Coffee Consumption and Risk of Type 2 Diabetes Mellitus Among Middle-aged Finnish Men and Women

Jaakko Tuomilehto, MD, PhD
Gang Hu, MD, PhD
Siamak Bidel, MD
Jaana Lindström, MSc
Pekka Jousilahti, MD, PhD

CENTURIES OF COFFEE DRINKING has made it the most consumed beverage in the world. During the last decade, research has attempted to make clear health benefits or detriments received from coffee drinking. Effects of coffee and caffeine on cardiovascular disease, hypertension, neurological diseases, different types of cancer, hormonal changes, gallstones, as well as diabetes mellitus (DM) have been studied through epidemiological, clinical, or experimental research. Type 2 DM is one of the diseases that is largely determined by lifestyle factors.

The role of coffee in relation to DM has not been investigated thoroughly. A large Dutch cohort study recently showed an inverse association between coffee consumption and the risk of DM. It is well known that caffeine stimulates insulin secretion of the pancreatic beta cells in vivo. However, coffee with its complex compounds may influence many other processes that may take part in the development of DM. According to international statistics, the Finnish population has the highest per capita coffee consumption in the world with 11.3 kg in 2000. Therefore, research into potential health effects of coffee in this population is of particular interest. Our large prospective study aimed at determining whether the suggested inverse relationship between coffee and type 2 DM exists among the Finnish population.

Context Only a few studies of coffee consumption and diabetes mellitus (DM) have been reported, even though coffee is the most consumed beverage in the world.

Objective To determine the relationship between coffee consumption and the incidence of type 2 DM among Finnish individuals, who have the highest coffee consumption in the world.

Design, Setting, and Participants A prospective study from combined surveys conducted in 1982, 1987, and 1992 of 6974 Finnish men and 7655 women aged 35 to 64 years without history of stroke, coronary heart disease, or DM at baseline, with 175682 person-years of follow-up. Coffee consumption and other study parameters were determined at baseline using standardized measurements.

Main Outcome Measures Hazard ratios (HRs) for the incidence of type 2 DM were estimated for different levels of daily coffee consumption.

Results During a mean follow-up of 12 years, there were 381 incident cases of type 2 DM. After adjustment for confounding factors (age, study year, body mass index, systolic blood pressure, education, occupational, commuting and leisure-time physical activity, alcohol and tea consumption, and smoking), the HRs of DM associated with the amount of coffee consumed daily (0-2, 3-4, 5-6, 7-9, 10 cups) were 1.00, 0.71 (95% confidence interval [CI], 0.48-1.05), 0.39 (95% CI, 0.25-0.60), 0.39 (95% CI, 0.20-0.74), and 0.21 (95% CI, 0.06-0.69) (P for trend = .001) in women, and 1.00, 0.73 (95% CI, 0.47-1.13), 0.70 (95% CI, 0.45-1.05), 0.67 (95% CI, 0.40-1.12), and 0.45 (95% CI, 0.25-0.81) (P for trend = .12) in men, respectively. In both sexes combined, the multivariate-adjusted inverse association was significant (P for trend < .001) and persisted when stratified by younger and older than 50 years; smokers and never smokers; healthy weight, overweight, and obese participants; alcohol drinker and non-drinker; and participants drinking filtered and nonfiltered coffee.

Conclusion Coffee drinking has a graded inverse association with the risk of type 2 DM; however, the reasons for this risk reduction associated with coffee remain unclear.

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addition, we evaluated a possible effect modification of the major determinants of type 2 DM and assessed the effects of different types of prepared coffee on the risk of DM.

