Coffee intake and incidence of hypertension[1–3]

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ABSTRACT

Background: The long-term longitudinal evidence for a relation between coffee intake and hypertension is relatively scarce.

Objective: The objective was to assess whether coffee intake is associated with the incidence of hypertension.

Design: This study was conducted on a cohort of 2985 men and 3383 women who had a baseline visit and follow-up visits after 6 and 11 y. Baseline coffee intake was ascertained with questionnaires and categorized into 0, >0–3, >3–6, and >6 cups/d. Hypertension was defined as a mean systolic blood pressure (SBP) ≥140 mm Hg over both follow-up measurements, a mean diastolic blood pressure (DBP) ≥90 mm Hg over both follow-up measurements, or the use of antihypertensive medication at any follow-up measurement.

Results: Coffee abstainers at baseline had a lower risk of hypertension than did those with a coffee intake of >0–3 cups/d [odds ratio (OR): 0.54; 95% CI: 0.31, 0.92]. Women who drank >6 cups/d had a lower risk than did women who drank >0–3 cups/d (OR: 0.67; 95% CI: 0.46, 0.98). Subjects aged ≥39 y at baseline had 0.35 mm Hg (95% CI: −0.59, −0.11 mm Hg) lower SBP per cup intake/d and 0.11 mm Hg lower DBP (95% CI: −0.26, 0.03 mm Hg) than did those aged <39 y at baseline, although the difference in DBP was not statistically significant.

Conclusions: Coffee abstinence is associated with a lower hypertension risk than is low coffee consumption. An inverse U-shaped relation between coffee intake and risk of hypertension was observed in the women. *Am J Clin Nutr* 2007;85:718–23.

KEY WORDS Coffee, hypertension, cohort study

INTRODUCTION

Coffee consumption has long been a suspected cause of hypertension, but the available evidence from various study designs is inconsistent. Many randomized experiments have been performed but with different coffee or caffeine intakes. In a recent meta-analysis of 16 trials with both coffee and caffeine interventions, we showed that for coffee trials with a median intake of 725 mL coffee/d there was a rise of 1.2 mm Hg in systolic blood pressure and of 0.5 mm Hg in diastolic blood pressure (1). These trials were designed for a short follow-up duration.

Most evidence on the relation between coffee and blood pressure stems from cross-sectional studies. This evidence, however, is inconsistent. Some of these studies showed a positive relation (2), no relation (3), or even an inverse relation (4). Such cross-sectional studies have important limitations with respect to causal inference.

Conclusive information about coffee as a cause for hypertension cannot be expected to come from randomized trials, because those would require unrealistically long-term interventions. Rather, long-term observational cohort studies will have to provide such information. There have been few follow-up studies on the relation between coffee intake and blood pressure or risk of hypertension (5, 6, 7). In 1017 young men, a small positive association between coffee intake and blood pressure rise over many years of follow-up was indicated to play a small role in the development of hypertension (6). In women participating in the Nurse's Health Studies, an inverse U-shaped relation was recently found between hypertension and caffeine consumption, but no association was found with caffeinated coffee consumption (7).

Because the long-term longitudinal evidence for a relation between coffee intake and hypertension is relatively scarce, we used a Dutch cohort study to address that issue. This cohort allowed for studying the relation of baseline coffee intake to the incidence of persistent hypertension on the basis of repeatedly measured blood pressure levels in subjects at 5 y intervals during a follow-up of 11 y. Our specific research question was whether coffee intake in subjects who are not hypertensive is associated with the incidence of hypertension.

