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## Original Contribution

# Coffee Intake and Incidence of Erectile Dysfunction

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Coffee intake is suggested to have a positive impact on chronic diseases, yet its role in urological diseases such as erectile dysfunction (ED) remains unclear. We investigated the association of coffee intake with incidence of ED by conducting the Health Professionals Follow-Up Study, a prospective analysis of 21,403 men aged 40–75 years old. Total, regular, and decaffeinated coffee intakes were self-reported on food frequency questionnaires. ED was assessed by mean values of questionnaires in 2000, 2004 and 2008. Multivariable adjusted Cox proportional hazards models were used to compute hazard ratios for patients with incident ED ($n$ = 7,298). No significant differences were identified for patients with incident ED after comparing highest (≥4 cups/day) with lowest (0 cups/day) categories of total (hazard ratio (HR) = 1.00, 95% confidence interval (CI): 0.90, 1.11) and regular coffee intakes (HR = 1.00, 95% CI: 0.89, 1.13). When comparing the highest category with lowest category of decaffeinated coffee intake, we found a 37% increased risk of ED (HR = 1.37, 95% CI: 1.08, 1.73), with a significant trend ($P$ trend = 0.02). Stratified analyses also showed an association among current smokers ($P$ trend = 0.005). Overall, long-term coffee intake was not associated with risk of ED in a prospective cohort study.

coffee; decaffeinated coffee; erectile dysfunction

Abbreviations: BMI, body mass index; CI, confidence interval; ED, erectile dysfunction; FFQ, food frequency questionnaire; HPFS, Health Professionals Follow-up Study; HR, hazard ratio.

Coffee is a rich source of caffeine, antioxidants and anti-inflammatory compounds (1–4), and has been implicated to have a potentially beneficial role against chronic diseases. Yet, the role of coffee intake in urological diseases, specifically in erectile dysfunction (ED), remains undetermined (5–9). The prevalence of ED in American men aged 20 years or older is 18.4%, which suggests that more than 18 million people are affected (10, 11). Further, in a prospective study, 17.7% of men (aged 40–75 years) reported incident ED during a 14-year follow-up (12). Among older men, these numbers substantially increase, which affects overall quality of life (11, 13, 14).

An inverse association between coffee intake and improved erectile function is biologically plausible. In addition to being a major source of polyphenols, coffee has the potential to increase testosterone levels (15–17), initiate a series of pharmacologic reactions that lead to the relaxation of the cavernous smooth muscle, and improve blood supply through penile arteries (18). In a previous cross-sectional analysis using the National Health and Nutrition and Examination Survey from 2001–2004, a nationally representative sample of the US noninstitutionalized male population, the equivalent of 2–3 cups of coffee per day was associated with a lower likelihood of ED (19). A further investigation of this association was conducted among men with comorbidities such as obesity, hypertension and diabetes, which are strong risk factors for ED. The findings remained the same among obese and hypertensive men, but not among men with diabetes.

Given the inherent limitations of the cross-sectional study design and a relatively small total sample size ($n$ = 3,724) in the National Health and Nutrition and Examination Survey analyses, we decided to investigate prospectively the association of caffeinated and decaffeinated beverages with risk of ED in the Health Professionals Follow-up Study (HPFS). In the HPFS, we used an analytic sample of 21,403 men, 7,298 patients with incident ED, and a follow-up period of 10 years. Additionally, we investigated these associations among

men with lifestyle factors and comorbid conditions such as obesity, hypertension, diabetes, history of smoking, and marital status.

## METHODS

The HPFS is an ongoing prospective cohort study that started in 1986 with 51,529 middle-aged US male health professionals which included dentists, pharmacists, optometrists, osteopaths physicians, podiatrists, and veterinarians. They are followed-up with mailed questionnaires every 2 years to update their information on lifestyle and health outcomes and every 4 years to assess usual diet (94% response rate) (20). The HPFS is approved by the Human Subjects Committee at the Harvard T.H. Chan School of Public Health.

