80)	0.81 (0.61–1.06)	<0.001

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Table 2—**Continued**

Mortality Cause	Coffee Consumption						
	<1 cup/mo	1 cup/mo to 4 cups/wk	5 to 7 cups/wk	2 to 3 cups/d	4 to 5 cups/d	≥6 cups/d	*P* Value for Trend
Cancer							
Deaths, *n*	679	691	1722	1409	378	132	–
Age-adjusted RR (95% CI)	1.0	0.98 (0.88–1.09)	0.96 (0.88–1.05)	1.08 (0.98–1.18)	1.22 (1.08–1.39)	1.60 (1.32–1.93)	<0.001
Age- and smoking-adjusted RR (95% CI)	1.0	0.96 (0.87–1.07)	0.91 (0.83–0.99)	0.94 (0.86–1.04)	0.97 (0.85–1.10)	1.15 (0.95–1.39)	0.45
Multivariable-adjusted RR (95% CI)†	1.0	1.01 (0.91–1.12)	0.95 (0.87–1.04)	0.94 (0.86–1.04)	0.91 (0.80–1.03)	1.05 (0.87–1.28)	0.26
Other causes							
Deaths, *n*	624	557	1356	904	209	66	–
Age-adjusted RR (95% CI)	1.0	0.80 (0.71–0.89)	0.75 (0.69–0.83)	0.75 (0.68–0.84)	0.81 (0.69–0.95)	1.06 (0.82–1.37)	0.12
Age- and smoking-adjusted RR (95% CI)	1.0	0.79 (0.70–0.88)	0.72 (0.65–0.79)	0.65 (0.59–0.72)	0.60 (0.51–0.70)	0.66 (0.51–0.85)	<0.001
Multivariable-adjusted RR (95% CI)†	1.0	0.89 (0.78–1.00)	0.86 (0.77–0.95)	0.70 (0.63–0.78)	0.59 (0.50–0.70)	0.60 (0.46–0.77)	<0.001

* CVD = cardiovascular disease; RR = relative risk.
† Adjusted for age (5-year categories); smoking status (never; past; and currently smoking 1 to 14, 15 to 24, and ≥25 cigarettes/day); body mass index (<23.0, 23.0 to 24.9, 25.0 to 27.9, 28.0 to 29.9, and ≥30.0 kg/m^2); physical activity (quintiles of metabolic equivalent tasks in h/wk for men, and <1.0, 1.0 to 1.9, 2.0 to 3.9, 4.0 to 6.9, and ≥7.0 h/wk for women); alcohol intake (never, 0.1 to 4.9, 5.0 to 9.9, 10.0 to 14.9, 15.0 to 29.9, and ≥30.0 g/d); parental history of myocardial infarction; menopausal status and use of hormone therapy for women (premenopausal, postmenopausal without hormone therapy, postmenopausal with past hormone therapy, and postmenopausal with current hormone therapy); multivitamin use; vitamin E supplement use; total caloric intake; quintiles of polyunsaturated, saturated, fish n-3, and trans fat intake; glycemic load; and folate intake.

caffeine intake on mortality through cross-classifications of both variables. Finally, we examined the association between decaffeinated coffee consumption and mortality.

In secondary analyses, we controlled the association between coffee consumption and mortality for hypertension, hypercholesterolemia, diabetes (these diseases could modify coffee consumption), and perceived health. In addition, we analyzed the association between continuous baseline coffee consumption and mortality, correcting the relative risk obtained by using the method of Rosner and colleagues (23). We performed all analyses by using SAS software, version 9.1 (SAS Institute, Cary, North Carolina).

This manuscript follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations (24). The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Role of the Funding Source

