

# Coffee consumption and the incidence of antihypertensive drug treatment in Finnish men and women<sup>1-3</sup>

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## ABSTRACT

**Background:** Only 2 prospective studies have previously investigated the association between coffee consumption and incident hypertension, and the findings are equivocal.

**Objective:** The objective was to determine the relation between coffee consumption and the incidence of antihypertensive drug treatment.

**Design:** We prospectively followed 24 710 Finnish subjects aged 25–64 y without a history of antihypertensive drug treatment, coronary heart disease, or stroke at baseline. Daily coffee consumption was assessed by questionnaires.

**Results:** During a mean follow-up period of 13.2 y, 2505 participants started antihypertensive drug treatment. The multivariate-adjusted (age, sex, study year, education, leisure-time physical activity, smoking, body mass index, high total cholesterol, history of diabetes, and alcohol, tea, fruit, vegetable, sausage, and bread consumption) hazard ratios for antihypertensive drug treatment associated with the amount of coffee consumed daily (0–1, 2–3, 4–5, 6–7, or ≥8 cups) were 1.00, 1.29 (95% CI: 1.09, 1.54), 1.26 (95% CI: 1.06, 1.49), 1.24 (95% CI: 1.04, 1.48), and 1.14 (95% CI: 0.94, 1.37) (*P* for trend = 0.024), respectively. This trend became marginally significant after additional adjustment for baseline systolic blood pressure (*P* for trend = 0.077).

**Conclusions:** The results indicate that coffee drinking seems to increase the risk of antihypertensive drug treatment, and this risk was higher in subjects with low-to-moderate coffee intakes; however, there was no significantly increased trend in drinkers of ≈1 cup (100 mL)/d or ≥8 cups/d. *Am J Clin Nutr* 2007;86:457–64.

**KEY WORDS** Coffee drinking, antihypertensive therapy, blood pressure, hypertension, epidemiology

## INTRODUCTION

Coffee is one of the most popularly consumed beverages in the world (1). During the past decade or so, research has attempted to clarify the health benefits or harms related to coffee drinking. The association between coffee consumption and blood pressure has been studied for ≥70 y (2). Two recent meta-analyses have shown a relation between coffee and caffeine intakes and an increase in blood pressure (3, 4). However, the data on the relation of coffee drinking and the risk of hypertension from prospective studies are still scarce (5, 6). According to international statistics, the Finns have the highest per capita coffee consumption in the world, at 11.4 kg/y (7). On the other hand, compared with many other populations, men and women in Finland have a

high prevalence of hypertension (8). Therefore, research into the potential health effects of coffee in this population is of particular interest. The aim of this study was to examine the association of coffee consumption with the incidence of antihypertensive drug treatment in a large prospective cohort of Finnish men and women.

## SUBJECTS AND METHODS

### Study sample

Four independent cross-sectional population surveys were carried out in the Kuopio and North Karelia provinces in eastern Finland and in the Turku-Loimaa region in southwestern Finland in 1982, 1987, 1992, and 1997 (9). The survey areas were expanded to the Helsinki capital area in 1992 and the northern province of Oulu in 1997. The sample has been stratified by area, sex, and 10-y age group according to the World Health Organization (WHO) MONItoring trends and determinants of CARDiovascular disease (MONICA) protocol (10). All 4 surveys included the age group 25–64 y. The subjects who participated in more than one survey were included only in the first survey cohort. The total sample size of the 4 surveys was 28 782. The participation rate varied by year from 74% to 88% (9). The final sample comprised 11 711 men and 12 999 women after the exclusion of the participants who received drug treatment for hypertension according to the National Social Insurance Institution's register for the reimbursement of drug costs (*n* = 2889) before the baseline survey or who reported on the questionnaire that they used antihypertensive drugs (*n* = 446) at the baseline survey, the participants with a history of coronary heart disease (*n* = 461) or stroke (*n* = 203) at baseline, and the participants

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with incomplete data on any variables required for this analysis ( $n = 73$ ). The participants gave informed consent (verbal consent in 1982–1992 and signed consent in 1997). The surveys were conducted according to the ethical rules of the National Public Health Institute, and the investigations were carried out in accordance with the Declaration of Helsinki.

### Measurements

A self-administered questionnaire was sent to the participants to be completed at home. The questionnaire included questions on medical history, socioeconomic factors, physical activity, smoking habits, and dietary habits. Education level, measured as the total number of school years, was divided into birth cohort specific tertiles. A detailed description of the questions about leisure-time physical activity was presented elsewhere (11–20). Self-reported leisure-time physical activity was classified into 3 categories: low, moderate, or high. On the basis of the responses, the participants were classified as never smokers, exsmokers, and current-smokers. Current smokers were categorized into those participants who smoked  $<20$  or  $\geq 20$  cigarettes/d. Subjects who reported having diabetes on the questionnaire or who had had a hospital discharge with a diagnosis of diabetes, or the approval for free-of-charge medication for diabetes from the National Social Insurance Institution's Register before the baseline survey were classified as having the history of diabetes at baseline.