SUBJECTS AND METHODS

The design of the Doetinchem Cohort Study is described in detail elsewhere (8). Briefly, the subjects were inhabitants of the Dutch city of Doetinchem who had participated in 2 subsequent general population screening projects for chronic disease risk

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factors: the Monitoring Project on Cardiovascular Disease Risk Factors [Peilstationsproject Hart- en Vaatziekten (PPHV)] (9) conducted between 1987 and1991, and the Monitoring Project on Risk Factors for Chronic Diseases–European Prospective Investigation into Cancer and Nutrition (MORGEN-EPIC) (10) conducted between 1993 and 1997. The subjects were invited for a third separate visit between 1998 and 2002. The response rate was 62% at baseline, 78% at the first follow-up, and again 78% at the third follow-up. Respondents who attended the baseline and at least one of the follow-up examinations were included in the present analysis ($n = 6368$). The median follow-up time was 11 y. The study was approved by the Medical Ethics Committee of the Organization for Applied Scientific Research-Zeist, Netherlands. All subjects signed an informed consent form.

Dietary variables and exposure categories

Coffee intake at baseline of PPHV was estimated by the question "How many cups of coffee do you drink per day?," a question on the type of coffee used (regular, decaffeinated, or other), and a question about the use of additives (none, milk, sugar, etc). In MORGEN-EPIC, the subjects were asked to indicate how frequently they usually drank coffee, the type of coffee [regular (instant), decaffeinated, or other], use of additives (sugar, milk, and type of milk) with color photographs to indicate the strength of coffee and the standard size of a cup equaling 125 g. In a food-frequency questionnaire, the respondents were instructed to record what, on average, they had eaten and drunk in the past year. The MORGEN-EPIC food-frequency questionnaire was also used in the third follow-up (11). Similar questions were asked about tea intake. Coffee intake at baseline was divided into 4 categories: 0 cups/d, >0–3 cups/d, >3–6 cups/d, and >6 cups/d. The category of >0–3 cups/d was chosen as the reference category rather than the non-coffee drinking category because it contained larger numbers of subjects and yielded more stable estimates.

At baseline of PPHV, the subjects filled out a mailed questionnaire about demography, family history of cardiovascular disease, other chronic disease (eg, diabetes mellitus), current medication use, prescribed diets, selected dietary habits, and reproductive history for women. Pregnant women were excluded from the study. Questionnaires were used to assess alcohol intake (glasses/d), smoking status (none, ever, or current smoking of cigarettes), educational level (low, medium, or high) based on highest educational level achieved, and occupational status (paid work, housekeeping, unemployed, or retired or other).

Anthropometric and biological variables

Body height was measured to the nearest 0.5 cm without shoes. Body weight was measured without shoes and heavy clothing to the nearest 0.1 kg.

At all visits, nonfasting blood samples were obtained by using a standardized protocol. Plasma total and HDL cholesterol were measured at the Clinical Chemistry Laboratory of the University Hospital "Dijkzigt" in Rotterdam, which is the Lipid Reference Laboratory for standardized cholesterol determinations in the Netherlands. Total cholesterol was measured enzymatically by using a Boehringer test kit (12). HDL-cholesterol concentrations were measured after precipitation of apolipoprotein B–containing lipoproteins with magnesium phosphotungstate (13).

Outcome measurements and definitions

In PPHV, blood pressure was measured by trained technicians using a random zero sphygmomanometer while the subject was in a sitting position. The cuff size (12 × 23 cm) was applied to the left upper arm. A larger cuff (15 × 33 cm) was used in 1.1% and a smaller cuff (9 × 18 cm) in 0.4% of all examined subjects. Systolic blood pressure was recorded at the appearance of sounds (first-phase Korotkoff) and diastolic blood pressure at the disappearance of sounds (fifth-phase Korotkoff). After the first measurement, the heart rate was measured for 30 s followed by a second blood pressure measurement. In MORGEN-EPIC and at the third visit, the blood pressure measurement procedure was identical to that performed in PPHV. No restrictions were made with regard to coffee drinking before the measurements were taken.