**METHODS**

**Participants**

We performed baseline surveys in 2 eastern Finnish provinces, North Karelia and Kuopio, and in the Turku-Loiarna region in southwestern Finland in 1982, 1987, and 1992. The survey was expanded to the Helsinki capital area in 1992. In the 3 surveys, the sample included participants aged 25 to 64 years. The 1982, 1987, and 1992 cohorts were combined in this analysis. The original random sample was stratified by sex and 4 equally large 10-year age groups according to the World Health Organization MONItoring trends and determinants of CArdiovascular disease (MONICA) protocol16,17 and consisted of 21,630 participants. The participation rate varied by year from 74% to 88%.18 Our analysis included 16,670 participants aged 35 to 64 years due to the few cases of type 2 DM in participants aged 25 to 34 years during the follow-up. The final sample comprised 6974 men and 7655 women after excluding participants diagnosed with coronary heart disease or stroke (n=590), participants with known DM at baseline (n=435), and participants with incomplete data on any variables required for this analysis (n=1016). We excluded participants with coronary heart disease and stroke because there may be bias regarding their exposure (coffee drinking due to their disease) or confounding factors (diet and physical activity, their survival probability is lower, and they may be using drugs that trigger DM). These surveys were conducted according to the ethical rules of the National Public Health Institute and the investigations were performed in accordance with the Declaration of Helsinki. At the time the baseline surveys were performed, oral informed consent was obtained from the participants and if not received, the survey data were not collected from these participants (they were considered nonresponders).

**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 alcohol, coffee, and tea consumption. Education level, measured as the total number of school years, was divided into birth cohort specific tertiles. Physical activity included occupational, commuting, and leisure-time physical activity. A detailed description of the questions is presented elsewhere, and these questions were the same as those used in the studies in the Nordic countries20,21 and similar to those used and validated in the Seven Countries study.21

The participants reported their occupational physical activity as light, moderate, or active. The daily commuting journey to or from work was grouped into 3 categories: using motorized transportation or not working outside the home (0 minutes of walking or cycling); walking or bicycling 1 to 29 minutes; and walking or bicycling 30 or more minutes. Self-reported leisure-time physical activity was classified as low, moderate, or high. Based on the responses, the participants were classified as never, ex-smokers, or current smokers. Current smokers were categorized into those participants who smoked less than 20 or 20 or more cigarettes per day.

The participants were asked, “How many cups of coffee or tea do you drink per day?” Coffee consumption was categorized into 5 categories: 0 to 2 cups, 3 to 4 cups, 5 to 6 cups, 7 to 9 cups, and 10 or more cups. Tea consumption was categorized as none, 1 to 2 cups, and 3 or more cups because only a few people drank tea. Alcohol consumption was categorized as none, 1 to 100, 101 to 300, or more than 300 g of alcohol per week. Because only a few women drank more than 300 g of alcohol per week, we combined the 2 higher categories in women.

At the study site, specially trained nurses measured height, weight, and blood pressure using the standardized protocol according to the World Health Organization MONICA project. Blood pressure was measured from the right arm of the participant who was seated for 5 minutes before the measurement was taken using a standard sphygmomanometer. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. In stratified analyses, the participants were classified in 3 categories: normal weight (BMI <23.0), overweight (25 to <30), and obese (≥30).

**Diagnosis of DM**

We ascertained incident cases of DM from the National Hospital Discharge Register and the Drug Register of the National Social Insurance Institution. These register data were linked to the risk factor survey data with the unique personal identification numbers assigned to every resident of Finland. Antidiabetic drugs prescribed by a physician are free of charge in Finland subject to approval of the application to the National Social Insurance Institution with a case history prepared by the treating physician attached. The physician confirms the diagnosis of DM on the basis of the World Health Organization criteria after 198022; before 1980, Finnish national guidelines were applied. All patients receiving free-of-charge medication (either oral antidiabetic agents or insulin) are entered into a register maintained by the National Social Insurance Institution. The National Hospital Discharge Register includes hospitalizations for patients admitted to hospitals with a primary or secondary diagnosis of DM in Finland nationwide. Follow-up of each participant in our present analysis continued until December 31, 1998, or until death.

**Statistical Analyses**

Sex-specific differences in risk factors based on different levels of coffee consumption were tested using univariate analysis of variance or logistic regression after adjustment for age and study year. The association between coffee consumption at baseline and the risk of type 2 DM was analyzed by using Cox proportional hazards regression...
models. Different levels of coffee consumption were included in the models as dummy variables. All analyses were adjusted for age, study year, BMI, systolic blood pressure, education, occupational, commuting, and leisure-time physical activity, alcohol and tea drinking, and smoking. 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. 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, men and women were combined in subgroup analyses adjusted for sex. Statistical significance was considered to be \( P < .05 \). All statistical analyses were performed with SPSS version 11.0 (SPSS Inc, Chicago, Ill).

