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## Coffee consumption and risk of hypertension in the Polish arm of the HAPIEE cohort study

Giuseppe Grosso<sup>1,2</sup>, Urszula Stepaniak<sup>2</sup>, Maciej Polak<sup>2</sup>, Agnieszka Micek<sup>2</sup>, Roman Topor-Madry<sup>2</sup>, Denes Stefler<sup>3</sup>, Krystyna Szafraniec<sup>2</sup>, and Andrzej Pajak<sup>2</sup>

<sup>1</sup>Department of Clinical and Molecular Biomedicine, Section of Pharmacology and Biochemistry, University of Catania, Catania, Italy <sup>2</sup>Department of Epidemiology and Population Studies, Jagiellonian University Medical College, Krakow, Poland <sup>3</sup>Department of Epidemiology and Public Health, University College of London, London, United Kingdom

### Abstract

**Background/objectives**—Coffee consumption has been hypothesized to be associated with blood pressure, but previous findings are not homogenous. The aim of this study was to evaluate the association between coffee consumption and the risk of developing hypertension.

**Subjects/Methods**—Data on coffee consumption, blood pressure, and use of anti-hypertensive medicament were derived from 2,725 participants of the Polish arm of the HAPIEE project (Health, Alcohol and Psychosocial factors In Eastern Europe) who were free of hypertension at baseline and followed up for an average of 5 years. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by multivariate logistic regression analyses and stratified for potential confounding factors.

**Results**—Coffee consumption was related with decreased age, smoking status, and total energy intake. Compared to persons who drink <1 cup coffee per day, systolic blood pressure was significantly associated with coffee consumption and the risk of hypertension was lower for individuals consuming 3–4 cups/day. Despite the analysis stratified by gender showed that the protective effect of coffee consumption on hypertension was significant only in women, the analysis after stratification by smoking status revealed a decreased risk of hypertension in non-smokers drinking 3–4 cups of coffee per day, in both sexes (OR 0.41, 95% CI: 0.21, 0.79 for men

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*Corresponding author:* Giuseppe Grosso, MD, Department of Clinical and Molecular Biomedicine, Section of Pharmacology and Biochemistry, University of Catania, V.le A. Doria 6, 95125, Catania, Italy Phone: +39.095.7384278 Fax: +39.095.7384220

giuseppe.grosso@studium.unict.it.

Urszula Stepaniak: mxbiela@cyf-kr.edu.pl

Maciej Polak: maciej.polak@uj.edu.pl

Agnieszka Micek: agnieszka.micek@uj.edu.pl

Roman Topor-Madry: mxtopor@cyf-kr.edu.pl

Denes Stefler: denes.stefler.10@ucl.ac.uk

Krystyna Szafraniec: mygomola@cyf-kr.edu.pl

Andrzej Pajak: mmpajak@cyf-kr.edu.pl

Conflict of interest

Authors declare no conflict of interest.

and OR 0.54, 95% CI: 0.29, 0.99 for women). Upper category coffee consumption (>4 cups per day) was not related with significant increased risk of hypertension.

**Conclusions**—Relation between coffee consumption and incidence of hypertension was related to smoking status. Consumption of 3-4 cups of coffee per day decreased risk of hypertension in non-smoking men and women only.

### Keywords

coffee; hypertension; blood pressure; polyphenols; smoking

## Introduction

Hypertension is one of the most common and important health problems in the modern world <sup>1</sup>. Elevated blood pressure is an established risk factor for coronary artery disease, stroke, kidney disease, all-cause mortality, and decreased life expectancy. The importance of preventing hypertension by adopting healthy lifestyle is undoubted. Together with low physical activity, excess in body weight, and unhealthy dietary habits (i.e., excessive sodium and low potassium intakes), coffee consumption has been considered detrimental due to results of studies reporting an association with increased risk of hypertension <sup>2</sup>. However, recent evidence demonstrated that underrated variables (such as socioeconomic status and concurrent smoking habits) have influenced results of previous studies and coffee may, in fact, be protective against hypertension <sup>3</sup>. Coffee is a mixture of several compounds that actively influence human homeostasis and metabolism, including caffeine, phenolic compounds, niacin, minerals (magnesium, potassium), and fiber. The major beneficial effects of coffee seems to depend on its content of chlorogenic acids, a family of polyphenols (mostly caffeic and ferulic acid) that demonstrates strong antioxidant properties through inhibiting production of inflammatory mediators <sup>4</sup>. Coffee has been reported to be the major source of chlorogenic acids in the diet <sup>5</sup>. Although the acute effect of caffeine intake is to increase blood pressure by blocking adenosine receptors in the vascular tissue, which leads to vasoconstriction in the general and micro circulation <sup>6</sup>, the health effect of long-term habitual consumption is not clear.