Hypertension was defined by using cutoffs according to the recommendations in the 7th report of the Joint National Committee (JNC) of the National Heart, Lung, and Blood Institute (14), which classifies stage 1 hypertension as a systolic blood pressure of 140–159 mm Hg or a diastolic blood pressure of 90–99 mm Hg and stage 2 hypertension as having systolic blood pressure of ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg, use of antihypertensive medication, or both. To have sufficient numbers of hypertensives in each category of coffee intake, these categories of hypertension were pooled to at least JNC stage 1 hypertension. Persistent hypertension was defined as having a mean systolic blood pressure ≥140 mm Hg or a mean diastolic blood pressure ≥90 mm Hg calculated over both follow-up measurements at a 5-y interval, the use of antihypertensive medication at any of the follow-up measurements, or both. The association between baseline coffee intake and incident hypertension as defined above was assessed among those who did not have hypertension at baseline. No hypertension at baseline was defined as having a systolic blood pressure <140 mm Hg and a diastolic blood pressure <90 mm Hg and no use antihypertensive medication.

Statistical analysis

The association between baseline coffee intake and incident hypertension as defined above was assessed among those who did not have hypertension at baseline as defined above. Logistic regression was used with presence of persistent hypertension (yes or no) as the dependent variable and baseline coffee intake and confounders as independent variables. Furthermore, effects of changes in coffee intake as a predictor of change of blood pressure were examined. A repeated-measures analysis with time-varying covariates was used with changes between repeated blood pressure measurements as dependent variables and time-varying changes in coffee intake and confounders as independent variables. In all analyses, we adjusted for the following possible confounders: age, sex, body height and weight, smoking, alcohol intake, tea intake, educational level, occupational status, and total energy intake.

All analyses were expressed as measures of association with corresponding 95% CIs, regarding intervals not including the respective null values as statistically significant. Analyses were performed by using SPSS version 11.0 or SAS Proc Mixed for repeated-measures analysis (SPSS Inc, Chicago, IL).

TABLE 1
Baseline characteristics of the study cohort (n = 6368)

	Men (n = 2985)	Women (n = 3383)	P[1]
Age (y)	40.7 ± 10.0[2]	40.1 ± 10.3	<0.0009
Body height (cm)	178.9 ± 6.8	165.9 ± 6.3	<0.0001
Body weight (kg)	81.1 ± 10.6	67.8 ± 10.8	<0.0001
Systolic blood pressure (mm Hg)	125.6 ± 13.6	117.5 ± 14.8	<0.0001
Diastolic blood pressure (mm Hg)	79.4 ± 10.3	75.5 ± 10.3	<0.0001
Total cholesterol (mmol/L)	5.6 ± 1.1	5.4 ± 1.0	<0.0001
HDL cholesterol (mmol/L)	1.1 ± 0.3	1.4 ± 0.3	<0.0001
Normotensive (%)[3]	77.0	85.5	<0.0001
Previous myocardial infarction (%)	0.9	0.1	<0.0001
Diabetes mellitus (%)	0.7	0.7	0.96
Current cigarette smoker (%)	34.9	33.8	0.35
Education level (%)			<0.0001
Low	55.3	68.7	
Middle	24.5	18.7	
High	20.2	12.6	
Occupational status (%)			<0.0001
Paid work	86	43.1	
Housekeeping	0.7	48.8	
Unemployed or retired	8.6	5.3	
Other	4.7	2.7	
Coffee intake			<0.0001
0 cups/d[4]	2.9	5.2	
≤3 cups/d	15.7	27.0	
3–6 cups/d	53.1	53.9	
>6 cups/d	28.3	13.5	
Coffee intake (g/d)	625 (125–3000)[5]	500 (62.5–2500)	<0.0001
Decaffeinated coffee user (no.)	327	509	<0.0001
Decaffeinated coffee intake (g/d)	375 (125–3125)	375 (62.5–1875)	0.03
Tea intake (g/d)	300 (150–3000)	300 (150–2250)	<0.0001
Alcohol intake (glasses/d)	1.1 (0–14)	0 (0–7)	<0.0001
Total energy intake (kJ)	8119.9 (1984.6)	6331.4 (1941.1)	<0.0001
Follow-up (y)	11.0 ± 0.18	11.0 ± 0.17	