The subjects' diet and food choices were assessed by 2 types questions (21). First, the participants were asked, "How many slices of bread and cups of coffee or tea do you have daily (1 cup of coffee = 1 dL; 1 cup of tea = 2 dL)?" (22–24). Second, the participants were asked about their frequency of consumption of vegetables and fruit over the past week ( $<1$  time/wk, 1–2 times/wk, 3–5 times/wk, and 6–7 times/wk) and of sausages over the past 12 mo ( $<1$  time/mo, 1–2 times/mo, 1 time/wk, 2 times/wk, almost daily, and  $>1$  time/d). Coffee consumption was categorized into 5 categories: 0–1 cup/d, 2–3 cups/d, 4–5 cups/d, 6–7 cups/d, and  $\geq 8$  cups/d. Tea consumption was categorized into 3 categories: none, 1–2 cups/d, and  $\geq 3$  cups/d because only a few participants drank tea. Ethanol consumption was categorized into 4 groups: none, 1–34, 35–209, and  $\geq 210$  g/wk in men and none, 1–34, 35–139, and  $\geq 140$  g/wk in women.

At the study site, specially trained nurses measured height, weight, and blood pressure using the standardized protocol of the WHO MONICA project (10). Height was measured without shoes and weight was measured with light clothing. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Blood pressure was measured from the right arm of the participant who was seated for 5 min before the measurement was taken with a standard sphygmomanometer. After blood pressure was measured, a venous blood specimen was drawn. Serum total cholesterol concentration was measured from fresh serum samples by using an enzymatic method (CHOD-PAP; Boehringer Mannheim, Mannheim, Germany). All samples were analyzed in the same laboratory at the National Public Health Institute. High cholesterol was defined as a serum total cholesterol concentration  $\geq 6.5$  mmol/L.

### Diagnosis of antihypertensive drug treatment

Data on the first initiation of antihypertensive drug treatment, which was the endpoint of the study, were received from the

records of the Social Insurance Institution's nationwide register on persons entitled to special reimbursement for antihypertensive drugs. In principle, every resident in Finland has been entitled to such a reimbursement since 1964. To obtain approval for reimbursement, the diagnosis of hypertension must be made by the patient's own physician on the basis of the WHO criteria for hypertension, and additionally, blood pressure levels must meet stricter criteria of the Social Insurance Institution for the reimbursement of antihypertensive drugs, which vary according to the presence of other cardiovascular disease risk factors or target organ involvement. The physician's statement documenting the details of the diagnosis of hypertension is then reviewed by the expert physician of the Social Insurance Institution. Computerized record linkage was done using the national personal identification number assigned for every person living permanently in Finland. All patients receiving special reimbursement for medication for hypertension are entered into a register maintained by the Social Insurance Institution. Follow-up of each cohort member continued until the date of the approval of special reimbursement for antihypertensive drugs, death, or until the end of year 2002. This method has been used in several studies in Finland (12, 16, 25); however, it leaves some hypertensive patients unrecognized because of the stricter criteria for antihypertensive drug treatment reimbursement of the Social Insurance Institution. Nevertheless, hypertension is a progressive disease, and it can be assumed that sooner or later also the patients considered hypertensive by the WHO criteria, but not by the Social Insurance Institution criteria will meet the latter criteria. Thus, we probably did not miss many hypertensive cases, but their diagnosis of hypertension was delayed when the Social Insurance Institution criteria were applied.

### Statistical analyses

Differences in risk factors based on different levels of coffee consumption were tested by using analysis of variance after adjustment for age, sex, and study year and after additional adjustment for BMI, leisure-time physical activity, smoking, high cholesterol, history of diabetes, and alcohol, tea, fruit, vegetables, sausage, and bread consumption in the analysis of baseline blood pressure levels and the prevalence of hypertension without drug treatment at baseline. The association between coffee consumption at baseline and the risk of incident hypertension (antihypertensive drug treatment) was analyzed by using Cox proportional hazards models. Different levels of coffee consumption were included in the models as dummy variables, and the significance of the trend over different categories of coffee consumption was tested in the same models by giving an ordinal numeric value for each dummy variable. The proportional hazards assumption in the Cox model was assessed with graphical methods and with models including time-by-covariate interactions (26). In general, all proportionality assumptions were appropriate. All analyses were adjusted for age, sex, study year, education, leisure-time physical activity, smoking, BMI, high cholesterol, history of diabetes, systolic blood pressure, and alcohol, tea, fruit, vegetables, sausage, and bread consumption at baseline. This reference category (0–1 cup/d) was chosen rather than the noncoffee drinking category for 3 reasons: 1) the risk of antihypertensive drug treatment incidence did not differ between coffee drinkers (1 cup/d) and coffee abstainers (hazard ratio: 0.84), 2) the risk of antihypertensive drug treatment incidence increased significantly in coffee drinkers (2 cups/d) compared with coffee