Studying the association between coffee consumption and blood pressure is challenging because the effects of coffee intake may vary when considered in short- or long-term, as well as in occasional or habitual consumers and because methodological issues <sup>3,7</sup>. Previous cross-sectional studies reported contrasting results <sup>8,9</sup>, but they may have suffer of reverse causation bias, as people with high blood pressure could have been advised to decrease coffee consumption in the past, which would result in a selective reduction of coffee consumption in hypertensive individuals <sup>10</sup>. Prospective epidemiological studies provide a better methodological approach to identify significant factors that may exert an effect on health during a reasonable long period of time, but they are scarce and their results are contrasting <sup>11-13</sup>. Also studies on urinary caffeine metabolites excretion related to coffee consumption demonstrated certain associations <sup>14</sup>. Several experimental studies have been conducted demonstrating an acute increase of blood pressure after consuming coffee (or caffeine), with the major limitations of short duration and of testing relatively high doses of coffee in the treatment groups <sup>15</sup>. A recent meta-analysis including prospective observational

studies reported inconsistent results<sup>16</sup>, whereas another pooled analysis including both epidemiological and experimental studies conducted on hypertensive subjects reported that caffeine intake produces an acute increase in BP for 3 h but there is no association between long-term coffee consumption and blood pressure<sup>17</sup>. Caffeine, whether considered the first responsible for blood pressure alteration, is metabolized by the liver CYP1A2 enzyme, whose activity is in turn influenced by several factors, such as cigarette smoking and oral contraceptives use<sup>18</sup>. Previous studies demonstrated that stratification of coffee drinkers and non-drinkers by smoking habits better describe the intercorrelations between such lifestyle behaviors and blood pressure<sup>14,19</sup>.

We previously reported a lower prevalence of metabolic syndrome in high coffee consumers among Polish participants of the Health, Alcohol and Psychosocial factors In Eastern Europe (HAPIEE) study<sup>9</sup>. However, a prospective evaluation over time of those individuals free of hypertension at baseline was lacking. The aim of this study was to assess the association between coffee consumption and risk to develop hypertension in the Polish urban sample of the HAPIEE study, also evaluating the relation between coffee consumption and blood pressure levels assessed at follow-up visits.

## Methods

### Study population

The HAPIEE study is a multicenter prospective cohort study investigating the role of biological, dietary, lifestyle, and environmental factors in cardiovascular and other chronic diseases<sup>20</sup>. The criteria for sample selection and the methods used were reported in detail elsewhere<sup>20</sup>. Briefly, a random sample of 10,729 subjects (aged 45–69 y) was recruited at the baseline survey conducted in 2002–2005 (response ratio of 59%) selected from population registers in the urban area of Krakow, Poland. The participants, after providing written informed consent, completed a structured questionnaire and were invited for clinical examination. For the purpose of this analysis, we selected individuals free of hypertension at baseline and used the following exclusion criteria: (i) did not agree to undergo follow-up visit; (ii) lack of information on blood pressure levels; (iii) lack of answer in more than 50% of food frequency questionnaire (FFQ). Application of the selection strategy showed in Figure 1 resulted in the final selection of 2,725 individuals free of hypertension at baseline and followed for an average of 5 years (last follow-up visit was conducted in 2008). Sample included in this analysis did not substantially differed from the original sample in background characteristics, but variables of interest, such as mean blood pressure levels (different by inclusion/exclusion criteria), BMI (lower among included individuals), smoking status and coffee consumption (higher among included individuals) differed as result of inclusion/exclusion criteria (Additional Table 1).

### Dietary assessment and categories of exposure

Dietary data were collected by using a FFQ based on the tool developed by Willett et al.<sup>21</sup> and subsequently adapted in the Whitehall II Study<sup>22</sup>. The FFQs consisted of 148 food and drink items representative of the diet during the preceding 3 months. A country-specific instruction manual that included photographs to facilitate the estimation of portion sizes was

used. Participants were asked how often, on average, they had consumed that amount of the item during the last three months, with nine responses ranging from 'never or less than once per month' to 'six or more times per day'. Moreover, participants were asked to include additional foods and frequency of consumption by manual entry.

Energy and micro-nutrients intakes were calculated through food composition tables in order to evaluate sodium and potassium intake<sup>23</sup>. The average coffee consumption was calculated (in ml) by following the portion sizes used in the study and then converted into 24-hour intake. We categorized daily coffee consumption according to standard cup of coffee (150 ml) in (i) <1 cup/d, (ii) 1-2 cups/d, (iii) 3-4 cups/d, and (iv) >4 cups/d.