**RESULTS**

A total of 381 cases of type 2 DM were identified during a mean follow-up of 12 years. In general, older persons were less likely to drink coffee (Table 1). After adjustment for age and study year, higher coffee consumption was associated with higher BMI and cigarette smoking, and lower blood pressure, education level, light occupational physical activity, leisure-time physical activity, tea consumption, and alcohol use.

**Coffee Consumption and Risk of Type 2 DM**

Age-adjusted and study year–adjusted hazard ratios (HRs) of DM in participants who drank 0 to 2, 3 to 4, 5 to 6, 7

### Table 1. Baseline Characteristics Among Men and Women by Volume of Coffee Consumption*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Daily Coffee Consumption, Cups</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤2</td>
<td>3-4</td>
</tr>
<tr>
<td>No. of participants</td>
<td>1251</td>
<td>1732</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>49.1 (8.4)</td>
<td>49.0 (8.5)</td>
</tr>
<tr>
<td>Body mass index, mean (SD)†</td>
<td>26.6 (3.7)</td>
<td>27.0 (3.6)</td>
</tr>
<tr>
<td>Blood pressure, mean (SD), mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>143 (19)</td>
<td>143 (19)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>89 (12)</td>
<td>88 (11)</td>
</tr>
<tr>
<td>Education, mean (SD), y‡</td>
<td>9.9 (4.2)</td>
<td>9.5 (3.8)</td>
</tr>
<tr>
<td>Physical activity, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Light occupational</td>
<td>573 (46)</td>
<td>737 (43)</td>
</tr>
<tr>
<td>Low leisure time</td>
<td>342 (27)</td>
<td>455 (26)</td>
</tr>
<tr>
<td>Walking or cycling to or from work &lt;30 min</td>
<td>1056 (84)</td>
<td>1472 (85)</td>
</tr>
<tr>
<td>Drinker, No. (%)§ Tea</td>
<td>847 (68)</td>
<td>766 (44)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>757 (61)</td>
<td>1065 (61)</td>
</tr>
<tr>
<td>Current smoker, No. (%)¶</td>
<td>211 (17)</td>
<td>379 (22)</td>
</tr>
<tr>
<td>Obesity, No. (%)¶</td>
<td>214 (17)</td>
<td>324 (19)</td>
</tr>
</tbody>
</table>

| No. of participants   | 1386 | 2544 | 2527 | 819 | 379  |
| Age, mean (SD), y    | 49.3 (8.8) | 49.7 (8.5) | 49.0 (8.4) | 47.1 (8.0) | 45.6 (7.6) | <.001   |
| Body mass index, mean (SD)† | 26.4 (4.9) | 26.4 (4.7) | 26.9 (4.8) | 27.3 (4.9) | 27.5 (5.0) | <.001   |
| Blood pressure, mean (SD), mm Hg |           |           |           |           |       |
| Systolic              | 141 (22) | 141 (22) | 141 (21) | 139 (20) | 138 (20) | .02 |
| Diastolic             | 84 (11) | 84 (11) | 84 (11) | 82 (11) | 82 (11) | <.001   |
| Education, mean (SD), y‡ | 10.0 (4.0) | 9.6 (3.7) | 9.1 (3.4) | 8.8 (3.2) | 8.6 (3.5) | <.001   |
| Physical activity, No. (%) |           |           |           |           |       |
| Light occupational    | 726 (52) | 1178 (46) | 1036 (41) | 300 (37) | 128 (34) | <.001   |
| Low leisure time      | 466 (34) | 763 (30) | 912 (36) | 333 (41) | 164 (43) | <.001   |
| Walking or cycling to or from work <30 min | 1085 (78) | 1890 (74) | 1923 (76) | 618 (76) | 292 (77) | .04   |
| Drinker, No. (%)§ Tea | 920 (66) | 1113 (44) | 645 (26) | 122 (15) | 48 (13) | <.001   |
| Alcohol               | 572 (41) | 1051 (41) | 905 (36) | 302 (37) | 145 (38) | .003   |
| Current smoker, No. (%)¶ | 93 (7) | 229 (9) | 346 (14) | 148 (18) | 147 (39) | <.001   |
| Obesity, No. (%)¶     | 278 (20) | 512 (20) | 577 (23) | 192 (23) | 82 (22) | <.001   |