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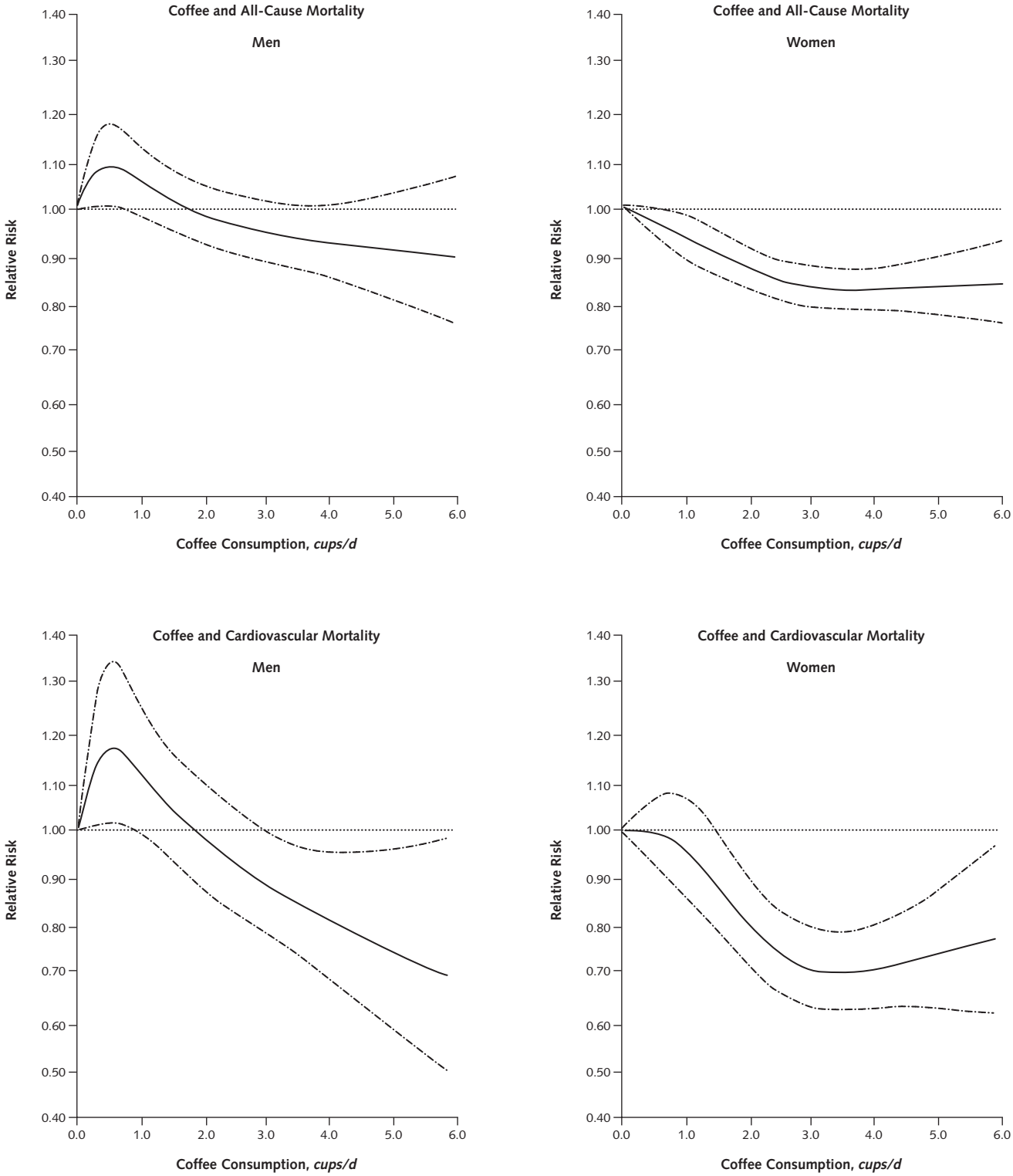
RESULTS

During 18 years of follow-up in the HPFS, we identified 6888 deaths (2049 from CVD and 2491 from cancer). During 24 years of follow-up in the NHS, we identified 11 095 deaths (2368 from CVD and 5011 from cancer). **Table 1** shows the baseline characteristics of the study population by levels of coffee consumption. Frequent coffee consumption was strongly associated with smoking. In addition, individuals who drank more coffee were more likely to drink alcohol and less likely to exercise and use multivitamin and vitamin E supplements.

In age-adjusted analyses, we observed that high coffee consumption was associated with a higher risk for all-cause mortality in men and women (**Table 2**). However, after adjustment for confounders (especially cigarette smoking), we observed an inverse association between coffee consumption and death from all causes in both men (P for trend = 0.008) and women (P for trend < 0.001). Among men, the relative risks for each category of coffee consumption did not reach statistical significance. However, among women, the relative risk for death from all causes in those consuming 5 to 7 cups of coffee per week was 7% lower than in nonconsumers; the decrease in all-cause mortality was 18% in those drinking 2 to 3 cups per day, 26% in those drinking 4 to 5 cups per day, and 17% in those drinking 6 or more cups per day. This reduction in death from all causes was partly due to the re-

Figure 1. **Nonlinear relationship between coffee consumption and total and cardiovascular mortality.**



Data were adjusted for the same variables as in Table 2.

duction in CVD deaths observed in women who consumed coffee (**Table 2** and **Figure 1**). The pooled relative risks for all-cause mortality in men and women combined across categories of coffee consumption were 1.0, 1.02 (95% CI, 0.96 to 1.07), 0.96 (CI, 0.92 to 1.01), 0.86 (CI, 0.82 to 0.91), 0.79 (CI, 0.73 to 0.85), and 0.83 (CI, 0.73 to 0.93).