### Demographic, lifestyle and clinical measurements

Socio-demographic and lifestyle characteristics included age, gender, educational and occupational level, smoking and alcohol drinking habits, medicaments and vitamin supplement use. Educational level was categorized as (i) low (primary/secondary), (ii) medium (high school), and (iii) high (university). Occupational level was categorized as (i) low (unskilled/unemployed workers), (ii) medium (partially skilled workers), and (iii) high (skilled workers). Physical activity included energy expenditure in leisure time by reporting type and duration of activity according to the predetermined questionnaire items. The overall amount of energy expenditure was estimated in kcal/d and categorized in low, moderately and high activity level. Individuals were categorized according to their smoking status as non-smoker and current smoker. Average alcohol consumption was categorized as (i) none or low (< 12 g/day) and (ii) alcohol drinker (>12 g/day). Medicaments use included oral contraceptive (OC), diabetes and hypercholesterolemia treatment.

Physical examination included measurement of height, weight, waist circumference and blood pressure using standard procedures<sup>20</sup>. Body mass index (BMI) was calculated according to the formula weight (kg)/height (m)<sup>2</sup>. Blood pressure was measured three times at the end of the physical examination and the final value was the mean among the three measurements. Participants were considered to have hypertension at baseline visit if they had a systolic and/or a diastolic blood pressure higher than 139 and 89 mmHg, respectively<sup>24</sup> or taking hypertensive medication within the last two weeks. These individuals were not included in this study. Among those free of hypertension, cases of new onset hypertension were identified according to the aforementioned criteria evaluated at follow-up visits.

### Statistical analysis

Characteristics of the study cohort were described by baseline coffee consumption categories. Taking into account the natural differences in hypertension risk between men and women, gender-specific analyses were conducted. Descriptive presentation relied on cross tabulations. Continuous variables are presented as means and standard deviations (SDs), categorical variables as frequencies and percentages. Variables were examined for normality (Kolmogorov). Chi-square test was used for comparisons of categorical variables, Kruskal-Wallis test was used for continuous variables.

Differences in mean systolic and diastolic blood pressure values by different categories of coffee consumption were tested by using analysis of covariance and linear contrast analysis because a dose-dependent effect was assumed. Similarly, mean differences between follow-up and baseline systolic and diastolic blood pressure values by different categories of coffee consumption were calculated.

The association between baseline coffee consumption and incident hypertension was assessed by logistic regression analyses. Crude (unadjusted), age-adjusted, and full-adjusted models were performed for the whole sample and separately by gender. Odds ratios (ORs) and 95% confidence intervals (CIs) of having hypertension with the lower category of coffee consumption as reference were calculated. The full-adjusted multivariate model was adjusted for variables hypothesized to be associated with hypertension according literature, such as age, gender, education, occupation, BMI, alcohol drinking (stratified in gender-specific cut-offs, such as 0, 0-12, 12-24, >24 ml/d for men and 0, 0-6, 6-12, >12 ml/d for women), smoking status, physical activity level, past history of CVD, diabetes at baseline, cholesterol therapy at baseline, use of OC at baseline, total energy intake, vitamin supplement use, and sodium and potassium intake. As an interaction was found for smoking status ( $P = 0.035$ ), the analysis was performed also after stratification of the sample by such variable. Statistical significance was accepted at  $p < 0.05$ . All statistical analyses were performed with SPSS for Windows 21.0 (SPSS Inc, Chicago, IL).

## Results

The baseline characteristics of the study cohort by coffee consumption categories are shown in Table 1. There were no substantial differences between men and women in coffee consumption. Coffee drinkers were characterized by slightly younger age, higher prevalence of smoking and had higher total energy intake. A further significant positive trend by coffee consumption was found with alcohol consumption among men, whereas in women drinking less coffee was related with higher prevalence of diabetes compared to high consumption. Figure 2 shows that number of cigarettes per day increased by increasing category of coffee consumption in both men and women ( $P < 0.001$ ).

Mean systolic and diastolic blood pressure values by coffee consumption categories are presented in Table 2. Only systolic blood pressure was significantly different among category of exposure, but gender-stratified analysis revealed that such association was mostly dependent on the relation present in women. No significant differences were found for diastolic blood pressure. The change of systolic and diastolic blood pressure at follow-up by categories of coffee consumption confirmed such findings, with significant higher increase in systolic blood pressure in lower rather than higher coffee consumers in both men and women, despite a linear trend was found only in the latter (Table 3).