### Outcome assessment

On the 2000 questionnaire, HPFS participants were asked to rate their ability (without treatment) to have and maintain an erection sufficient for intercourse. Each question included a time grid with year/month increments (before 1986, 1986–1989, 1990–1994, 1995 or later, and in the past 3 months) to allow participants to report historically if and when erectile function changed. Participants were again asked to report their current function (without treatment) in 2004 and 2008. Response options on the 5-point scale included very poor, poor, fair, good, and very good. Only men who at baseline in 1998 were without prior diagnosis of ED; prostate, bladder, or testicular cancer; or CVD were included in our analyses. Date of diagnosis was defined as the date of return of the 2000 questionnaire, and we censored at first report of ED. Reports of poor or very poor erectile function in any of the periods from 2000 to 2008 were considered incident cases of ED (21, 22).

### Coffee intake assessment

Dietary data, including coffee intake, was collected from HPFS participants using food frequency questionnaires (FFQ), which calculated the cumulative dose of coffee intake. FFQ were administered in 1998 and subsequently every 4 years through 2010. In the FFQ, participants reported how frequently they consumed a specified portion of a food item over the previous year, with 9 possible answers ranging from "never or less than once a month" to "6 or more times per day." The FFQ included questions to assess the daily intake (number of cups) of regular and decaffeinated coffee. Previously, Feskanich et al. (23) conducted a validation study and found a high correlation ($r = 0.93$) between participant reports of coffee intake on the FFQ compared with 2 1-week diet records separated by 6 months.

### Statistical analysis

Each participant contributed person-time from the date of return of the 1998 questionnaire to the date of first report of ED or the end of follow-up in 2010. Coffee intake data was categorized according to levels of regular, decaffeinated and total (regular and decaffeinated) coffee intake. Because cardiovascular diseases share many similar diet risk factors as ED, we stopped updating the coffee intake and diet intake information when any cardiovascular disease was diagnosed during follow-up. In order to avoid bias due to reverse causality, we conducted analyses using cumulative average intake with a lag of 4 years to avoid using data on coffee intake from completed FFQ immediately before ED diagnosis (24) or development of cardiovascular disease and prostate, bladder or testicular cancers during follow-up.

Cox proportional hazards regressions were conducted to adjust for potential confounding by ED risk factors that were previously identified in this cohort and in other studies. We used left-truncated Cox proportional hazards for time-varying covariates, with a counting process data structure using age in months as the time scale. We also stratified based on calendar year to estimate the hazard ratios for coffee intake in relation to the risk of ED by using the lowest intake of quintile as the referent group (25, 26). Covariates were updated every other year. Multivariable models were adjusted for smoking (never, past, or current 1–14, 15–24, ≥25 cigarettes/day), BMI (weight in kilograms divided by height in meters squared; <25.0, 25.0–29.9, or ≥30.0), alcohol consumption (gram/day; 0, 0.1–4.9, 5.0–14.9, 15.0–29.9, or ≥30.0), total physical activity (metabolic equivalent task/week; quintiles), history of diabetes (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), history of cardiovascular disease (yes vs. no), energy intake (kcal/day; quintiles), marital status (married, divorced, separated, widowed, or never married), race (white, African-American, Asian-American, or other), Alternative Healthy Eating Index score (quintiles), difficulty of falling into sleep (yes vs. no), waking up during the night (yes vs. no), not feeling rested upon waking (yes vs. no), medication for lowering cholesterol (yes vs. no), medication for lowering blood pressure (yes vs. no) and sleep medicine (yes vs. no). To test for a linear trend across categories of coffee intake, we modeled intake as a continuous variable using the median intake for each category.

We conducted further stratified analyses to determine whether comorbidities and lifestyle factors such as hypertension, BMI, smoking, alcohol consumption and marital status modify the association between coffee intake and ED. Multiplicative interaction terms were incorporated into the models and likelihood-ratio tests were used to test for interaction. All analyses were conducted with SAS software, version 9 (SAS Institute, Inc., Cary, North Carolina). All $P$ values were 2-sided and $P < 0.05$ indicated statistical significance.