[1] Differences in continuous data were tested by using Student's t test; difference in median no. of glasses alcohol/d was tested by using Mann-Whitney U test; and differences in proportional data were tested by using chi-square tests.
[2] $\bar{x}$ ± SD (all such values).
[3] Systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg and no antihypertensive treatment (14).
[4] 1 cup = 125g.
[5] Median; min-max in parentheses (all such values).

RESULTS

The baseline characteristics at the first round (1987 to 1991) of the Doetinchem cohort are shown in **Table 1**. The prevalence of hypertension, as defined in Methods, at baseline was 23% in the men and 14.5% in the women.

The associations between baseline coffee intake and the subsequent development of persistent hypertension among normotensives at baseline are shown in **Table 2**. The interaction between sex and coffee intake in relation to hypertension was borderline statistically significant (P = 0.08), and therefore we decided to do both sex-specific analyses and analysis of the total group. The unadjusted odds ratios indicated a lower risk among noncoffee drinkers than in those who drank >0–3 cups/d. After adjustment, this association was slightly attenuated but was still detectable in the total group. Furthermore, women who drank >6 cups/d had a lower risk of hypertension than did women who drank >0–3 cups/d. Among coffee drinking women, there was a statistically significant trend over coffee intake categories (P = 0.023). Because age played a central role in confounding adjustments, we further explored to what extent the association between baseline coffee intake and later blood pressure differed with age. In linear regression models with the mean systolic or diastolic blood pressure from the last 2 visits as the dependent variable and coffee intake (cups), age, and a coffee intake × age interaction term as independent variables, there was a statistically signficant interaction for systolic blood pressure (P < 0.0001) as well as for diastolic blood pressure (P < 0.0001). The association between baseline coffee intake and systolic and diastolic blood pressure by median age at baseline and after full adjustment in the subjects who were not treated for hypertension at baseline is shown in **Figure 1**. Below the median age, there was no significant relation between coffee and blood pressure. In the group above the median, there was an inverse relation for systolic blood pressure (linear regression coefficient: −0.35 mm Hg · cup^{-1} · d^{-1}; 95% CI: −0.59, −0.11 mm Hg · cup^{-1} · d^{-1}) and diastolic blood pressure (−0.11 mm

TABLE 2
Relative risk for persistent hypertension occurrence in 11 y follow-up by baseline categories of coffee intake in 5189 normotensive subjects in the study cohort[1]

Coffee intake	Total cohort	No hypertension	Hypertension	OR (95% CI)	OR adjusted (95% CI)[2]
	n	*n*	*n*		
Men					
0 cups/d	65	59	6	0.40 (0.17, 0.96)[3]	0.60 (0.24, 1.49)
>0–3 cups/d	379	302	77	1.00	1.00
>3–6 cups/d	1195	928	267	1.13 (0.85, 1.50)	1.08 (0.79, 1.47)
>6 cups/d	658	515	143	1.09 (0.80, 1.49)	1.03 (0.72, 1.46)
Women					
0 cups/d	166	155	11	0.38 (0.20, 0.71)[3]	0.51 (0.26, 1.01)
>0–3 cups/d	794	668	126	1.00	1.00
>3–6 cups/d	1542	1275	267	1.11 (0.88, 1.40)	0.83 (0.64, 1.07)
>6 cups/d	390	331	59	0.95 (0.68, 1.32)	0.67 (0.46, 0.98)[3]
Total					
0 cups/d	231	214	17	0.38 (0.23, 0.64)[3]	0.54 (0.31, 0.92)[3]
>0–3 cups/d	1173	970	203	1.00	1.00
>3–6 cups/d	2737	2203	534	1.16 (0.97, 1.38)	0.93 (0.76, 1.12)
>6 cups/d	1048	846	202	1.14 (0.92, 1.42)	0.83 (0.65, 1.07)