**TABLE 1**  
Baseline characteristics of 24 710 Finnish subjects by coffee consumption

Characteristics	Coffee consumption (cups/d) <sup>1</sup>					P <sup>2</sup>
	0–1	2–3	4–5	6–7	≥8	
Total participants (n)	2681	5336	7430	5084	4179	
Male (%)	45.1	40.6	42.6	49.3	63.6	
Age (y)	40.6 ± 0.2 <sup>3</sup>	43.6 ± 0.2	44.4 ± 0.1	44.7 ± 0.2	42.5 ± 0.2	< 0.001
BMI (kg/m <sup>2</sup> )	25.4 ± 0.08	25.6 ± 0.05	25.8 ± 0.05	26.0 ± 0.06	26.3 ± 0.06	< 0.001
Education (y)	11.5 ± 0.06	11.3 ± 0.05	10.8 ± 0.04	10.2 ± 0.05	9.9 ± 0.05	< 0.001
Bread consumption (slices/d)	5.4 ± 0.05	5.1 ± 0.04	5.4 ± 0.03	5.8 ± 0.04	6.2 ± 0.05	< 0.001
Low leisure-time physical activity (%)	27.6	25.4	26.5	30.7	34.6	< 0.001
Daily consumption of vegetables (%)	28.7	29.0	25.7	18.8	15.3	< 0.001
Daily consumption of fruit (%)	36.0	34.6	32.3	27.1	20.5	< 0.001
Almost-daily consumption of sausage (%)	17.7	18.8	18.9	19.6	18.5	0.001
Tea drinker (%)	71.2	56.0	35.5	21.7	12.9	< 0.001
Alcohol drinker (%)	49.6	58.5	54.6	50.6	52.6	< 0.001
Current smoker (%)	16.8	20.1	26.8	33.6	52.4	< 0.001
History of diabetes (%)	1.3	1.1	1.3	1.5	1.7	0.22
Total cholesterol ≥6.5 mmol/L (%)	17.5	22.0	26.0	28.6	28.3	< 0.001

<sup>1</sup> 1 cup = 100 mL.

<sup>2</sup> ANOVA with each row variable as the dependent variable and the coffee categories as the independent variable; all data, except age, were adjusted for age, sex, and study year. P values from ANOVA.

<sup>3</sup>  $\bar{x} \pm SE$  (all such values).

abstainers (hazard ratio: 1.22), and 3) the reference group contained larger numbers of participants, which made the statistical comparisons more stable. To assess whether the effect differed between the sexes, first-level interactions between coffee consumption and sex were analyzed. Because no statistically significant interactions were found ( $\chi^2 = 3.76$ , 4 df,  $P > 0.25$ ), men and women were combined in the analyses adjusted for sex. Statistical significance was set at  $P < 0.05$ . All statistical analyses were performed with SPSS for WINDOWS 14.0 (SPSS Inc, Chicago, IL).

## RESULTS

During a mean follow-up period of 13.2 y, 2505 people started antihypertensive treatment. In general, older persons were more likely to drink coffee than were younger ones (Table 1). After adjustment for age, sex, and study year, coffee consumers had a higher BMI, had less leisure-time physical activity, had higher serum total cholesterol, and were more often current smokers. Coffee drinking had an inverse association with education, tea drinking, and the daily consumption of fruit and vegetables.

At baseline, persons who drank more than one cup of coffee daily had a slightly, but significantly, higher diastolic and systolic blood pressure—adjusted for age, sex, and study year—than did those who drank only 0–1 cups (Table 2). Further adjustment for BMI and other confounding factors did not affect the results.

Age-, sex-, and study year–adjusted hazard ratios for antihypertensive drug treatment associated with the amount of coffee consumed daily (0–1, 2–3, 4–5, 6–7, and ≥8 cups) were 1.00, 1.35 (95% CI: 1.14, 1.60), 1.36 (95% CI: 1.16, 1.60), 1.35 (95% CI: 1.14, 1.59), and 1.27 (95% CI: 1.07, 1.51) ( $P$  for trend = 0.003), respectively (Table 3). After further adjustment for education, leisure-time physical activity, smoking, BMI, high total cholesterol, history of diabetes, and alcohol, tea, fruit, vegetable, sausage, and bread consumption, this association remained significant ( $P$  for trend = 0.024) but became marginally significant

after additional adjustment for baseline systolic blood pressure ( $P$  for trend = 0.077). Age, alcohol consumption, BMI, serum total cholesterol, history of diabetes, and baseline systolic blood pressure had a positive association, and leisure-time physical activity and current smoking had an inverse association with the risk of antihypertensive drug treatment (data not shown).