Table 3. **Caffeinated Coffee Consumption and Relative Risks for All-Cause Mortality in Men and Women, by Stratification Variables***

Stratification Variable	Coffee Consumption					*P* Value for Trend	*P* Value for Interaction
	<1 cup/mo	1 cup/mo to 4 cups/wk	5 to 7 cups/wk	2 to 3 cups/d	≥4 cups/d		
Men							
Smoking status							
Never	1.0	1.01 (0.85–1.18)	0.95 (0.80–1.12)	0.79 (0.64–0.97)	0.63 (0.40–0.99)	0.003	–
Past	1.0	1.15 (0.99–1.33)	1.06 (0.93–1.22)	1.02 (0.88–1.18)	0.86 (0.68–1.10)	0.06	–
Current†	1.0	1.16 (0.78–1.71)	1.12 (0.79–1.60)	0.94 (0.66–1.33)	0.92 (0.62–1.37)	0.18	0.62
Alcohol							
Abstainer	1.0	0.99 (0.84–1.16)	1.04 (0.89–1.22)	1.06 (0.89–1.27)	0.76 (0.57–1.01)	0.34	–
Drinker	1.0	1.08 (0.98–1.19)	1.01 (0.92–1.10)	0.94 (0.85–1.04)	0.92 (0.80–1.07)	0.01	0.36
BMI							
<30 kg/m^2	1.0	1.05 (0.96–1.14)	1.02 (0.94–1.10)	0.95 (0.87–1.04)	0.86 (0.75–0.99)	0.005	–
≥30 kg/m^2	1.0	1.19 (0.92–1.55)	0.99 (0.78–1.27)	0.95 (0.73–1.23)	1.17 (0.82–1.66)	0.79	0.57
Women							
Smoking status							
Never	1.0	1.01 (0.91–1.12)	0.93 (0.85–1.03)	0.70 (0.63–0.79)	0.68 (0.55–0.82)	<0.001	–
Past	1.0	0.97 (0.87–1.08)	0.92 (0.84–1.01)	0.89 (0.81–0.98)	0.89 (0.78–1.01)	0.03	–
Current†	1.0	1.00 (0.81–1.24)	1.00 (0.84–1.19)	0.82 (0.69–0.96)	0.72 (0.60–0.86)	<0.001	0.36
Alcohol							
Abstainer	1.0	1.05 (0.93–1.18)	0.94 (0.85–1.04)	0.83 (0.74–0.93)	0.76 (0.65–0.88)	<0.001	–
Drinker	1.0	0.94 (0.86–1.02)	0.91 (0.85–0.98)	0.80 (0.74–0.87)	0.75 (0.68–0.83)	<0.001	0.47
BMI							
<30 kg/m^2	1.0	0.93 (0.86–1.01)	0.88 (0.82–0.93)	0.81 (0.76–0.87)	0.78 (0.71–0.85)	<0.001	–
≥30 kg/m^2	1.0	1.02 (0.86–1.19)	0.93 (0.81–1.07)	0.78 (0.66–0.90)	0.77 (0.61–0.96)	<0.001	0.37

* Models adjusted for the same covariates as in Table 2, except for the stratification variable. Values are relative risks and 95% CIs. BMI = body mass index.
† Additional adjustment for cigarettes per day.

Coffee consumption was not significantly associated with risk for cancer death after adjustment for potential confounders in either cohort (**Table 2**). In addition, regular coffee consumption was associated with lower risk for death from "other causes," mainly in women. In particular, we observed inverse associations between coffee consumption and death from chronic liver disease and cirrhosis (135 cases, multivariable relative risks across categories of coffee consumption were 1.0, 0.91, 0.81, 0.41, and 0.35; P for trend < 0.001) and diabetes death (152 cases, relative risks across categories of coffee consumption were 1.0, 0.80, 0.65, 0.49, and 0.57; P for trend $= 0.02$).

The inverse association between coffee consumption and death from all causes remained significant in nonsmokers, alcohol drinkers, and nonobese men (**Table 3**). We did not find substantial differences in the association between coffee consumption and all-cause mortality among women across all categories of smoking status, alcohol consumption, and body mass index.

We attempted to separate the effects of coffee consumption (including decaffeinated coffee) from caffeine intake on all-cause mortality (**Table 4**). In the cross-classification analyses, we observed no clear pattern among men, but among women, the inverse association between coffee and all-cause mortality in those who drank 2 or more cups of coffee per day was independent of the amount of caffeine ingested. Because these analyses suggested that components in coffee other than caffeine could explain the association observed, we next examined whether decaffeinated coffee was associated with mortality. We found that higher decaffeinated coffee consumption was also associated with a slightly lower risk for all-cause and CVD mortality, especially in women (**Table 5**).