[1] Hypertension was defined as having at least stage 1 hypertension (mean systolic blood pressure over both follow-up measurements ≥140 mm Hg, mean diastolic blood pressure over both follow-up measurements ≥90 mm Hg, or the use of antihypertensive medication at any of both follow-up measurements) (14). Normotensive subjects at baseline were defined as having a systolic blood pressure <140 mm Hg and a diastolic blood pressure <90 mmHg and use of no antihypertensive medication. Odds ratios (ORs) were obtained from logistic regression with persistent hypertension (yes or no) as the dependent variable and dummy categories of coffee intake and adjustment factors as independent variables. The category of >0–3 cups coffee/d was the reference group. The interaction between sex and coffee intake in relation to hypertension was borderline statistically significant ($P = 0.08$). Among coffee drinking women, there was a statistically significant trend over coffee intake categories ($P = 0.023$).

[2] Adjusted for baseline age, height and weight, smoking, alcohol intake, tea intake, education level, occupational status, and total energy intake. For the analysis of the total cohort, sex was added to the adjustment model.

[3] The OR was statistically significant.

Hg · cup^{-1}·d^{-1}; 95% CI: −0.26, 0.03 mm Hg · cup^{-1} · d^{-1}), although the latter was not statistically significant.

No statistically significant associations between change of coffee intake and blood pressure change were observed among the cohort members not receiving antihypertensive drug treatment at any visit. No clear association was evident between intake of every extra cup of coffee and either systolic blood pressure (−0.08 mm Hg/cup change in coffee intake; 95% CI: −0.23, 0.07 mm Hg/cup change in coffee intake; $P = 0.31$) or diastolic blood pressure (−0.05 mm Hg/cup change in coffee intake; 95% CI: −0.16, 0.06 mm Hg/cup change in coffee intake; $P = 0.37$) over the total follow-up time. Adjustment for the change in confounders, such as age, body height and weight, total cholesterol, energy intake, tea intake, alcohol intake, smoking, education level, and sex, did not significantly change these findings (systolic blood pressure: 0.06 mm Hg/cup change in coffee intake; 95% CI: −0.11, 0.22 mm Hg/cup change in coffee intake; $P = 0.48$; diastolic blood pressure: −0.06 mm Hg/cup change in coffee intake; 95% CI: −0.18, 0.06 mm Hg/cup change in coffee intake; $P = 0.34$). Exclusion of non-coffee drinkers from the analysis did not significantly influence these findings.

Finally, we found in our cohort a lower risk of persistent hypertension in the 231 total abstainers from coffee than in the 411 users of strictly decaffeinated coffee. Using stage 1 or stage 2 hypertension as outcome, the unadjusted odds ratio was 0.35 (95% CI: 0.20, 0.60). Adjustment for confounding attenuated this odds ratio to a nonsignificant 0.72 (95% CI: 0.34, 1.49).

DISCUSSION

Our study indicates that both abstainers from coffee and, in women only, heavy consumers (>6 cups/d) have lower risks of hypertension than do low coffee consumers (>0–3 cups/d). An association between higher coffee consumption and lower blood pressure seems to be present only after middle age.

Nonresponses may have been related to coffee intake or blood pressure, but not likely to specific associations between coffee and blood pressure. We cannot rule out that professional advice to lower coffee consumption to persons with higher baseline intakes has led to a spurious association between higher intake and lower blood pressure. However, we analyzed persons who were normotensive at baseline to whom such advice was unlikely given. Although there may be residual or unmeasured confounding, we accounted for most confounders that are known to be risk factors for high blood pressure. We had no baseline information about intake of caffeine-containing sodas, which was recently shown to be associated with incidence of hypertension (7). We can only speculate about the effects of adjustment for that intake, but consumption of such sodas in the Netherlands in middle-aged persons in that period was probably low. A strong feature of our study is that it pertains to a large sample from the general population with >10 y of follow-up. Moreover, our outcome classification—the incidence of hypertension persisting over a 5-y period—better reflects true hypertension incidence than does measurement at a single occasion. This outcome was based on actual blood pressure measurements or hypertension treatment,