Because the survey measurement of blood pressure was not diagnostic and some participants may have received a diagnosis of hypertension soon after the survey, we carried out additional analyses in which subjects who used antihypertensive drug treatment during the first year of follow-up were excluded ( $n = 126$ ) (Table 3). After adjustment for all potential confounders (age, sex, study year, education, leisure-time physical activity, smoking, BMI, high total cholesterol, history of diabetes, and alcohol, tea, fruit, vegetable, sausage, and bread consumption), hazard ratios for antihypertensive drug treatment associated with the amount of coffee consumed daily (0–1, 2–3, 4–5, 6–7, or ≥8 cups) were 1.00, 1.27 (95% CI: 1.07, 1.52), 1.25 (95% CI: 1.05, 1.49), 1.24 (95% CI: 1.03, 1.48), and 1.15 (95% CI: 0.95, 1.39) ( $P$  for trend = 0.057), respectively.

After exclusion of the participants who were aware of having hypertension at baseline ( $n = 3850$ ), multivariable-adjusted hazard ratios for antihypertensive drug treatment associated with the amount of coffee consumed daily (0–1, 2–3, 4–5, 6–7, or ≥8 cups) were 1.00, 1.29 (95% CI: 1.02, 1.64), 1.23 (95% CI: 0.98, 1.55), 1.19 (95% CI: 0.93, 1.51), and 1.18 (95% CI: 0.92, 1.51), respectively.

In additional analyses, we found similar associations between coffee consumption and the risk of antihypertensive drug treatment after excluding those who had high serum cholesterol or who reported diabetes at baseline ( $n = 6450$ ). After adjustment for all potential confounders, hazard ratios for antihypertensive drug treatment associated with the amount of coffee consumed daily (0–1, 2–3, 4–5, 6–7, or ≥8 cups) were 1.00, 1.36 (95% CI: 1.11, 1.68), 1.32 (95% CI: 1.08, 1.62), 1.25 (95% CI: 1.01, 1.55), and 1.13 (95% CI: 0.90, 1.42) ( $P$  for trend = 0.016), respectively.

TABLE 2

Baseline blood pressure levels in 24 710 Finnish subjects by coffee consumption

Characteristics	Coffee consumption (cups/d) <sup>1</sup>					P <sup>2</sup>
	0–1 (n = 2681)	2–3 (n = 5336)	4–5 (n = 7430)	6–7 (n = 5084)	≥8 (n = 4179)	
Systolic blood pressure (mm Hg) <sup>3</sup>	133.9 ± 0.3 <sup>4</sup>	135.9 ± 0.2	135.7 ± 0.2	135.9 ± 0.2	135.4 ± 0.3	< 0.001
Systolic blood pressure (mm Hg) <sup>5</sup>	134.3 ± 0.3	136.1 ± 0.2	135.8 ± 0.2	135.7 ± 0.2	135.0 ± 0.3	< 0.001
Systolic blood pressure (mm Hg) <sup>6</sup>	134.7 ± 0.3	136.3 ± 0.2	135.8 ± 0.2	135.6 ± 0.2	134.8 ± 0.3	< 0.001
Diastolic blood pressure (mm Hg) <sup>3</sup>	81.0 ± 0.2	82.4 ± 0.1	82.2 ± 0.1	81.7 ± 0.1	81.2 ± 0.2	< 0.001
Diastolic blood pressure (mm Hg) <sup>5</sup>	81.4 ± 0.2	82.6 ± 0.1	82.2 ± 0.1	81.6 ± 0.1	80.9 ± 0.2	< 0.001
Diastolic blood pressure (mm Hg) <sup>6</sup>	81.4 ± 0.2	82.5 ± 0.1	82.2 ± 0.1	81.6 ± 0.1	81.0 ± 0.2	< 0.001
Prevalence of hypertension (%) <sup>3,7</sup>	39.4	43.5	43.0	42.9	42.5	0.004
Prevalence of hypertension (%) <sup>5,7</sup>	40.5	44.1	43.1	42.5	41.4	0.004
Prevalence of hypertension (%) <sup>6,7</sup>	41.4	44.4	43.1	42.1	40.8	0.002

<sup>1</sup> 1 cup = 100 mL.<sup>2</sup> ANOVA with each row variable as the dependent variable and the coffee categories as the independent variable.<sup>3</sup> Adjusted for age, sex, and study year.<sup>4</sup>  $\bar{x} \pm SE$  (all such values).<sup>5</sup> Adjusted for age, sex, study year, and BMI.

<sup>6</sup> Adjusted for age, sex, study year, education, leisure-time physical activity (low, moderate, or high), cigarette smoking (never, past, or current smoking of 1–19 or ≥20 cigarettes/d), alcohol consumption (none or 1–34, 35–209, or ≥210 g/wk in men; none or 1–34, 35–139, or ≥140 g/wk in women), tea consumption (none or 1–2 or ≥3 cups/d), frequency of vegetable consumption (<1, 1–2, 3–5, or 6–7 times/wk), frequency of fruit consumption (<1, 1–2, 3–5, or 6–7 times/wk), frequency of sausage consumption (<1 time/mo, 1–2 times/mo, 1 time/wk, 2 times/wk, almost daily, or >1 time/d), bread consumption (slices/d), BMI, history of diabetes, and total cholesterol ≥6.5 mmol/L.