We conducted various sensitivity analyses to evaluate the robustness of our results. First, we performed analyses excluding individuals in the lowest category of coffee consumption (<1 cup per month) to test whether specific characteristics of this group confounded the association, and we obtained similar results. We also conducted analyses excluding participants who reduced their coffee consumption in the 10 years preceding the study, excluding the first 4 years of follow-up (when participants could have undiagnosed diseases), by using only the most recent coffee consumption level (to assess short-term effects) and adjusting the models for high blood pressure, hypercholesterolemia, or type 2 diabetes; perceived health; and pack-years of smoking. The estimates remained similar to those in the main analyses. Finally, after correction for measurement error, the relative risk for the association between baseline coffee consumption (as a continuous variable) and risk for all-cause mortality in men was 1.01 (CI, 0.99 to 1.04), which was the same as the uncorrected value of 1.01 (CI, 1.00 to 1.03). In women, the validation data set necessary to conduct the correction was unavailable.

DISCUSSION

In these 2 large cohort studies, we did not find a detrimental effect of coffee consumption on mortality. On the contrary, our results showed a modest inverse association between coffee and all-cause mortality in both men and women. This association was mainly explained by a reduction in CVD deaths. Our data also suggest that this association was due to components in coffee other than caffeine.

Previous studies examined the effect of coffee on all-cause mortality in different populations. Legrady and colleagues (25) followed a cohort of 2000 men during 19 years and found that those who drank 6 or more cups of coffee per day had 1.7 times (CI, 1.27 to 2.30) higher risk for death from coronary heart disease compared with those consuming l cup per day or less. In addition, a Norwegian study (26) found an increased risk for death from coronary heart disease after a follow-up of 6 years, but later found that the association was weakened with longer follow-up (27). In contrast, other studies observed that coffee consumption was inversely associated with mortality (1–5). For example, Kleemola and colleagues (2), after 10-year follow-up of a large middle-age population, found that men who consumed 7 or more cups of coffee per day had a relative risk for all-cause mortality of 1.01 (CI, 0.84 to 1.22), but women who consumed that amount of coffee had a significantly decreased risk for all-cause mortality (0.62 [CI, 0.44 to 0.84]). These researchers attributed their findings to possible subclinical diseases that led to a reduction in coffee consumption. However, Andersen and colleagues (6), after analyzing a cohort of postmenopausal women followed during 15 years, concluded that consumption of coffee was inversely associated with all-cause mortality (relative risk, 0.87 [CI, 0.76 to 1.00], for those drinking 6 or more cups per day in comparison with nondrinkers) and CVD mortality (relative risk, 0.87 [CI, 0.69 to 1.09]), and attributed the results to the effect of coffee on reducing chronic inflammation.

Our findings are consistent with the possible beneficial effects of coffee on inflammation, endothelial function, and risk for type 2 diabetes. We previously reported an inverse association of caffeinated coffee consumption with surface leukocyte adhesion molecules (E-selectin) and with

Table 4. **Relative Risks for All-Cause Mortality, by Combinations of Coffee Consumption Level (Including Decaffeinated Coffee) and Caffeine Intake***

Characteristic, by Total Coffee Consumption Level	Quintile of Caffeine Intake		
	Quintile 1 to Quintile 2	Quintile 3	Quintile 4 to Quintile 5
Men			
<1 cup/mo to 4 cups/wk			
Median caffeine intake, *mg/d*	33	164	338
Person-years	175 021	28 477	11 715
Deaths, *n*	1602	237	99
Multivariable-adjusted RR (95% CI)	1.0	0.97 (0.83–1.12)	0.91 (0.73–1.13)
5 to 7 cups/wk			
Median caffeine intake, *mg/d*	71	179	307
Person-years	71 136	85 037	54 586
Deaths, *n*	923	959	596
Multivariable-adjusted RR (95% CI)	1.00 (0.91–1.10)	0.96 (0.88–1.06)	1.00 (0.90–1.12)
≥2 cups/day			
Median caffeine intake, mg/d	46	192	451
Person-years	33 971	26 837	214 186
Deaths, *n*	351	316	1805
Multivariable-adjusted RR (95% CI)	0.92 (0.80–1.05)	1.09 (0.94–1.25)	0.91 (0.84–0.98)
Women†			
<1 cup/mo to 4 cups/wk			
Median caffeine intake, *mg/d*	98	302	511
Person-years	313 837	62 955	143 116
Deaths, *n*	2022	415	962
Multivariable-adjusted RR (95% CI)	1.0	0.90 (0.81–1.00)	0.79 (0.73–0.86)
5 to 7 cups/wk			
Median caffeine intake, *mg/d*	161	292	397
Person-years	234 597	126 844	41 575
Deaths, *n*	1570	859	314
Multivariable-adjusted RR (95% CI)	0.98 (0.92–1.05)	1.01 (0.93–1.10)	1.04 (0.92–1.17)
≥2 cups/day			
Median caffeine intake, mg/d	175	314	506
Person-years	83 305	126 042	446 278
Deaths, *n*	456	662	2481
Multivariable-adjusted RR (95% CI)	0.84 (0.76–0.93)	0.80 (0.73–0.88)	0.84 (0.78–0.89)

* Models adjusted for the same covariates as in Table 2. RR = relative risk.
† Follow-up since 1984. The person-years and cases are different for women from previous tables because of the different years of follow-up.