Over an average follow-up period of 5 years, 1735 new cases of hypertension occurred. The association between baseline coffee consumption and incidence hypertension is showed in Table 4. The multivariate-adjusted models demonstrated a decreased risk of hypertension in participants consuming 3-4 cups of coffee per day (OR 0.75, 95% CI: 0.58, 0.95) whereas for those with higher consumption the increase in risk was not significant. After

stratification by gender, the association remained significant only in women. Since coffee consumption was significantly associated with smoking status at univariate analysis, an additional model was built by stratifying by such variable (Table 5). As expected, since smoking was strictly correlated with coffee drinking, The risk of hypertension among smokers was not associated with coffee consumption significantly, whereas among non-smokers the intake of coffee of up to 3-4 cups per day decreased the risk of hypertension both in men and in women (OR 0.41, 95% CI: 0.21, 0.79 and OR 0.54, 95% CI: 0.29, 0.99, respectively.)

## Discussion

In this study we prospectively evaluated the association of coffee consumption with blood pressure and with incidence of hypertension in a well-established cohort in Eastern Europe, taking into account its daily intake and potential confounding factors. We found that excessive coffee consumption (>4 cups per day) was not significantly associated with incident cases of hypertension, which may be associated to other untested variables or the lack of statistical power due to low number of individuals in this category of exposure. Non-smoking participants, consuming up to 3-4 cups of coffee per day had decreased risk (by about 50%) of hypertension. Coffee consumption correlated inversely with blood pressure in women.

The acute effects of caffeine intake are well-known <sup>6</sup>, but the effect of chronic coffee consumption on blood pressure is still unclear. Recent meta-analysis of randomized clinical trials analyzed the effects of coffee and caffeine intake reporting that blood pressure elevations appeared to be significant only for caffeine but not for coffee intake <sup>8</sup>. This finding suggests that despite the acute ingestion of caffeine increases blood pressure, when ingested through coffee, the hypertensive effect of caffeine may be somehow attenuated. It is likely that other components of coffee may counteract the negative effect of caffeine. Experimental studies reported that acute raise in blood pressure due to coffee intake develops rapidly tolerance and that intravenous caffeine is responsible of rise in muscle sympathetic activity and blood pressure in both habitual and non-habitual coffee drinkers, but coffee intake led to increased blood pressure only in non-habitual coffee drinkers <sup>25</sup>. These findings may support the hypothesis that habitual coffee drinkers are less likely to show a blood pressure response after caffeine intake and less average blood pressure levels than non-drinkers. Moreover, coffee is rich in blood pressure-lowering minerals (i.e., potassium and magnesium) and antioxidant compounds (polyphenols) that may outweigh the hypertensive effects of caffeine <sup>4</sup>. From a mechanistic point of view, genetic and concurrent lifestyle habits (such as smoking status) may influence the activity of key enzymes, as CYP1A2, able to metabolize caffeine and, consequently, influence blood pressure abnormalities. Taking into account such variables may explain much of gender differences often occurring in this type of studies and further research is needed to better clarify such potential correlations.

Overall, coffee ameliorates metabolism-related parameters under laboratory and experimental conditions <sup>26</sup>. There is evidence that the main phenolic compounds of coffee can regulate the cellular processes leading to inflammatory response <sup>27</sup>. Oxidative stress

plays an important role in the process that leads to metabolism impairment and development of chronic conditions such as hypertension, since a state of subclinical inflammation is heavily involved in the pathogenesis of such pathological conditions. Therefore, consumption of coffee may inhibit inflammation and thus reduce the risk of cardiovascular and other inflammatory diseases. The antioxidant properties of polyphenols contained in coffee mostly depend on chlorogenic acids<sup>28</sup>. This particular family of molecules exhibits anti-inflammatory activity in a concentration-dependent manner through inhibiting production of inflammatory mediators (TNF- $\alpha$  and IL-6) in human peripheral blood mononuclear cells<sup>4</sup>. Investigations during the last decade have demonstrated their potential anti-hypertensive effects and beneficial role in improving endothelial and vascular function<sup>29</sup>. Two randomized clinical trials conducted on humans demonstrated a significant lowering effect on blood pressure of purified chlorogenic acids up to 10/7 mm Hg after 12 weeks of treatment compared to placebo<sup>30,31</sup>. Chlorogenic acids have been found to reduce NAD(P)H-dependent super-oxide production<sup>32,33</sup>, to attenuate the proliferation of vascular smooth muscle cells through inhibiting intracellular superoxide anion generation<sup>34</sup>, and to interact with the renin-angiotensin aldosterone system by inhibiting angiotensin-converting enzyme activity demonstrated both in vitro and in vivo<sup>35,36</sup>. Among the chlorogenic acids metabolites, ferulic acid seems to have the greatest effect on blood pressure<sup>37,38</sup>. The administration of ferulic acid greatly increases nitric oxide bioavailability and enhanced acetylcholine-induced endothelial-dependent vasodilation<sup>39</sup>.