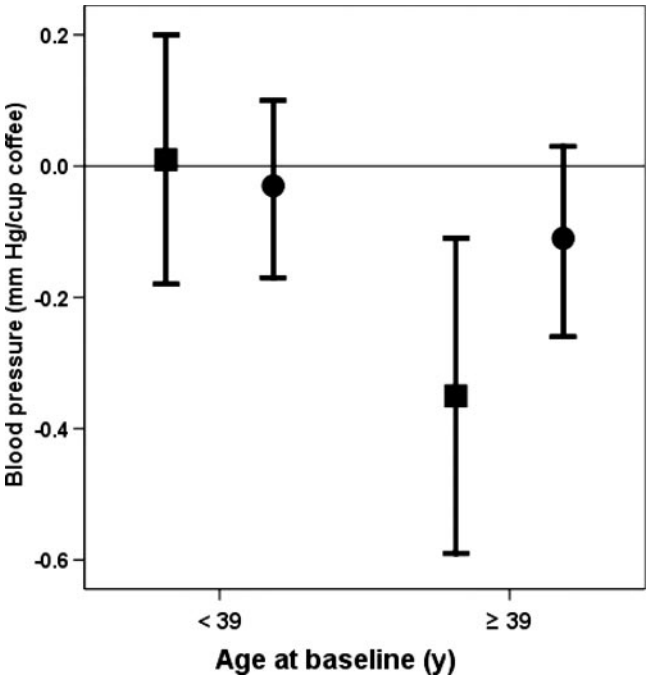

FIGURE 1. Linear regression coefficients (95% CIs) representing the difference in mean systolic (■) and diastolic (●) blood pressures over the 2 follow-up visits per each extra daily cup of coffee at baseline, separated by those aged below and above the median age (39 y) at baseline in the study cohort. Data pertain to 5694 subjects without antihypertensive treatment at any visit. All estimates are adjusted for sex, height and weight, smoking, alcohol intake, tea intake, total cholesterol, HDL cholesterol, education level, occupational status, and total energy intake. In linear regression models with the mean systolic or diastolic blood pressure from the 2 follow-up visits as the dependent variable and coffee intake (in cups), age, and an coffee intake × age interaction term as independent variables, there was a statistically significant interaction for systolic blood pressure and for diastolic blood pressure ($P < 0.0001$ for both). 95% CIs not crossing the null line are considered statistically significant.

rather than on self-reporting of a physician diagnosis, such as in the Nurse's Health Study (7). Finally, although we have addressed a limited number of hypotheses concerning the association between coffee intake and hypertension, we cannot rule out chance as an explanation, neither for the main effects nor for the interactions with age.

Our findings in men agree with those of a previous report on a long-term follow-up conducted in 1017 males showing a nonsignificant relation between coffee intake and hypertension incidence, despite a small positive effect on blood pressure levels (6). Our findings in women may be compatible with recent findings in the women participating in the Nurse's Health Studies I and II, where an inverse U-shaped association was found between caffeinated coffee intake and hypertension risk (7). Among normotensives at baseline, we showed a lower hypertension risk for coffee abstainers than for users of >0–3 cups/d.