Table 5. **Decaffeinated Coffee Consumption and Relative Risks for All-Cause and Disease-Specific Mortality in Men and Women***

Mortality Cause	Decaffeinated Coffee Consumption					*P* Value for Trend
	<1 cup/mo	1 cup/mo to 4 cups/wk	5 to 7 cups/wk	2 to 3 cups/d	≥4 cups/d	
Men						
All causes						
Person-years	294 554	213 006	131 207	50 843	11 355	–
Deaths, *n*	2783	2059	1479	481	86	–
Age-adjusted RR (95% CI)	1.0	0.85 (0.81–0.90)	0.85 (0.80–0.90)	0.92 (0.84–1.01)	1.00 (0.81–1.24)	0.20
Multivariable-adjusted RR (95% CI)	1.0	0.96 (0.90–1.03)	0.93 (0.86–1.01)	0.91 (0.82–1.01)	0.81 (0.64–1.03)	0.02
CVD						
Deaths, *n*	777	668	439	146	19	–
Age-adjusted RR (95% CI)	1.0	0.98 (0.89–1.09)	0.88 (0.78–0.99)	0.99 (0.84–1.19)	0.81 (0.51–1.28)	0.23
Multivariable-adjusted RR (95% CI)	1.0	1.10 (0.97–1.24)	0.97 (0.85–1.12)	0.95 (0.78–1.17)	0.83 (0.52–1.31)	0.16
Cancer						
Deaths, *n*	979	746	540	180	46	–
Age-adjusted RR (95% CI)	1.0	0.89 (0.81–0.98)	0.90 (0.81–1.00)	0.97 (0.83–1.14)	1.49 (1.11–2.00)	0.20
Multivariable-adjusted RR (95% CI)	1.0	0.96 (0.86–1.07)	0.95 (0.84–1.07)	0.95 (0.80–1.13)	1.20 (0.87–1.66)	0.81
Women†						
All causes						
Person-years	760 095	387 614	314 893	99 778	16 169	–
Deaths, *n*	5023	2252	1921	486	59	–
Age-adjusted RR (95% CI)	1.0	0.73 (0.69–0.76)	0.72 (0.68–0.75)	0.74 (0.67–0.81)	0.76 (0.59–0.99)	<0.001
Multivariable-adjusted RR (95% CI)	1.0	0.92 (0.87–0.97)	0.89 (0.84–0.94)	0.85 (0.77–0.94)	0.78 (0.61–1.00)	<0.001
CVD						
Deaths, *n*	1096	441	401	114	10	–
Age-adjusted RR (95% CI)	1.0	0.66 (0.59–0.73)	0.68 (0.61–0.76)	0.78 (0.64–0.94)	0.58 (0.31–1.08)	<0.001
Multivariable-adjusted RR (95% CI)	1.0	0.84 (0.75–0.95)	0.85 (0.75–0.95)	0.89 (0.73–1.09)	0.55 (0.30–1.04)	0.04
Cancer						
Deaths, *n*	2126	1021	852	233	30	–
Age-adjusted RR (95% CI)	1.0	0.81 (0.75–0.87)	0.78 (0.72–0.84)	0.83 (0.72–0.95)	0.87 (0.60–1.24)	<0.001
Multivariable-adjusted RR (95% CI)	1.0	0.97 (0.90–1.05)	0.93 (0.85–1.01)	0.94 (0.82–1.08)	0.86 (0.60–1.23)	0.14

* Models adjusted for the same covariates as in Table 2, plus caffeinated coffee consumption. CVD = cardiovascular disease; RR = relative risk.
† Follow-up since 1984. The person-years and cases are different for women from previous tables because of the different years of follow-up.