*Adjusted for age and study year.
†Calculated as weight in kilograms divided by the square of height in meters.
‡Defined as the total number of school years.
§Defined as drinking 1 or more cups per day of tea or 1 or more grams per week of alcohol.
¶Defined as smoking 1 or more cigarettes per day.
*Defined as body mass index of 30 or higher.
The risk of DM did not differ between total coffee abstainers and light coffee drinkers (HR, 1.20; 95% CI, 0.74-1.97). Sex-adjusted and multivariate-adjusted (including coffee consumption) HRs of DM by tea consumption of 0, 1 to 2, or more cups were 1.00, 0.81 (95% CI, 0.63-1.05), and 0.98 (95% CI, 0.67-1.42; P for trend=.27), respectively. To avoid the potential bias from subclinical disease, additional analyses were also performed excluding cases of type 2 DM, which occurred during the first 4 years of follow-up (n=27). The sex-adjusted and multivariate-adjusted HRs by coffee consumption of 0 to 2, 3 to 4, 5 to 6, 7 to 9, and 10 or more cups did not vary and were 1.00, 0.74 (95% CI, 0.55-1.00), 0.54 (95% CI, 0.39-0.74), 0.54 (95% CI, 0.36-0.81), and 0.41 (95% CI, 0.25-0.68; P for trend<.001), respectively.

The risk of DM was significantly reduced in those participants who drank at least 10 cups of coffee (HR, 0.45; 95% CI, 0.25-0.81). When data for men and women were combined, sex-adjusted and multivariate-adjusted HRs were 1.00, 0.76 (95% CI, 0.57-1.01), 0.54 (95% CI, 0.40-0.73), 0.55 (95% CI, 0.37-0.81), and 0.39 (95% CI, 0.24-0.64; P for trend<.001), respectively.

The risk of DM was present in participants aged 35 to 49 years (P for trend=.23) and 50 to 64 years (P for trend=.001; Table 3). Similarly, the inverse association was observed in nonsmokers (P for trend=.001), in overweight participants (P for trend=.01), and in nondrinkers (P for trend<.001). A nonsignificant association was observed in smokers (P for trend=.07), in healthy weight participants (P for trend=.35), in participants who were obese (P for trend=.05), in alcohol drinkers (P for trend=.25), in filtered coffee drinkers (P for trend=.07), and in pot-boiled coffee drinkers (P for trend=.06). There were 22 incident cases of DM among participants aged 25 to 34 years at baseline who were not included in the analyses. An additional analysis including the youngest age group also did not change the results.

The type of coffee consumption was assessed in the surveys from 1987 and 1992. More than 80% of Finnish coffee consumers used filtered coffee at baseline. There was no interaction be-