## RESULTS

During 10 years of follow-up among the 21,403 participants (median age of 62 years), a total of 7,298 men (34%) reported incident ED. Baseline characteristics of the participants according to categories of coffee intake in 1998 are shown in Tables 1 and 2. Overall, in 1998, 65% of cohort participants reported drinking at least 1 cup of coffee (total coffee) per day, and 11% reported consuming 4 or more cups of coffee daily. Men with higher total coffee intake had higher physical activity level, were more likely to be current smokers, and consumed more alcohol (Table 1). Similar results were observed among men with higher intake of regular coffee; in addition, they

**Table 1.** Baseline Age-Adjusted Characteristics by Total Coffee Consumption, Health Professionals Follow-up Study, 1998–2010

| Characteristic | Coffee Intake, cups/day | | | | | | | | | | *P* for Trend |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | None (*n* = 2,753) | | 0.01–0.50 (*n* = 2,506) | | 0.50–0.99 (*n* = 2,208) | | 1.00–3.99 (*n* = 11,576) | | ≥4.00 (*n* = 2,360) | | |
| | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | |
| Age, years | | 60.3 (8.1) | | 61.3 (8.5) | | 62.6 (8.7) | | 62.5 (8.5) | | 61.2 (7.6) | |
| BMI[a] | | 25.5 (3.7) | | 25.3 (3.4) | | 25.7 (3.3) | | 26.1 (3.4) | | 26.5 (3.5) | <0.0001 |
| Physical activity, METs/week | | 37.9 (41.1) | | 37.9 (43.1) | | 38.2 (40.1) | | 36.4 (39.2) | | 33.8 (36.5) | <0.0001 |
| Currently married | 91 | | 88 | | 90 | | 89 | | 90 | | 0.71 |
| Smoking status | | | | | | | | | | | |
| Never | 79 | | 68 | | 61 | | 47 | | 34 | | <0.0001 |
| Past | 19 | | 30 | | 37 | | 49 | | 55 | | <0.0001 |
| Current | 2 | | 2 | | 2 | | 5 | | 12 | | <0.0001 |
| Self-reported disease | | | | | | | | | | | |
| Hypertension | 13 | | 14 | | 16 | | 15 | | 12 | | 0.59 |
| High cholesterol | 40 | | 45 | | 46 | | 46 | | 43 | | <0.0001 |
| Difficulty falling asleep[b] | 21 | | 20 | | 21 | | 21 | | 19 | | 0.99 |
| Waking during the night[b] | 55 | | 54 | | 58 | | 59 | | 58 | | <0.0001 |
| Not feeling rested upon waking[b] | 23 | | 23 | | 23 | | 23 | | 24 | | 0.99 |
| Medication | | | | | | | | | | | |
| Low blood pressure | 19 | | 23 | | 25 | | 24 | | 20 | | 0.005 |
| Lower cholesterol | 11 | | 11 | | 14 | | 13 | | 12 | | 0.0002 |
| Sleep medication[b] | 3 | | 3 | | 3 | | 4 | | 3 | | 0.04 |
| Alcohol consumption, g/day | | 4.7 (9.7) | | 8.4 (12.1) | | 9.7 (12.4) | | 13.0 (14.4) | | 13.8 (15.7) | <0.0001 |
| Calories, kcal/day | | 1,972 (604) | | 1,967 (394) | | 1,944 (601) | | 2.011 (602) | | 2.092 (692) | <0.0001 |
| AHEI score | | 49.7 (11.7) | | 52.7 (11.4) | | 52.2 (11.2) | | 51.3 (11) | | 49.8 (10.7) | 0.72 |
| Regular coffee | | 0 (0) | | 0.1 (0.1) | | 0.4 (0.3) | | 1.6 (1.0) | | 3.6 (1.5) | <0.0001 |
| Decaffeinated coffee | | 0 (0) | | 0.1 (0.1) | | 0.3 (0.3) | | 0.7 (0.8) | | 1.3 (1.5) | <0.0001 |