<sup>7</sup> Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or both at baseline.

Because the participants might have changed their coffee drinking habits during the follow-up, we also carried out additional sensitivity analyses restricting the follow-up periods to the first 10 y. The trend between coffee consumption and the risk of antihypertensive drug treatment remained almost the same when the follow-up time of the study cohorts was restricted to the first 10 y (Table 4).

The relative risks of antihypertensive drug treatment by the coffee consumption among the different subpopulations are shown in Table 5. No significant interactions between coffee consumption and smoking ( $P > 0.9$ ), coffee consumption and BMI ( $P > 0.1$ ), and coffee consumption and alcohol drinking were found on the risk of incident antihypertensive drug treatment ( $P > 0.1$ ).

## DISCUSSION

The results of our large population-based prospective study showed that coffee drinking was associated with a modestly increased risk of antihypertensive drug treatment. The increased risk showed no dose-response relation, but a threshold was observed between those who drank >1 cup/d and those who drank only 0–1 cups/d.

The evidence concerning the effects of coffee intake on blood pressure or hypertension is inconsistent. A recent meta-analysis based on 16 clinical trials with ≥7 d of intervention has shown that pooling of coffee and caffeine trials (a median intake of 725 mL/d in coffee trials and a median intake of 410 mg/d in caffeine trials) was associated with an increase of 2.04 mm Hg for systolic blood pressure and of 0.73 mm Hg for diastolic blood pressure (4). When coffee trials and caffeine trials were analyzed separately, elevations in blood pressure appeared to be larger for caffeine (systolic: 4.16 mm Hg; diastolic: 2.41 mm Hg) than for coffee (systolic: 1.22 mm Hg; diastolic: 0.49 mm Hg). The Johns Hopkins Precursors Study examined the long-term effect of

coffee drinking on blood pressure and the risk of hypertension among 1017 white male former medical students (5). It has been suggested that coffee drinking is associated with small increases in blood pressure, but such weak associations of coffee consumption on the risk of hypertension disappear after adjustment for risk factors for hypertension (5). In another analysis that included 2 large cohort studies of women, the Nurses' Health Studies I and II, a modest inverse U-shaped association between caffeine intake and the development of hypertension was found in both cohorts (6). When they assessed the frequency of the use of different caffeine-containing beverages in relation to the risk of incident hypertension, a marginally significantly inverse association between caffeinated or decaffeinated coffee intake and the risk of hypertension was found. Evidence of a relation between coffee consumption and blood pressure comes mostly from cross-sectional studies; however, the results are inconsistent. Some of these studies found that habitual consumption of coffee was associated with slightly elevated blood pressure (27, 28), whereas others indicated no association (29, 30) or a small inverse association (31–33).

The mechanism of the association between moderate or high coffee intake and the risk of hypertension is incompletely understood. Experimental studies have shown that caffeine can acutely raise plasma concentrations of several stress hormones, such as epinephrine, norepinephrine, and cortisol (4, 34, 35), and all of these factors may lead to an increase in blood pressure (4, 35, 36). However, such experiments have been limited to short periods of observation. Longer-term clinical trials of coffee consumption and blood pressure or hypertension are warranted to examine the mechanisms underlying the relation between coffee consumption and hypertension. In the present study, coffee consumption was positively associated with age, alcohol consumption, BMI, and current cigarette smoking and inversely associated with education level, leisure-time physical activity, and tea,

TABLE 3

Hazard ratios (HRs) for the development of hypertension in 24 710 Finnish subjects by coffee consumption