Table 2. Development of Type 2 Diabetes by Volume of Coffee Consumption

<table>
<thead>
<tr>
<th>Daily Coffee Consumption, Cups</th>
<th>≤2</th>
<th>3-4</th>
<th>5-6</th>
<th>7-9</th>
<th>≥10</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of new cases</td>
<td>41</td>
<td>48</td>
<td>67</td>
<td>28</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>14,191</td>
<td>20,054</td>
<td>25,704</td>
<td>11,480</td>
<td>10,426</td>
<td></td>
</tr>
<tr>
<td>Adjustment for age and study year, HR (95% CI)</td>
<td>1.00</td>
<td>0.83 (0.54-1.25)</td>
<td>0.88 (0.60-1.30)</td>
<td>0.86 (0.53-1.39)</td>
<td>0.69 (0.40-1.19)</td>
<td>.74</td>
</tr>
<tr>
<td>Multivariate adjustment, HR (95% CI)*</td>
<td>1.00</td>
<td>0.73 (0.47-1.13)</td>
<td>0.70 (0.45-1.05)</td>
<td>0.67 (0.40-1.12)</td>
<td>0.45 (0.25-0.81)</td>
<td>.12</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of new cases</td>
<td>46</td>
<td>68</td>
<td>48</td>
<td>13</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>15,821</td>
<td>30,367</td>
<td>32,036</td>
<td>10,523</td>
<td>4980</td>
<td></td>
</tr>
<tr>
<td>Adjustment for age and study year, HR (95% CI)</td>
<td>1.00</td>
<td>0.72 (0.49-1.04)</td>
<td>0.49 (0.32-0.73)</td>
<td>0.47 (0.25-0.87)</td>
<td>0.26 (0.08-0.85)</td>
<td>.002</td>
</tr>
<tr>
<td>Multivariate adjustment, HR (95% CI)*</td>
<td>1.00</td>
<td>0.71 (0.48-1.05)</td>
<td>0.39 (0.25-0.60)</td>
<td>0.39 (0.20-0.74)</td>
<td>0.21 (0.06-0.69)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Men and Women Combined†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of new cases</td>
<td>87</td>
<td>116</td>
<td>115</td>
<td>41</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>30,112</td>
<td>50,421</td>
<td>57,740</td>
<td>22,003</td>
<td>15,406</td>
<td></td>
</tr>
<tr>
<td>Adjustment for age and study year, HR (95% CI)</td>
<td>1.00</td>
<td>0.79 (0.59-1.04)</td>
<td>0.67 (0.50-0.88)</td>
<td>0.66 (0.46-0.96)</td>
<td>0.53 (0.33-0.85)</td>
<td>.02</td>
</tr>
<tr>
<td>Multivariate adjustment, HR (95% CI)*</td>
<td>1.00</td>
<td>0.76 (0.57-1.01)</td>
<td>0.54 (0.40-0.73)</td>
<td>0.55 (0.37-0.81)</td>
<td>0.39 (0.24-0.64)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio.
*Adjusted for age, study year, body mass index, systolic blood pressure, education, occupational physical activity (light, moderate, and active), walking or cycling to or from work (0, 1-29, and ≥30 min/d), leisure time physical activity (low, moderate, and high), cigarette smoking (never, past, and current smoking of 1-19 or ≥20 cigarettes/d), alcohol consumption (0, 1-100, 101-300, and >300 g/wk), and tea consumption (none, 1-2, and ≥3 cups/d).
†Also adjusted for sex.
tween the type of coffee and the amount of coffee for the risk of type 2 DM (χ² = 2.63, 0.85, and 2.13 for men, women, and for men and women combined, respectively; all P > 0.10). Men and women who drank pot-boiled coffee without filtering showed a similar inverse trend in risk of type 2 DM vs participants who drank filtered coffee (Table 3). However, men who drank pot-boiled coffee showed a 2.9 times higher risk for development of DM (HR, 2.86; 95% CI, 1.76-4.63) compared with men who drank filtered coffee after multivariate adjustment for risk factors of DM, including the amount of coffee consumed (Table 4). This association was also observed among men and women combined.

COMMENT

This study revealed unequivocal evidence for an inverse and graded association between coffee consumption and type 2 DM independent of other risk factors for type 2 DM. Because the Finnish population drinks more coffee than other populations, we had power to determine the risk of DM at high levels of coffee consumption. The significant inverse association between coffee consumption and the risk of type 2 DM was found in both sexes.

In a previous study among the Finnish population, no association between the coffee consumption and incidence of type 2 DM was observed. This may be due to the fact that the Finnish population drinks more coffee than other populations. Therefore, we had power to determine the risk of DM at high levels of coffee consumption.