Abbreviations: AHEI, Alternative Healthy Eating Index; BMI, body mass index; MET, metabolic equivalent of task; SD, standard deviation.
[a] Weight (kg)/height (m)$^2$.
[b] Variables were ascertained in 2004 questionnaire.

were less likely to be hypertensive and had poorer diet quality as measured by Alternative Healthy Eating Index scores (Table 2). High decaffeinated coffee drinkers had higher BMI and higher cholesterol levels, consumed more alcohol, and were more likely to be current or former smokers and hypertensive, but had slightly higher diet quality scores (Table 3).

Age-adjusted associations tended to show positive trends, but after adjusting for potential confounders including history of cardiovascular disease and lifestyle risk factors, we did not find any statistically significant association between greater intakes of total coffee (*P* for trend = 0.37) or regular coffee (*P* for trend = 0.90) and ED (Table 4). No significant differences were identified after comparing the highest (≥4 cups/day) and lowest (0 cups/day) categories of total coffee (hazard ratio (HR) = 1.00, 95% confidence interval (CI): 0.90, 1.11) and regular coffee (HR = 1.00, 95% CI: 0.89, 1.13) intakes. However, in comparing highest (≥4 cups/day) with lowest (0 cups/day) categories of decaffeinated coffee, there was a 37% increased risk of ED (HR = 1.37, 95% CI: 1.08, 1.73), and the trend was significant (*P* for trend = 0.02).

Further analyses were conducted to assess possible reverse causation, that is, if development of ED led to a change in coffee habits. Thus, we examined coffee intake with a 4-year lag period between total, regular, and decaffeinated coffee intakes and ED (Table 5). We did not find any statistically significant trend associated between intakes of total (*P* for trend = 0.63), regular (*P* for trend = 0.74) and decaffeinated (*P* for trend = 0.64) coffee and ED. Also, there were no significant differences between the highest and lowest categories of total (HR = 0.92, 95% CI: 0.81, 1.04) and regular (HR = 0.89, 95% CI: 0.77, 1.02) coffee intakes. After comparing the highest category of decaffeinated coffee intake with the lowest ((≥4 vs. 0 cups/day), we found a 43% increased risk of ED (HR = 1.43, 95% CI: 1.10, 1.87).

In stratified and multivariable analyses, we examined the association between coffee and ED across strata of smoking status (Table 6). We also stratified across strata of BMI categories, hypertension, marital status, and alcohol consumption (Web Tables 1–4, available at https://academic.oup.com/aje). No significant results were reported among strata of smoking

**Table 2.** Baseline Age-Adjusted Characteristics by Regular Coffee Consumption, Health Professionals Follow-up Study, 1998–2010