	Coffee consumption (cups/d) <sup>1</sup>					P for trend <sup>2</sup>
	0–1	2–3	4–5	6–7	≥8	
All subjects						
Participants (n)	2681	5336	7430	5084	4179	
Cases of hypertension (n)	183	514	785	585	438	
Person-years (y)	33 023	65 944	97 508	71 094	57 963	
Incident rate/1000 person-years	5.54	7.79	8.05	8.22	7.56	
Age-, sex-, and study year-adjusted HR (95% CI)	1.00	1.35 (1.14, 1.60)	1.36 (1.16, 1.60)	1.35 (1.14, 1.59)	1.27 (1.07, 1.51)	0.003
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.35 (1.14, 1.60)	1.35 (1.14, 1.60)	1.32 (1.11, 1.57)	1.27 (1.05, 1.53)	0.008
Multivariate HR (95% CI) <sup>4</sup>	1.00	1.29 (1.09, 1.54)	1.26 (1.06, 1.49)	1.24 (1.04, 1.48)	1.14 (0.94, 1.37)	0.024
Multivariate HR (95% CI) <sup>5</sup>	1.00	1.27 (1.07, 1.51)	1.20 (1.01, 1.42)	1.21 (1.01, 1.44)	1.13 (0.94, 1.36)	0.077
Exclusion of subjects who were diagnosed with incident hypertension during the first year of follow-up (n = 126)						
Participants (n)	2674	5306	7388	5055	4161	
Cases of hypertension (n)	176	484	743	556	420	
Person-years (y)	33 020	65 927	97 488	71 077	57 953	
Incident rate/1000 person-years	5.33	7.34	7.62	7.82	7.25	
Age-, sex-, and study year-adjusted HR (95% CI)	1.00	1.33 (1.12, 1.58)	1.34 (1.13, 1.58)	1.32 (1.12, 1.57)	1.26 (1.06, 1.50)	0.011
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.33 (1.11, 1.59)	1.34 (1.13, 1.59)	1.32 (1.10, 1.58)	1.28 (1.06, 1.55)	0.017
Multivariate HR (95% CI) <sup>4</sup>	1.00	1.27 (1.07, 1.52)	1.25 (1.05, 1.49)	1.24 (1.03, 1.48)	1.15 (0.95, 1.39)	0.057
Multivariate HR (95% CI) <sup>5</sup>	1.00	1.26 (1.05, 1.50)	1.20 (1.01, 1.42)	1.21 (1.01, 1.45)	1.15 (0.95, 1.39)	0.13

<sup>1</sup> 1 cup = 100 mL.<sup>2</sup> Wald test.<sup>3</sup> Cox proportional hazard model adjusted for age, sex, study year, education, leisure-time physical activity (low, moderate, or high), cigarette smoking (never, past, or current smoking of 1–19 or ≥20 cigarettes/d), alcohol consumption (none or 1–34, 35–209, or ≥210 g/wk in men; none or 1–34, 35–139, or ≥140 g/wk in women), tea consumption (none or 1–2 or ≥3 cups/d), frequency of vegetable consumption (<1, 1–2, 3–5, or 6–7 times/wk), frequency of fruit consumption (<1, 1–2, 3–5, or 6–7 times/wk), frequency of sausage consumption (<1 time/mo, 1–2 times/mo, 1 time/wk, 2 times/wk, almost daily, or >1 time/d), and bread consumption (slices/d).<sup>4</sup> Adjusted for the above variables and for BMI, history of diabetes, and total cholesterol ≥6.5 mmol/L.<sup>5</sup> Adjusted for the above variables and for baseline systolic blood pressure.

vegetable, and fruit consumption. All of these factors may be partly responsible for the association between coffee drinking and the risk of hypertension. In our study, age, alcohol consumption, BMI, high total cholesterol, history of diabetes, and

baseline systolic blood pressure had a positive association, and leisure-time physical activity and current smoking had an inverse association with the risk of antihypertensive drug treatment. The results from prospective studies have shown

TABLE 4

Hazard ratios (HRs) for the development of hypertension during the first 10 y of follow-up by coffee consumption

	Coffee consumption (cups/d) <sup>1</sup>					P for trend <sup>2</sup>
	0–1	2–3	4–5	6–7	≥8	
Participants (n)	2681	5336	7430	5084	4179	
Cases of hypertension (n)	109	318	468	340	242	
Person-years	22 884	45 593	64 630	45 195	37 033	
Incident rate/1000 person-years	4.76	6.97	7.24	7.52	6.53	
Age- and study year-adjusted HR (95% CI)	1.00	1.36 (1.09, 1.68)	1.38 (1.12, 1.69)	1.39 (1.12, 1.72)	1.27 (1.01, 1.59)	0.033
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.35 (1.08, 1.68)	1.37 (1.10, 1.70)	1.35 (1.07, 1.70)	1.25 (0.98, 1.60)	0.060
Multivariate HR (95% CI) <sup>4</sup>	1.00	1.30 (1.04, 1.63)	1.28 (1.03, 1.59)	1.26 (1.01, 1.59)	1.12 (0.87, 1.43)	0.083
Multivariate HR (95% CI) <sup>5</sup>	1.00	1.26 (1.01, 1.58)	1.17 (0.93, 1.46)	1.22 (0.97, 1.54)	1.09 (0.86, 1.40)	0.20

<sup>1</sup> 1 cup = 100 mL.<sup>2</sup> Wald test.<sup>3</sup> Cox proportional hazard model adjusted for age, sex, study year, education, leisure-time physical activity (low, moderate, or high), cigarette smoking (never, past, or current smoking of 1–19 or ≥20 cigarettes/d), alcohol consumption (none or 1–34, 35–209, or ≥210 g/wk in men; none or 1–34, 35–139, or ≥140 g/wk in women), tea consumption (none or 1–2 or ≥3 cups/d), frequency of vegetable consumption (<1, 1–2, 3–5, or 6–7 times/wk), frequency of fruit consumption (<1, 1–2, 3–5, or 6–7 times/wk), frequency of sausage consumption (<1 time/mo, 1–2 times/mo, 1 time/wk, 2 times/wk, almost daily, or >1 time/d), and bread consumption (slices/d).<sup>4</sup> Adjusted for the above variables and for BMI, history of diabetes, and total cholesterol ≥6.5 mmol/L.<sup>5</sup> Adjusted for the above variables and for baseline systolic blood pressure.