### Table 3. Development of Type 2 Diabetes by Volume of Coffee Consumption Among Various Subpopulations*

<table>
<thead>
<tr>
<th>Daily Coffee Consumption, Cups</th>
<th>≤2</th>
<th>3–4</th>
<th>5–6</th>
<th>7–9</th>
<th>≥10</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–49</td>
<td>1.00</td>
<td>0.65 (0.37–1.13)</td>
<td>0.63 (0.37–1.11)</td>
<td>0.57 (0.29–1.15)</td>
<td>0.42 (0.20–0.91)</td>
<td>.23</td>
</tr>
<tr>
<td>50–64</td>
<td>1.00</td>
<td>0.82 (0.59–1.16)</td>
<td>0.53 (0.37–0.76)</td>
<td>0.57 (0.35–0.92)</td>
<td>0.38 (0.20–0.74)</td>
<td>.001</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1.00</td>
<td>0.77 (0.53–1.12)</td>
<td>0.44 (0.29–0.66)</td>
<td>0.41 (0.22–0.76)</td>
<td>0.42 (0.18–1.00)</td>
<td>.001</td>
</tr>
<tr>
<td>Ever or current</td>
<td>1.00</td>
<td>0.71 (0.45–1.13)</td>
<td>0.69 (0.44–1.09)</td>
<td>0.71 (0.41–1.22)</td>
<td>0.39 (0.21–0.73)</td>
<td>.07</td>
</tr>
<tr>
<td>Body mass index†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>1.00</td>
<td>0.53 (0.19–1.45)</td>
<td>0.65 (0.25–1.66)</td>
<td>0.36 (0.09–1.48)</td>
<td>0.15 (0.02–1.29)</td>
<td>.35</td>
</tr>
<tr>
<td>25–29.9</td>
<td>1.00</td>
<td>0.74 (0.46–1.18)</td>
<td>0.48 (0.29–0.80)</td>
<td>0.53 (0.28–1.01)</td>
<td>0.26 (0.10–0.68)</td>
<td>.01</td>
</tr>
<tr>
<td>≥30</td>
<td>1.00</td>
<td>0.86 (0.58–1.28)</td>
<td>0.59 (0.39–0.88)</td>
<td>0.59 (0.35–1.01)</td>
<td>0.56 (0.31–1.02)</td>
<td>.05</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.00</td>
<td>0.79 (0.55–1.13)</td>
<td>0.46 (0.32–0.68)</td>
<td>0.40 (0.23–0.70)</td>
<td>0.45 (0.25–0.83)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Drinker</td>
<td>1.00</td>
<td>0.79 (0.47–1.32)</td>
<td>0.78 (0.47–1.32)</td>
<td>0.97 (0.53–1.78)</td>
<td>0.38 (0.16–0.93)</td>
<td>.25</td>
</tr>
<tr>
<td>Type of coffee‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filtered</td>
<td>1.00</td>
<td>0.63 (0.34–1.16)</td>
<td>0.51 (0.27–0.96)</td>
<td>0.47 (0.19–1.17)</td>
<td>0.15 (0.03–0.66)</td>
<td>.07</td>
</tr>
<tr>
<td>Pot-boiled without filter</td>
<td>1.00</td>
<td>0.90 (0.40–2.01)</td>
<td>0.39 (0.17–0.80)</td>
<td>0.48 (0.18–1.28)</td>
<td>0.33 (0.09–1.18)</td>
<td>.06</td>
</tr>
</tbody>
</table>

*Adjusted for age, study year, body mass index, systolic blood pressure, education, occupational physical activity (light, moderate, and active), walking or cycling to or from work (0, 1-29, and ≥30 min/d), leisure time physical activity (low, moderate, and high), cigarette smoking (never, past, and current smoking of 1–19 or ≥20 cigarettes/d), alcohol consumption (0, 1–100, 101–300, and ≥300 g/wk), tea consumption (none, 1–2, and ≥3 cups/d), and sex.†Calculated as weight in kilograms divided by the square of height in meters.‡This analysis only includes surveys conducted from 1987 and 1992.