The main concern regarding the effects of coffee intake on blood pressure depends on the discrepancy between the results obtained with purified molecules of chlorogenic acids against the lack of a clear anti-hypertensive effect of coffee consumption in human studies, the latter reporting controversial results<sup>40-42</sup>. Findings of prospective cohort studies are indeed inconsistent<sup>12-14</sup>. The overall effect of coffee consumption on risk of hypertension has been outputted in a meta-analysis<sup>43</sup> showing an inverse J-shaped risk, with an increasing risk of hypertension for low to moderate consumption and a decreased risk for high consumption of coffee. There are some aspects of the studies included in the meta-analysis that should be taken into account. Two of them included individuals with untreated hypertension<sup>11,15</sup>. Of the studies conducted on healthy individuals<sup>12-14</sup>, adjusting for important potential confounding factors (i.e., sodium or potassium intake) or stratified analysis by subgroups of individuals with specific characteristics that are supposed to influence blood pressure (i.e., smokers) were often lacking. We reported opposite findings, suggesting that moderate consumption of coffee may even be protective and the effect of excessive chronic consumption is less evident. A separate analysis by smoking status determined the conclusions in our study. From a biological point of view, it seems possible that, even if the tolerance for the caffeine-induced pressure effect develops in habitual coffee drinkers<sup>6,44</sup>, the effects of excessive intake of caffeine reduce such tolerance<sup>45</sup>. Nevertheless, despite coffee is rich in blood pressure-lowering minerals (i.e., potassium and magnesium) and antioxidants (chlorogenic acid, flavonoids, etc.) that may outweigh potential adverse effects of caffeine<sup>4</sup>, these compounds could counterbalance caffeine's pressure effect above a certain level of consumption<sup>8</sup>. It has been hypothesized that other compounds produced during the roasting process, may be responsible for neutralizing the anti-hypertensive effects of chlorogenic acids. Among the most investigated candidates,

hydroxyhydroquinone (HHQ), a particular fraction of chlorogenic acids discovered in roasted coffee after temperature treatment, demonstrated to eliminate the anti-hypertensive effects of chlorogenic acids<sup>29, 46, 47</sup> and, inversely, daily consumption of HHQ-free coffee led to a decrease of blood pressure in a marginally dose-dependent manner<sup>48</sup>. The current hypothesis is that the production of HHQ-derived superoxide may neutralize chlorogenic acids-enhanced NO bioactivity, therefore concealing the anti-hypertensive effects of chlorogenic acids<sup>47, 49</sup>.

Some limitations of this study should be considered when interpreting results. Despite our study was population-based and comprised a large number of men and women from a homogeneous population, the availability of prospective information and the restriction of the analysis to participants free of hypertension at baseline, reduced the overall sample. Moreover, the sample was recruited in an urban area and cannot be considered nationally representative and the selection process may have produced a selection bias toward healthier individuals with healthier behaviors compared with excluded participants. However, the number of subjects included is comparable with previous studies and we consider a strength the inclusion of only healthy subjects and the assessment of hypertension by direct measurement of blood pressure together with anti-hypertensive therapy use, since the use of only drug-treated hypertension as an endpoint is a serious limitation of previous studies, which probably contributed to the elimination of the undiagnosed hypertension. However, we found an unusual high prevalence and incidence of hypertension cases with apparently no reason to explain it. Another limitation was that information on the pattern of coffee drinking, such as type, time, and brewing method, was limited. The inclusion in the analysis of decaffeinated coffee depended on its very small consumption in our sample (which did not allow to perform the analysis separately). Moreover, information regarded only the baseline investigation and was self-reported. Finally, due to the nature of the investigation, coffee consumption may be strongly associated with other lifestyle factors that we were not able to identify and analyze (such as genetic information), thus potential confounders may still remain. However, compared with previous investigations, we included a large variety of well-known cofactors associated with both coffee consumption either blood pressure. Finally, last category of exposure included fewer individuals than others and this could have affected the statistical power. Nevertheless, we preferred to consider for analysis this category as separate due to a different biological effect with a lower coffee consumption.

In conclusion, average consumption of 3-4 cups of coffee per day decreased the risk of hypertension among non-smokers and coffee intake seemed to be inversely associated with systolic blood pressure. In the present study, excessive daily coffee consumption did not increase the risk of hypertension significantly and background characteristics, such as smoking status, must be carefully considered when exploring the effects of coffee consumption.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.