From short-term randomized trials, it is known that coffee and caffeine have a blood pressure–raising effect (1). The prevailing explanation for such effect is that caffeine antagonizes endogenous adenosine, resulting in vasoconstriction and elevated total peripheral vascular resistance (15). The question is how low coffee intake is associated with a higher risk of hypertension, whereas high coffee intake is not. One explanation could be that effects of coffee on blood pressure do depend on consumption habits, with higher blood pressure levels observed in nonhabitual than in habitual coffee consumers (16, 17). Thus, a higher hypertension risk in consumers of >0–3 cups/d than in nondrinkers and consumers of >6 cups/d may be based on a lower adaptation to the effects of coffee when used in moderate to low amounts. Alternatively, coffee may have more general protective effects, because our finding of heavier coffee intake leading to lower blood pressure does not seem to be specific. A lower risk for type 2 diabetes mellitus in heavy coffee users compared with non- or moderate users was first shown by one of us (18) and recently confirmed by others (19-23) and is somewhat stronger in women than in men (21). In agreement with our findings for hypertension, it was shown that women with low coffee use (<1 cup/d) had a higher risk of type 2 diabetes mellitus than did non-coffee users (20). However, it remains unclear whether and to what extent an association between coffee intake and blood pressure can explain the association with diabetes mellitus. Some studies could only adjust for known hypertension (18, 23), which may be misclassified and leave residual confounding by blood pressure as an explanation. One study adjusted for systolic blood pressure levels, whereas diastolic blood pressure levels were most strongly associated with diabetes mellitus risk (21). In other studies, there was no explicit adjustment for blood pressure or hypertension (19, 20, 22). Finally, there may be a blood pressure–lowering compound in coffee that explains lower hypertension risk with higher intake. It was recently shown in a cross-sectional study that higher habitual tea intake was associated with lower risk of hypertension (24). This effect of tea combined with our observations on coffee may indicate a central role of serum potassium concentrations. A higher intake of potassium is clearly associated with lower blood pressure (25), and tea and particularly coffee are rich sources of potassium in Western diets (26). This, however, would not explain the observed lower hypertension risk in coffee abstainers.

Overall, higher baseline coffee intake in our study was associated with lower later blood pressure only from middle age onwards, wheras there was no such relation in younger persons. We can only speculate about the mechanisms for such age-dependent effects. It may agree with the results from short-term randomized trials, in which blood pressure–raising effects of coffee were reported to be stronger in younger than in older subjects (1) and which may point at more habituation to coffee in older persons (15, 16). Alternatively, if there is a protective salt constituent in coffee, such as potassium, it may be through increasing salt-sensitivity and higher blood pressure levels observed with increasing age (27, 28) that the protective effects of higher coffee intake become apparent. Finally, there is recent evidence to suggest that genetically determined slow caffeine metabolism in relation to cardiovascular disease risk is present only in relatively younger persons (29).

From a public health point of view, a direct implication of our study may be to reduce the incidence of hypertension by measures aimed at refraining from moderate coffee intake, but that would be unpractical if at all effective. The most important merit of our study is the elucidation of the role of coffee intake through its relation with hypertension in increasing the risk of cardiovascular disease. Although there are reports claiming coffee to be hazardous (30, 31), the larger cohorts show no association between coffee intake and cardiovascular morbidity or mortality (32) or with the prognosis of myocardial infarction (33). We consider it likely that the extent to which coffee intake explains

hypertension risk is too small to be detected in relation to cardiovascular disease. A practical implication from our findings would therefore be to abstain from professional advice concerning coffee intake in normotensive individuals, which indeed agrees with the latest clinical guidelines on hypertension (14). We cannot preclude that associations between coffee intake and cardiovascular outcomes are different among hypertensive individuals (34). In conclusion, coffee abstinence was associated with a lower hypertension risk than was low coffee consumption, and an inverse U-shaped relation between coffee intake and risk of hypertension was observed in women.

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WMMV was the project leader. WMMV, HBBdM, and MO were involved in the design and conduct of the cohort. CSPMU, HCB, and DEG analyzed the data. All authors played a role in data-interpretation and writing of the manuscript. CSPMU was provided an unrestricted grant by the organization on Physiological Effects of Coffee (PEC) in Paris. No other authors had any conflicts of interest.

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