### Table 4. Development of Type 2 Diabetes by Different Type of Coffee Consumption According to Sex and Age*

<table>
<thead>
<tr>
<th>No. of New Diabetes Cases</th>
<th>Filtered Coffee</th>
<th>Pot-Boiled Coffee Without Filter</th>
<th>Person-Years</th>
<th>Filtered Coffee</th>
<th>Pot-Boiled Coffee Without Filter</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–49</td>
<td>40</td>
<td>36</td>
<td>25410</td>
<td>6915</td>
<td>1.00</td>
<td>2.86 (1.76–4.63)</td>
</tr>
<tr>
<td>50–64</td>
<td>23</td>
<td>25</td>
<td>9409</td>
<td>3992</td>
<td>1.00</td>
<td>2.72 (1.49–4.96)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–49</td>
<td>38</td>
<td>26</td>
<td>29,652</td>
<td>7943</td>
<td>1.00</td>
<td>1.30 (0.76–2.24)</td>
</tr>
<tr>
<td>50–64</td>
<td>32</td>
<td>22</td>
<td>11,430</td>
<td>4876</td>
<td>1.00</td>
<td>1.29 (0.72–2.33)</td>
</tr>
<tr>
<td>Men and women combined†</td>
<td>78</td>
<td>62</td>
<td>54,871</td>
<td>14,858</td>
<td>1.00</td>
<td>2.04 (1.43–2.92)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–49</td>
<td>23</td>
<td>15</td>
<td>34,034</td>
<td>5990</td>
<td>1.00</td>
<td>2.71 (1.33–5.53)</td>
</tr>
<tr>
<td>50–64</td>
<td>55</td>
<td>47</td>
<td>20,837</td>
<td>8888</td>
<td>1.00</td>
<td>1.87 (1.24–2.82)</td>
</tr>
</tbody>
</table>

*Adjusted for age, study year, body mass index, systolic blood pressure, education, occupational physical activity (light, moderate, and active), walking or cycling to or from work (0, 1–29, and ≥30 min/d), leisure time physical activity (low, moderate, and high), cigarette smoking (never, past, and current smoking of 1–19 or ≥20 cigarettes/d), alcohol consumption (0, 1–100, 101–300, and ≥300 g/wk), tea consumption (none, 1–2, and ≥3 cups/d), and coffee consumption (0–2, 3–4, 5–6, 7–9, ≥10 cups/d). This analysis only includes surveys conducted from 1987 and 1992.†Also adjusted for sex.
inci
dence of type 2 DM was observed. One possible explanation for the dif
erent results is that at the time of their baseline survey, in 1973 and 1977, most
Finnish individuals drank pot-boiled coffee. At the end of the 1960s, 75% of
the Finnish population drank boiled coffee but by 1987 this proportion had
decreased to 24%, although 69% drank filtered coffee. However, although we
were able to determine the type of the coffee consumed in our surveys in 1987
and 1992, there was no interaction
effect between type of coffee and amount of coffee on the risk of type 2
DM in either men or women. Never
theless, there was a significant, almost 3-fold, increase in the risk of diabetes
among men who drank pot-boiled cof
fe compared with men who drank fil
tered coffee.
Van Dam and Feskens
investigated the association between coffee consumption and risk of type 2
DM in a prospective study. They also ob
ained similar inverse associations be
 tween coffee consumption and the risk of type 2 DM, similar to our results. Re
cently, data from large US cohorts of
men and women also showed that long
term coffee consumption and total ca
feine intake were significantly associ
ated with a reduced risk of type 2 DM.
A Japanese cross-sectional study com
prising 1916 men and 2704 women
aged 40 to 50 years found that coffee
 intake or caffeine intake from coffee was
 inversely associated with the preva
lence of fasting hyperglycemia (fast
ing plasma glucose, \( \geq 110 \text{ mg/dL} \) (\( \geq 6.1 \text{ mmol/L} \)).

Although the biological mechanism
behind the inverse association be
 tween coffee consumption and the risk
of DM is unknown, several putative
mechanisms can be proposed. The pro
ective effect of coffee may be due to the
hibition of glucose-6-phosphatase ac
 tivity by chlorogenic acid. Hepatic glu
cose-6-phosphatase may be a key con
 trol site in the homeostatic regulation of
blood glucose concentration, and
glucose-6-phosphatase is widely held
to be a significant factor in the abnor
mally high rates of hepatic glucose pro
duction observed in the diabetic state.
Reduced glucose-6-phosphatase hy
drolysis or its inhibition may reduce
plasma glucose output leading to re
duced plasma glucose concen
tration. Hypoglycemic effect of chloro
genic acid has been presented in
streptozotocin-induced diabetic rats as
well. Johnston et al suggest that
chlorogenic acid might have an antago
nistic effect on glucose transport. It is
possible that habitual differences be
 tween the coffee consumers and differ
ent manufacturing process of coffee
from green seeds may also result in dif
ferent effects. For instance, roasting and
some other manipulation of process
ning coffee will partly destroy chloro
genic acid and may oxidize some other
compounds to form new compounds, leading subsequently to differential
metabolic effects.