## Acknowledgements

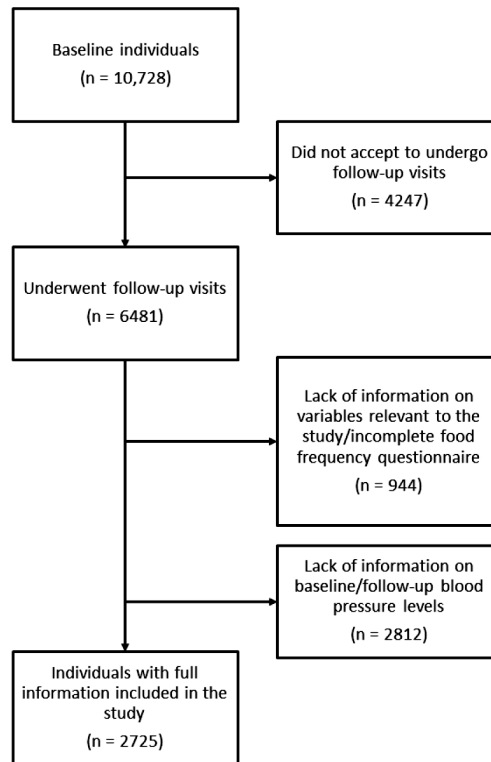
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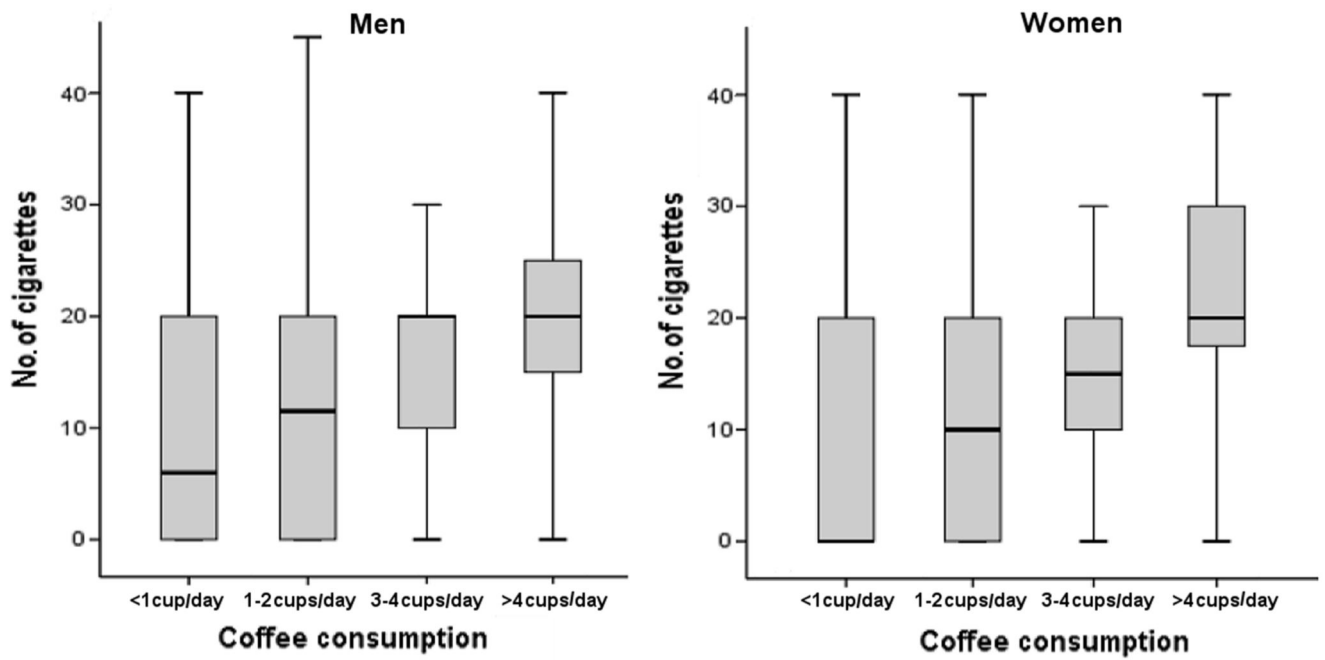
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**Figure 1.**  
Flow-chart of individuals included for the analysis.



**Figure 2.** Incidence of hypertension by coffee consumption and smoking status at baseline in 2725 participants of the HAPIEE cohort.

Table 1

Background characteristics by category of coffee consumption in 2725 participants of the HAPIEE cohort free of hypertension at baseline.