C-reactive protein (a monocyte activator in the endothelial wall) in women with diabetes and an inverse association of decaffeinated coffee consumption with C-reactive protein in healthy women (7). In addition, Yukawa and colleagues (28) found that regular coffee consumption reduced susceptibility to low-density lipoprotein oxidation. Coffee may favorably affect endothelial atherosclerotic plaques through this pathway because oxidized low-density lipoprotein is present in atherosclerotic lesions (29). Also, the phenolic compounds of coffee (chlorogenic acid, ferulic acid, and *p*-coumaric acid) have a strong antioxidant capacity (30). Chlorogenic acid might also improve glucose tolerance (31). In addition, coffee contains many other substances, including magnesium, trigonelline, and quinides, that have been associated with improved insulin sensitivity (32). All these mechanisms can counterbalance some of the potential harmful effects of caffeine, such as the acute stimulation of the release of epinephrine, a potent inhibitor of insulin activity, and the acute increase in blood pressure and homocysteine levels (33–35). Thus, these mechanisms also support our finding of an inverse association between coffee and all-cause mortality independent of caffeine intake. Finally, in our analysis, coffee consumption in women was associated with a slight reduction in mortality due to chronic liver disease and cirrhosis. Previous studies have shown that coffee consumption may have a protective effect on hepatic cancer (36), and various components of coffee have been associated with this favorable effect, including caffeine; coffee oils, such as kahweol and cafestol; and phenolic components (37, 38).

We have extended the previous analyses by using larger cohorts of men and women and assessing the cumulative coffee consumption instead of consumption only at the start of follow-up. The cumulative consumption reflects long-term exposure to coffee and may therefore be more appropriate for the study of all-cause and disease-specific mortality. In addition, we have been able to better control for potential confounders because information about incident diseases and risk factors has been updated every 2 years. We believe that our results were not confounded by morbidity because we performed several additional analyses to address this problem. In particular, we controlled our models for hypertension, hypercholesterolemia, and type 2 diabetes. In addition, we excluded the first 4 years of follow-up to avoid subclinical morbidity, and we adjusted the association for perceived health. On the other hand, some measurement error in the assessment of coffee consumption is inevitable because we estimated

the consumption from self-reports; however, the dietary questionnaire has been shown to reflect long-term intake (39), the validation data showed that coffee was among the most accurately reported items in the food frequency questionnaire (14), and the relative risk for the association between continuous baseline coffee consumption and all-cause mortality corrected for measurement error was very similar to the uncorrected one. In addition, the inverse association between coffee consumption and mortality was stronger in women. Possible reasons for this include a shorter follow-up in men, different distribution of causes of death for men and women, and different age ranges. However, formal tests for heterogeneity in the associations between the 2 cohorts were not statistically significant. Finally, because our study was conducted among health care professionals, extrapolation of results to the general population should be made with caution.

In conclusion, the data from 2 large cohort studies of men and women suggest that regular coffee consumption is not associated with increased deaths in either men or women. The possibility of a modest benefit of coffee consumption on all-cause and CVD mortality needs to be further investigated.

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Appendix Table. **Cohort Studies Addressing the Association between Coffee Consumption and All-Cause and Disease-Specific Mortality***