In addition to the inhibitory effects of chlorogenic acid on glucose-6-
phosphatase affecting glucose regula
tion at hepatic stage, it has also been
reported to inhibit glucose transport
ers (sodium-dependent glucose trans
porter) at the intestinal stage. Coffee
may also influence the secretion of gas
trointestinal peptides such as glucagon-
like peptide 1 and gastric inhibitory
polypeptide, both of which are known
for their glucose lowering effects.

Coffee also contains magnesium, approxi
mately 11 mg per 100 g of dry cof
fe. This component is another pos
sible factor, which may result in positive
effects on glucose tolerance and pre
vention of type 2 DM. There is a sig
ificant inverse correlation between se
rum magnesium and the incidence of
type 2 DM; both serum and ionized
magnesium were consistently found to
be decreased in patients with DM.

It is well known that caffeine and the
ophylline are strong stimulants of pan
creatic beta cells. Stimulation of insu
lin secretion may be beneficial in people
at risk of type 2 DM who usually have
impaired insulin secretion. In addi
tion, caffeine may increase insulin sen
sitivity. It has also been suggested that
the thermogenic effect of caffeine may
overcome the energy imbalance accom
panied by unfavorable lifestyle and im
prove glucose homeostasis.

The inverse association between cof
fee consumption and the risk of DM
tended to be stronger in women than
in men, although the sex-interaction
was not statistically significant. Previ
ous studies have revealed that caffeine
may be positively associated with
plasma estrogen, plasma estradiol, and
sex hormone-binding globulin levels
and inversely related to testosterone
among postmenopausal women.
In addition phytoestrogens may
have beneficial effects in patients with
DM. Phytoestrogens content of coffee
and effects of caffeine on hormonal level
may explain the effects of coffee on the
risk of diabetes in women. Neverthe
less, in most populations, the preva
lence of type 2 DM is lower in women
than in men at premenopausal age.

A limitation of our study was that a
ucose tolerance test was not per
formed in the baseline and follow-up
surveys. Therefore, we could have
 missed some cases of asymptomatic
diet-treated diabetes, although the clin
ical diagnosis of diabetes from the hos
pital discharge register may have in part
avoided this potential underdiagnos
sis. Another source of misclassifica
ion may be that we used self-report for
data on coffee intake. However, the mis
classification of exposure is most prob
ably not systematically related to the
outcome and vice versa. Therefore, it
should not cause biased results but may
only weaken the observed association.
Finally, we cannot completely ex
clude the effects of residual confound
ing due to measurement error in the
assessment of confounding factors and
unmeasured factors such as diet (whole
grain consumption, intake of fiber, satu
rated and polyunsaturated fat, glyce
mic load of the diet, and total energy
intake). The Finnish population typi
cally drink their coffee without milk or
only add a very small volume of milk.

In conclusion, we found a strong and
graded inverse relationship between
coffee consumption and the risk of type
2 DM among Finnish men and women,
with the highest coffee

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consumption in the world. The mechanisms or process by which coffee contents may exert their beneficial effects on DM are nevertheless unclear. Several components of coffee may affect glucose regulation, such as chlorogenic acid on glucose-6-phosphatase, antioxidant activity of polyphenols on α-glucosidase, caffeine on insulin secretion on pancreatic beta cells, cumulative effects of phytoestrogens, and magnesium, which are suggested as the biological basis of our findings. Expanded investigation is required to explore these mechanisms, including randomized controlled trials.

Author Contributions: Dr Tuomilehto had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Tuomilehto, Hu, Jousilahti.

Acquisition of data: Tuomilehto, Hu.

Analysis and interpretation of data: Tuomilehto, Hu, Bidel, Lindstrom.

Drafting of the manuscript: Tuomilehto, Hu, Bidel, Lindstrom, Jousilahti.

Critical revision of the manuscript for important intellectual content: Hu, Bidel, Lindstrom, Statistical expertise: Tuomilehto, Hu, Lindstrom. Obtained funding: Tuomilehto, Hu, Jousilahti. Administrative, technical, or material support: Tuomilehto. Study supervision: Jousilahti.

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REFERENCES