TABLE 5

Hazard ratios (HRs) for the development of hypertension by coffee consumption and stratified by sex, smoking, BMI, alcohol consumption, and different types of coffee

	Coffee consumption (cups/d) <sup>1</sup>					P for interaction <sup>2</sup>
	0–1	2–3	4–5	6–7	≥8	
Sex						>0.25
Male (n = 11 711)						
Participants (n)	1209	2168	3168	2508	2658	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.14 (0.90, 1.44)	1.12 (0.90, 1.41)	1.10 (0.87, 1.40)	1.05 (0.82, 1.34)	
Female (n = 12 999)						
Participants (n)	1472	3168	4262	2576	1521	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.46 (1.13, 1.90)	1.40 (1.08, 1.81)	1.38 (1.05, 1.81)	1.19 (0.88, 1.60)	
Smoking						>0.90
Never or ever (n = 17 307)						
Participants (n)	2234	4264	5441	3379	1989	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.36 (1.12, 1.65)	1.37 (1.13, 1.66)	1.33 (1.08, 1.62)	1.22 (0.98, 1.52)	
Current (n = 7403)						
Participants (n)	447	1072	1989	1705	2190	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.08 (0.74, 1.58)	0.96 (0.67, 1.37)	0.97 (0.67, 1.41)	0.92 (0.64, 1.32)	
BMI						>0.10
<25 kg/m <sup>2</sup> (n = 11 543)						
Participants (n)	1504	2628	3495	2171	1745	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.34 (0.99, 1.83)	1.45 (1.08, 1.96)	1.26 (0.91, 1.75)	1.20 (0.84, 1.72)	
≥25 kg/m <sup>2</sup> (n = 13 167)						
Participants (n)	1177	2708	3935	2913	2434	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.27 (1.03, 1.56)	1.22 (1.00, 1.49)	1.21 (0.99, 1.50)	1.12 (0.90, 1.40)	
Alcohol consumption						>0.10
Never drinker (n = 11 431)						
Participants (n)	1351	2216	3371	2511	1982	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.42 (1.11, 1.83)	1.40 (1.10, 1.78)	1.44 (1.12, 1.85)	1.39 (1.06, 1.81)	
Alcohol drinker (n = 13 279)						
Participants (n)	1330	3120	4059	2573	2197	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.17 (0.92, 1.48)	1.12 (0.89, 1.42)	1.05 (0.82, 1.35)	0.92 (0.71, 1.20)	
Different type of coffee <sup>4</sup>						
Filtered coffee (n = 14 391)						
Participants (n)	1892	3394	4339	2567	2199	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.29 (1.01, 1.66)	1.24 (0.97, 1.58)	1.11 (0.85, 1.45)	1.11 (0.84, 1.47)	
Pot-boiled coffee without filter (n = 3271)						
Participants (n)	1376	392	585	512	406	
Multivariate HR (95% CI) <sup>3</sup>	1.00	1.16 (0.75, 1.78)	1.53 (1.04, 2.24)	1.43 (0.96, 2.16)	0.97 (0.60, 1.56)	

<sup>1</sup> 1 cup = 100 mL.

<sup>2</sup> Likelihood ratio test.

<sup>3</sup> Cox proportional hazard model adjusted for age, sex (except in the analysis by sex), study year, education, leisure-time physical activity (low, moderate, or high), cigarette smoking (never, past, or current smoking of 1–19 or ≥20 cigarettes/d, except in the analysis by smoking status), alcohol consumption (none or 1–34, 35–209, or ≥210 g/wk in men; none or 1–34, 35–139, or ≥140 g/wk in women, except in the analysis by alcohol status), tea consumption (none or 1–2 or ≥3 cups/d), frequency of vegetable consumption (<1, 1–2, 3–5, or 6–7 times/wk), frequency of fruit consumption (<1, 1–2, 3–5, or 6–7 times/wk), frequency of sausage consumption (<1 time/mo, 1–2 times/mo, 1 time/wk, 2 times/wk, almost daily, or >1 time/d), bread consumption (slices/d), BMI, history of diabetes, and total cholesterol ≥6.5 mmol/L.

<sup>4</sup> This analysis only included surveys conducted in 1987, 1992, and 1997; subjects who reported no coffee drinking were included in the analyses of both filtered coffee and pot-boiled coffee as a reference group.

that alcohol consumption is one of the important modifiable risk factors for hypertension (37, 38). In the present study, we adjusted for alcohol consumption and all other factors and also conducted some analyses stratified by smoking status, BMI, and alcohol consumption. We found that the positive trend between coffee drinking and the risk of incident antihypertensive drug treatment attenuated after adjustment for these factors. The statistically significant trend was only found in some subgroups, including women, nonsmokers, and non-alcohol drinkers. The possible reason for the statistically significant trend in women but not in men is that the incidence

rate of antihypertensive drug treatment in the reference group was lower in women than in men; however, the difference of incident rates in subjects who drank ≥2 cups of coffee daily was smaller or almost the same in women as in men. Thus, relative risks became higher in women than in men.