| Characteristics | Coffee Intake, cups/day | | | | | | | | | | *P* for Trend |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | None (*n* = 4,058) | | 0.01–0.50 (*n* = 4,112) | | 0.50–0.99 (*n* = 2,732) | | 1.00–3.99 (*n* = 9,167) | | ≥4.00 (*n* = 1,334) | | |
| | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | |
| Age, years | | 61.7 (8.7) | | 62.3 (8.5) | | 62.5 (8.6) | | 62.0 (8.3) | | 60.3 (7.2) | |
| BMI[a] | | 25.6 (3.5) | | 25.6 (3.3) | | 26.0 (3.5) | | 26.2 (3.4) | | 26.4 (3.4) | <0.0001 |
| Physical activity, METs/week | | 38.3 (42.8) | | 37.4 (39.3) | | 36.6 (38.9) | | 36.2 (39.3) | | 32.2 (34.9) | <0.0001 |
| Currently married | 91 | | 90 | | 89 | | 89 | | 88 | | <0.0001 |
| Smoking status | | | | | | | | | | | |
| Never | 72 | | 61 | | 52 | | 45 | | 34 | | <0.0001 |
| Past | 26 | | 36 | | 45 | | 49 | | 52 | | <0.0001 |
| Current | 2 | | 3 | | 4 | | 5 | | 14 | | <0.0001 |
| Self-reported disease | | | | | | | | | | | |
| Hypertension | 15 | | 16 | | 17 | | 14 | | 10 | | 0.0002 |
| High cholesterol | 43 | | 47 | | 47 | | 45 | | 42 | | 0.47 |
| Difficulty falling asleep[b] | 22 | | 22 | | 24 | | 20 | | 21 | | 0.09 |
| Waking during the night[b] | 56 | | 57 | | 59 | | 59 | | 56 | | 0.02 |
| Not feeling rested upon waking[b] | 23 | | 24 | | 23 | | 23 | | 22 | | 0.29 |
| Medication | | | | | | | | | | | |
| Low blood pressure | 22 | | 24 | | 25 | | 22 | | 18 | | 0.10 |
| Lower cholesterol | 12 | | 13 | | 14 | | 13 | | 11 | | 0.97 |
| Sleep medication[b] | 3 | | 3 | | 3 | | 4 | | 3 | | 0.40 |
| Alcohol consumption, g/day | | 6.2 (11.1) | | 10.0 (13.3) | | 10.9 (12.6) | | 13.5 (14.7) | | 13.9 (15.7) | <0.0001 |
| Calories, kcal/day | | 1,944 (587) | | 1,976 (605) | | 1,980 (607) | | 2,033 (606) | | 2,100 (642) | <0.0001 |
| AHEI score | | 50.7 (11.7) | | 52.3 (11.2) | | 52.2 (10.9) | | 50.9 (11) | | 48.8 (10.6) | <0.0001 |
| Total coffee | | 0.3 (0.7) | | 0.9 (1.0) | | 1.5 (0.9) | | 2.7 (1.0) | | 5.0 (0.9) | <0.0001 |
| Decaffeinated coffee | | 0.3 (0.7) | | 0.7 (1.0) | | 0.8 (0.9) | | 0.6 (0.8) | | 0.3 (0.6) | <0.0001 |

Abbreviations: AHEI, Alternative Healthy Eating Index; BMI, body mass index; MET; metabolic equivalent of task; SD, standard deviation.
[a] Weight (kg)/height (m)$^2$.
[b] Variables were ascertained in the 2004 questionnaire.

status for total (*P* for interaction = 0.11) and regular (*P* for interaction = 0.80) coffee intakes, Table 4). However, among current smokers there was a positive trend associated between decaffeinated coffee intake and ED (*P* for trend = 0.005 and *P* for interaction = 0.06).

Among categories of BMI (<25.0, 25.0–29.9, or ≥30.0), the associations of total, regular and decaffeinated coffee intake with ED did not reach statistical significance (*P* for interaction = 0.07, 0.16, and 0.88, respectively; Web Table 1). Similar findings were identified after stratifying for history of hypertension (*P* for interaction = 0.25, 0.25, and 0.72, respectively; Web Table 2), marital status (*P* for interaction = 0.32, 0.67, and 0.08, respectively, Web Table 3), and alcohol consumption (*P* for interaction = 0.70, 0.99, and 0.93, respectively; Web Table 4). Further stratified analyses were conducted by age (<70 or ≥70), history of diabetes (yes vs. no), medication for lowering blood pressure (yes vs. no), and difficulty of falling into sleep (yes vs. no), but no significant associations were found (data not shown).

## DISCUSSION

In the present large observational study that investigated prospectively the association of coffee intake with ED, we observed no significant associations between intakes of total and regular coffee and ED. For decaffeinated coffee intake, there was a significant association after comparing the highest with the lowest intake and also a significant trend. In stratified analyses, none of the modifiable lifestyle factors influenced the association of coffee intake with ED, though the positive association between decaffeinated coffee and ED was observed most strongly in the stratum of current smokers, and possibly suggests residual confounding.