Author, Year (Reference)	Sex	Age Range, *y*	Participants, *n*	Exposure	Outcome	Cases of Mortality, *n*	Mean Follow-up, *y*	Adjustment for Confounding Factors	Multivariable-Adjusted Result	Comments
Iwai et al., 2002 (1)	Men and women	40–79	2855	Coffee at baseline	All-cause mortality	361	9.9	Age, physical activity, education, history of chronic diseases, smoking, alcohol use (only in men)	For consumption of ≥2 cups/d, the RR was 0.43 (95% CI, 0.30–0.63) for men and 0.76 (CI, 0.45–1.27) for women.	Inverse association between coffee and all-cause mortality in men
Kleemola et al., 2000 (2)	Men and women	30–59	20 179	Coffee at baseline	All-cause and CHD mortality	All-cause, 1645; CHD, 975	10	Age, smoking, cholesterol level, blood pressure level, history of MI	Men: For consumption of ≥7 cups/d, the RR for all-cause mortality was 1.01 (CI, 0.84–1.22) and the RR for CHD mortality was 1.22 (CI, 0.90–1.65); women: For consumption of ≥7 cups/d, the RR for all-cause mortality was 0.62 (CI, 0.44–0.87) and the RR for CHD mortality was 0.57 (CI, 0.28–1.16).	Inverse association between coffee and all-cause mortality in women; no association between coffee and CHD mortality in men or women
Woodward and Tunstall-Pedoe, 1999 (3)	Men and women	40–59	11 000	Coffee at baseline	All-cause and CHD mortality	All-cause, 573; CHD, 357	7.7	Age, housing tenure, activity at work, activity in leisure, smoking, BMI, Bortner score, cotinine, SBP, fibrinogen, total cholesterol level , HDL cholesterol level, TG, alcohol use, vitamin C, tea consumption	Men: For consumption of ≥5 cups/d, the RR for all-cause mortality was 0.77 and the RR for CHD mortality was 0.58; women: For consumption of ≥5 cups/d, the RR for all-cause mortality was 0.79 and the RR for CHD mortality was 1.18.	Inverse association between coffee and all-cause mortality in men and women; inverse association between coffee and CHD mortality in men
Rosengren and Wilhelmsen, 1991 (4)	Men	51–59	6765	Coffee at baseline	All-cause, CHD, and cancer mortality	All-cause, 478; CHD, 169; cancer, NA	7.1	Age, SBP, BMI, diabetes, alcohol abuse, family history of MI, mental stress, physical activity, occupational class	For consumption of ≥9 cups/d, the RR for all-cause mortality was 0.6 (CI, 0.3–0.9), the RR for CHD mortality was 1.4 (CI, 0.8–2.4), and the RR for cancer mortality was 0.9 (CI, 0.4–2.1).	Inverse association between coffee and all-cause mortality; no association between coffee and CHD and cancer mortality
Murray et al., 1981 (5)	Men	≥35	16 911	Coffee at baseline	CHD and non-CHD mortality	CHD, 721; non-CHD, 985	11.5	Age, smoking, urban or rural residence	For consumption of ≥7 cups/d, the RR for all-cause mortality was 0.86, and the RR for CHD mortality was 0.91.	Inverse association between coffee and all-cause and CHD mortality
Andersen et al., 2006 (6)	Women	55–69	41 836	Coffee at baseline	All-cause, CHD, cancer, and inflammatory disease mortality	All-cause, 4265; CHD, 1411; cancer, 1733; inflammatory disease, 713	15	Age; smoking; alcohol consumption; BMI; waist–hip ratio; education; physical activity; use of estrogen; MV; energy intake; consumption of whole and refined grain, red meat, fish and seafood, total fruit and vegetables	For consumption of 4–5 cups/d, the RR for all-cause mortality was 0.81 (CI, 0.72–0.91), the RR for CVD mortality was 0.81 (CI, 0.66–0.99), the RR for cancer mortality was 0.84 (CI, 0.70–1.02), and the RR for inflammatory mortality was 0.67 (CI, 0.50–0.90).	Parabolic association between coffee and all-cause and CVD mortality; no association with cancer mortality; inverse association with inflammatory mortality
Lopez-Garcia et al., 2006 (8)	Men and women	30–55	128 493	Cumulative exposure	CHD mortality	1417	Men, 14; women, 20	Age, smoking, BMI, physical activity, alcohol consumption, parental history of MI, menopausal status, use of hormone therapy, aspirin, MV, vitamin E, hypertension, hypercholesterolemia, diabetes mellitus	Men: For consumption of ≥6 cups/d, the RR for CHD mortality was 0.60 (CI, 0.26–1.36); women: For consumption of ≥6 cups/d, the RR for CHD mortality was 0.61 (CI, 0.37–1.02).	Weak inverse association between coffee and CHD mortality
LeGrady et al., 1987 (25)	Men	40–56	1910	Coffee at 1 year baseline	All-cause, CHD, non-CHD mortality	All-cause, 452; CHD, 220; non-CHD, 232	19	Age, DBP, cholesterol level, smoking	For consumption of ≥6 cups/d, the RR for all-cause mortality was 1.33 (CI, 1.07–1.65), the RR for CHD mortality was 1.71 (CI, 1.27–2.30), and the RR for non-CHD mortality was 1.02 (CI, 0.73–1.41).	Direct association between coffee and all-cause and CHD mortality
Tverdal et al., 1990 (26)	Men and women	35–54	38 564	Coffee at baseline	CHD mortality	174	6.4	Age, cholesterol level, HDL cholesterol level, SBP, smoking	Men: For consumption of ≥9 cups/d, the RR for CHD mortality was 2.2 (CI, 1.1–4.5); women: For consumption of ≥9 cups/d, the RR for CHD mortality was 5.1 (CI, 0.4–60.3).	Direct association between coffee and CHD mortality