The habit of coffee consumption among the Finns is somewhat different from other Western populations. Most Finns drink coffee daily; whereas the cup size is ≈1 dL, overall coffee consumption is the highest in the world (7). Of 24 710 participants in the present study, ≈7.3% of Finns (n = 1809) reported no coffee consumption, and 3.5% of Finns (n = 872) reported drinking 1

cup coffee/d. According to international statistics, Finns have the highest per capita coffee consumption in the world, at 11.4 kg/y (7). The use of decaffeinated coffee is not popular in Finland. In our surveys of 1987, 1992, and 1997 that collected details about different types of coffee consumption ( $n = 16654$ ),  $\approx 8\%$  of participants reported no coffee consumption,  $\approx 80\%$  of participants drank filtered coffee, and  $\approx 12\%$  of participants drank unfiltered pot-boiled coffee. Only 0.4% of the participants drank decaffeinated or noncaffeinated coffee. The positive trend between coffee drinking and the risk of hypertension was found in both filtered coffee drinkers and in pot-boiled coffee drinkers (Table 5).

A lower risk of incident antihypertensive drug treatment was found in none to very light coffee drinkers (0–1 cup/d) and the heaviest coffee drinkers ( $\geq 8$  cups/d) compared with light-moderate coffee drinkers (2–7 cups/d) at baseline, which is in keeping with a previous finding (5, 6). In the Nurses' Health Study, the risk of incident hypertension increased by 14% (95% CI: 9%, 19% for Nurses' Health Study I) and 15% (95% CI: 9%, 21% for Nurses' Health Studies II) for those in the third quintile of caffeine consumption, whereas those in the highest quintile were not at an increased risk of hypertension compared with women in the lowest quintile of caffeine consumption (6). In the Johns Hopkins Precursors Study, relative risk of hypertension was significantly greater in those drinking 3–4 cups/d (relative risk: 1.49, 95% CI: 1.01, 2.20) but not in those drinking  $\geq 5$  cups/d (relative risk: 1.07) than in the men who abstained at baseline (5). Klag et al (5) suggested that the amount of coffee consumed during the long follow-up had an effect. They also indicated when the most recent, rather than baseline, coffee intake was considered, the risk of hypertension was higher in the heaviest coffee drinkers (5).

There were several strengths and limitations of our study. Our study was population-based and comprised a large number of men and women from a homogeneous population. The mean follow-up, 13.2 y, was long and resulted in the largest number of cases of drug-treated hypertension reported without any loss of follow-up. A limitation of our study was that we used self-reported data on coffee intake only at baseline. However, the misclassification of exposure during the follow-up was probably not systematically related to the outcome, but may have weakened the observed association. We also carried out some additional analyses to restrict the follow-up periods at the first 10 y to avoid the potential bias due to a possible change in coffee consumption during the follow-up. Second, we did not assess the effect of caffeine on the risk of incident antihypertensive drug treatment since we had no information about the consumption of cola beverage and chocolate. It is understood, however, that coffee has many other compounds besides caffeine that can influence the atherosclerotic process. Even though our analyses were adjusted for physical activity, smoking, and tea, alcohol, fruit, vegetable, sausage, and bread intakes, residual confounding due to measurement error in the assessment of confounding factors, and unmeasured factors such as diet (eg, dietary intake of sodium, potassium, and fiber), cannot be excluded. Finally, the use of only drug-treated hypertension as an endpoint was a limitation, but, on the other hand, it certainly minimized the problem of false positivity. Because the participants may have already received a diagnosis of hypertension and were advised to reduce their coffee consumption without drug treatment having been initiated, we carried out additional analyses in which subjects

who used antihypertensive drug treatment during the first year of follow-up, who were aware of having hypertension at baseline, or who had high cholesterol or who reported diabetes at baseline to avoid the potential bias were excluded.

In conclusion, this study showed that coffee drinking seemed to increase the risk of antihypertensive drug treatment, and this risk was increased in subjects with low-to-moderate intakes, but there was no significantly increased trend for 1 cup/d or  $\geq 8$  cups/d. On the basis of this large study in a population with the per capita coffee consumption in the world, it is obvious that coffee drinking may not be a major risk factor for hypertension. Even though the risk of hypertension associated with coffee consumption was relatively small, it may have some public health importance because coffee is the most consumed drink, other than water (1), and hypertension is a major health problem in the world (8). On the other hand, because coffee consumption seems to reduce the risk of type 2 diabetes (22, 24, 39–41), the relation between coffee consumption and cardiovascular disease risk is complicated, and further studies are needed.

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