	Men, coffee consumption				Women, coffee consumption				P for trend
	<1 cup/d	1-2 cups/d	3-4 cups/d	>4 cups/d	<1 cup/d	1-2 cups/d	3-4 cups/d	>4 cups/d	
No of subjects	334	473	319	25	401	674	479	20	
Age (years), mean (SD)	56.7 (7.1)	56.3 (8.8)	55.5 (6.9)	56.3 (6.8)	55.8 (6.6)	55.3 (6.5)	54.5 (6.1)	52.8 (7)	0.001
BMI, mean (SD)	26.7 (3.4)	26.6 (3.3)	26.5 (3.4)	25.7 (3.8)	26.1 (4)	26.2 (4.1)	26.6 (4.1)	25.3 (4.4)	0.252
Baseline systolic blood pressure, mean (SD)	123.9 (9.6)	124.3 (9.1)	124.1 (8.3)	124.3 (10.2)	119.1 (10.9)	119.8 (10.4)	119.2 (10.6)	117.5 (13.3)	0.900
Baseline diastolic blood pressure, mean (SD)	78.1 (6.3)	78.4 (6.8)	78.4 (6.1)	78.8 (8.2)	76.6 (7)	77 (6.7)	76.9 (6.7)	74.8 (6.2)	0.855
Current smoker, n (%)	138 (41.6)	194 (41.3)	147 (46.1)	17 (68)	118 (29.5)	229 (34.1)	173 (36.2)	11 (57.9)	0.010
Oral contraceptives use, n (%)	-	-	-	-	12 (3.0)	27 (4.0)	7 (1.5)	1 (5.0)	0.088
Low educational level, n (%)	30 (9)	37 (7.8)	17 (5.3)	0	43 (10.8)	58 (8.6)	37 (7.7)	2 (10)	0.155
Low occupational level, n (%)	187 (57.2)	297 (64.8)	186 (60)	11 (48.8)	167 (43.6)	276 (42.4)	200 (42.7)	6 (30)	0.847
Low physical activity level, n (%)	84 (27)	120 (27.2)	85 (27.9)	5 (20.8)	102 (26.6)	200 (31)	126 (28)	6 (31.6)	0.853
Alcohol intake >12 g/d, n (%)	11 (3.3)	24 (5.1)	21 (6.6)	4 (16)	10 (2.5)	19 (2.8)	13 (2.7)	0	0.976
Diabetes or diabetic treatment, n (%)	20 (6)	34 (7.2)	17 (5.3)	0	19 (4.7)	22 (3.3)	11 (2.3)	0	0.031
Hypercholesterolemia treatment, n (%)	25 (7.5)	44 (9.3)	19 (6)	3 (12)	49 (12.2)	98 (14.5)	51 (10.6)	3 (15)	0.492
Total energy intake (kcal/d), mean (SD)	2136.1 (668.7)	2182.7 (626.9)	2314.4 (705.3)	2347.6 (578.3)	2091.9 (623.5)	2059.2 (572.1)	2153.6 (605.8)	2365.2 (734.4)	0.032
Vitamin supplement use, n (%)	38 (11.4)	77 (16.3)	51 (16)	2 (8)	98 (24.4)	165 (24.5)	95 (19.8)	3 (15)	0.063
Sodium intake, mean (SD)	3436.2 (1324.1)	3514.3 (1167.6)	3598.4 (1209.9)	3577.3 (1164.7)	3273.3 (1068.4)	3124.2 (994.1)	3343.6 (1102)	3798.9 (1630)	0.071
Potassium intake, mean (SD)	3713 (1366.8)	3722.1 (1189.3)	3874.1 (1342.2)	3729.6 (1030.9)	3637.3 (1362.4)	3653.9 (1231.4)	3688 (1126.1)	4170.7 (1508.6)	0.270

**Table 2**

Systolic and diastolic blood pressure measures at follow-up by category of coffee consumption in 2725 participants of the HAPIEE cohort free of hypertension at baseline.

	Coffee consumption				<i>P</i> for trend
	<1 cup/d	1-2 cups/d	3-4 cups/d	>4 cups/d	
Systolic blood pressure, mean (SD)					
Overall	141.3 (20.9)	140.3 (20.6)	138.5 (19.7)	136.9 (16.2)	0.004
Men	141.3 (19.8)	142.3 (20.4)	140.3 (17.9)	138.8 (19.5)	0.427
Women	141.4 (21.9)	138.9 (20.7)	137.3 (20.8)	134.5 (18.1)	0.003
Diastolic blood pressure, mean (SD)					
Overall	85.5 (11.5)	86 (11.4)	85.7 (10.9)	86.5 (8.5)	0.697
Men	85.9 (11.1)	86.8 (11.2)	86.5 (10.1)	86.7 (7.3)	0.547
Women	85.2 (11.9)	85.4 (11.5)	85.2 (11.4)	86.2 (10)	0.909

**Table 3**

Mean differences between follow-up and baseline systolic and diastolic blood pressure measures by category of coffee consumption in 2725 participants of the HAPIEE cohort free of hypertension at baseline.