Stensvold et al., 1996 (27)	Men and women	35–54	38 564	Coffee at baseline	CHD mortality	476	12	Age, cholesterol level, HDL cholesterol level, SBP, smoking	For consumption of ≥9 cups/d, the RR for CHD mortality was 1.3.	No association between coffee and CHD mortality when Tverdal et al. study (26) was continued for 6 more years
Greenberg et al., 2007 (40)	Men and women	32–86	6594	Caffeinated beverages at baseline	CVD, CHD, and cerebrovascular disease mortality	CVD, 426; CHD, 347; cerebrovascular disease, 79	8.8	Age, smoking, BMI, sex, race, physical activity, alcohol use, income, education, American-style diet	In participants age ≥65 years who consumed ≥4 cups/d, the RR for CVD mortality was 0.53 (CI, 0.38–0.75), the RR for CHD mortality was 0.47 (CI, 0.32–0.69), and the RR for cerebrovascular death was 0.88 (CI, 0.42–1.83).	Inverse association between caffeinated beverages and CVD and CHD mortality among elderly but not younger participants
Hart and Smith, 1997 (41)	Men	35–64	5766	Coffee at baseline	CHD mortality	625	17	Age, DBP, cholesterol level, smoking, social class, education, BMI, angina	For consumption of ≥4.5 cups/d, the RR for CHD mortality was 1.49 (CI, 0.89–2.47).	No association between coffee and CHD mortality
Jazbec et al., 2003 (42)	Men and women	35–59	3364	Coffee at baseline	All-cause and CVD mortality	All-cause, 950; CVD, 435	27	Age, region, smoking, DBP, feeling of well-being, history of stomach ulcer	Men: For consumption of 1–2 cups/d, the RR for all-cause mortality was 0.78 (CI, 0.61–0.98) and the RR for CVD mortality was 0.82 (CI, 0.58–1.16); women: For consumption of 1–2 cups/d, the RR for all-cause mortality was 0.63 (CI, 0.46–0.86) and the RR for CVD mortality was 0.67 (CI, 0.43–1.05).	Inverse association between coffee and all-cause mortality
Lindsted et al., 1992 (43)	Men	≥30	9484	Coffee at baseline	All-cause and CVD mortality	NA	25	Age, BMI, heart disease, hypertension, race, exercise, sleep, marital status, education, smoking, diet history	For consumption of ≥1–2 cups/d, the RR for all-cause mortality was 1.15 (CI, 1.05–1.26) and the RR for CVD mortality was 1.09 (CI, 0.82–1.46).	Weak direct association between coffee and all-cause and CVD mortality
Jacobsen et al., 1986 (44)	Men and women	NA	16 555	Coffee at baseline	All-cause and cancer mortality	All-cause, 4032; cancer, 886	11.5	Age, residence, smoking	For consumption of ≥7 cups/d, the RR for all-cause mortality was 0.95 ($P = 0.15$) and the RR for cancer mortality was 1.14 ($P = 0.49$).	No association between coffee and all-cause and cancer mortality
Happonen et al., 2004 (45)	Men	42–60	1971	Coffee at baseline	CHD mortality	269	14	Age, smoking, ischemia, diabetes, income, serum insulin level, DBP, HDL cholesterol level, LDL cholesterol level, maximum oxygen uptake, waist–hip ratio	Heavy drinkers (≥814 mL/d) had an RR for CHD mortality of 1.43 (CI, 1.06–1.94).	Direct association between coffee and CHD mortality
Paganini-Hill et al., 2007 (46)	Men and women	44–101	13 624	Coffee at baseline	All-cause mortality	11 386	23	Age, sex, smoking, physical activity BMI, alcohol use, hypertension, angina, heart attack, stroke, diabetes, rheumatoid arthritis, cancer	For consumption of 2–3 cups/d, the RR for all-cause mortality was 0.89 (CI, 0.85–0.94).	Parabolic association between coffee and all-cause mortality
Dawber et al., 1974 (47)	Men and women	30–62	5209	Coffee at baseline	All-cause and CHD mortality	All-cause, 321; CHD, NA	12	Age, smoking	Men: For consumption of ≥6 cups/d, the RR for all-cause mortality was 1.01 and the RR for CHD mortality was 0.92.	Direct association between coffee and all-cause mortality in men; no association between coffee and CHD mortality in men or women
Vandenbroucke et al., 1986 (48)	Men and women	40–65	3091	Coffee at baseline	All-cause mortality	NA	25	Age, smoking, alcohol use, BMI, living parents, cholesterol level, SBP	Men: For consumption of ≥5 cups/d, the RR for all-cause mortality was 1.42 (CI, 0.94–2.15); women: For consumption of ≥5 cups/d, the RR for all-cause mortality was 0.83 (CI, 0.52–1.30).	Direct association between coffee and all-cause mortality in men
Kurozawa et al., 2005 (49)	Men and women	40–79	110 688	Coffee at baseline	Hepatocellular carcinoma mortality	258	11	Age, sex, education, history of diabetes and liver diseases, smoking, alcohol use	For consumption of ≥1 cups/d, the RR for cancer mortality was 0.50 (CI, 0.31–0.79).	Inverse association between coffee and hepatocellular carcinoma mortality

*Obtained from a MEDLINE search through February 2008 using the keywords *coffee* and *caffeine* in combination with *mortality* and *death*. BMI = body mass index; CHD = coronary heart disease; CVD = cardiovascular disease; DBP = diastolic blood pressure; HDL = high-density lipoprotein; LDL = low-density lipoprotein; MI = myocardial infarction; MV = multivitamin use; NA = not available; SBP = systolic blood pressure; TG = triglyceride.