	Coffee consumption				P for trend
	<1 cup/d	1-2 cups/d	3-4 cups/d	>4 cups/d	
Systolic blood pressure, mmHg (mean, SD)					
Overall	19.2 (22.5)	17.4 (21.3)	17.0 (21.5)	14.8 (14.9)	0.047
Men	16.3 (20.5)	17.4 (21.0)	16.4 (18.0)	13.5 (15.9)	0.859
Women	21.7 (23.9)	17.4 (21.6)	17.4 (21.8)	16.2 (14.0)	0.013
Diastolic blood pressure, mmHg (mean, SD)					
Overall	7.5 (12.6)	7.7 (12.4)	7.9 (11.7)	8.5 (8.1)	0.514
Men	7.2 (11.5)	8.1 (12.1)	8.1 (10.9)	6.6 (8.6)	0.502
Women	7.8 (13.4)	7.4 (12.5)	7.8 (12.1)	10.6 (7.1)	0.752



**Table 4**

Uni- and multivariate adjusted odds ratios (95% confidence intervals)<sup>a</sup> of hypertension by categories of coffee consumption in 2725 participants of the HAPIEE cohort free of hypertension at baseline, overall and by gender.

	Coffee consumption			
	<1 cup/d	1-2 cups/d	3-4 cups/d	>4 cups/d
Overall				
Hypertension cases, n (%)	493 (67.1)	739 (64.4)	470 (58.9)	33 (73.3)
Unadjusted	1	0.89 (0.73, 1.08)	0.70 (0.57, 0.86)	1.35 (0.68, 2.66)
Age-adjusted	1	0.89 (0.73, 1.07)	0.70 (0.57, 0.86)	1.41 (0.71, 2.78)
Multivariate <sup>a</sup>	1	0.86 (0.68, 1.07)	0.75 (0.58, 0.95)	1.58 (0.85, 3.64)
Men				
Hypertension cases, n (%)	224 (67.1)	321 (67.9)	198 (62.1)	21 (84)
Unadjusted	1	1.03 (0.77, 1.39)	0.80 (0.58, 1.11)	2.57 (0.86, 7.69)
Age-adjusted	1	1.05 (0.77, 1.41)	0.81 (0.58, 1.12)	2.63 (0.87, 7.91)
Multivariate <sup>a</sup>	1	1.04 (0.73, 1.49)	0.92 (0.62, 1.35)	2.42 (0.66, 8.91)
Women				
Hypertension cases, n (%)	269 (67.1)	418 (62)	272 (56.8)	12 (60)
Unadjusted	1	0.80 (0.61, 1.0)	0.64 (0.48, 0.85)	0.74 (0.29, 1.84)
Age-adjusted	1	0.79 (0.61, 1.0)	0.64 (0.48, 0.84)	0.72 (0.28, 1.81)
Multivariate <sup>a</sup>	1	0.74 (0.55, 1.0)	0.65 (0.47, 0.90)	1.09 (0.36, 3.33)

<sup>a</sup>Adjusted for age, gender (except when analyses were stratified by sex), education, occupation, BMI, alcohol drinking, smoking status, physical activity level, past history of CVD, diabetes at baseline, cholesterol therapy at baseline, total energy intake, vitamin supplement use, oral contraceptives use, and sodium and potassium intakes.

**Table 5**

Adjusted odds ratios (95% confidence intervals)<sup>a</sup> of hypertension in smokers and non-smokers by baseline categories of coffee consumption in 2725 participants of the HAPIEE cohort free of hypertension at baseline, overall and by gender.

	Coffee consumption			
	<1 cup/d	1-2 cups/d	3-4 cups/d	>4 cups/d
Smokers				
Overall, multivariate <sup>a</sup>	1	0.96 (0.73, 1.26)	0.96 (0.73, 1.26)	1.41 (0.41, 4.86)
Men	1	1.48 (0.94, 2.34)	1.51 (0.91, 2.34)	2.32 (0.22, 24.47)
Women	1	0.73 (0.51, 1.04)	0.73 (0.49, 1.07)	1.01 (0.23, 4.50)
Non-smokers				
Overall, multivariate <sup>a</sup>	1	0.63 (0.41, 0.96)	0.44 (0.28, 0.69)	0.89 (0.31, 2.53)
Men	1	0.52 (0.27, 0.98)	0.41 (0.21, 0.79)	1.52 (0.28, 8.03)
Women	1	0.75 (0.42, 1.34)	0.54 (0.29, 0.99)	0.68 (0.16, 2.88)

<sup>a</sup>Adjusted for age, gender (except when analyses were stratified by sex), education, occupation, BMI, alcohol drinking, physical activity level, past history of CVD, diabetes at baseline, cholesterol therapy at baseline, total energy intake, vitamin supplement use, oral contraceptives use, and sodium and potassium intakes.