Coffee intake has potential health benefits for various health outcomes (27–30). Yet, the present prospective investigation, which included 21,403 men followed for 10 years with a 34% rate of patients with incident ED (*n* = 7,298), did not support this association. Unlike in other studies in which investigators found potential associations that could potentially be the result

**Table 3.** Baseline Age-Adjusted Characteristics by Decaffeinated Coffee Consumption, Health Professionals Follow-up Study, 1998–2010

| Characteristic | Coffee Intake, cups/day | | | | | | | | | | *P* for Trend |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | None ($n$ = 6,787) | | 0.01–0.50 ($n$ = 7,280) | | 0.50–0.99 ($n$ = 3,041) | | 1.00–3.99 ($n$ = 4,088) | | ≥4.00 ($n$ = 207) | | |
| | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | % | Mean (SD) | |
| Age, years | | 61.2 (8.3) | | 61.5 (8.3) | | 62.6 (8.5) | | 63.4 (8.3) | | 63.3 (8.3) | |
| BMI[a] | | 25.9 (3.6) | | 25.8 (3.3) | | 26.0 (3.3) | | 26.3 (3.4) | | 26.8 (3.5) | <0.0001 |
| Physical activity, METs/week | | 36.1 (40) | | 37.2 (40.8) | | 36.4 (36.9) | | 36.6 (39.1) | | 34.6 (38.9) | 0.60 |
| Currently married | 88 | | 89 | | 90 | | 92 | | 95 | | <0.0001 |
| Smoking status | | | | | | | | | | | |
| Never | 59 | | 56 | | 51 | | 41 | | 31 | | <0.0001 |
| Past | 35 | | 41 | | 45 | | 53 | | 59 | | <0.0001 |
| Current | 6 | | 3 | | 4 | | 5 | | 11 | | 0.90 |
| Self-reported disease | | | | | | | | | | | |
| Hypertension | 13 | | 13 | | 16 | | 17 | | 20 | | <0.0001 |
| High cholesterol | 41 | | 45 | | 47 | | 49 | | 51 | | <0.0001 |
| Difficulty falling asleep[b] | 19 | | 22 | | 22 | | 21 | | 23 | | 0.03 |
| Waking during the night[b] | 53 | | 58 | | 62 | | 62 | | 62 | | <0.0001 |
| Not feeling rested upon waking[b] | 21 | | 23 | | 25 | | 24 | | 17 | | 0.008 |
| Medication | | | | | | | | | | | |
| Low blood pressure | 20 | | 22 | | 26 | | 26 | | 25 | | <0.0001 |
| Lower cholesterol | 11 | | 12 | | 14 | | 15 | | 12 | | <0.0001 |
| Sleep medication[b] | 3 | | 3 | | 3 | | 4 | | 3 | | 0.0007 |
| Alcohol consumption, g/day | | 9.8 (14.3) | | 11.1 (13.1) | | 11.8 (13.4) | | 12.7 (14.7) | | 14.6 (17.2) | <0.0001 |
| Calories, kcal/day | | 1,992 (614) | | 2,014 (602) | | 2,000 (611) | | 1,999 (595) | | 2,110 (604) | 0.40 |
| AHEI score | | 49.3 (11.5) | | 52.2 (10.9) | | 52.0 (11) | | 51.8 (10.8) | | 51.0 (10.4) | <0.0001 |
| Regular coffee | | 1.3 (1.6) | | 1.4 (1.3) | | 1.3 (1.2) | | 1.2 (1.2) | | 1.1 (1.2) | <0.0001 |
| Decaffeinated coffee | | 1.3 (1.6) | | 1.6 (1.3) | | 2.0 (1.2) | | 3.0 (1.3) | | 5.6 (1.3) | <0.0001 |

Abbreviations: AHEI, Alternative Healthy Eating Index; BMI, body mass index; MET; metabolic equivalent of task; SD, standard deviation.
[a] Weight (kg)/height (m)$^2$.
[b] Variables were ascertained in the 2004 questionnaire.

of residual confounding (31), we controlled for a large number of confounders (e.g., sleep problems).

Relatively few studies have investigated the independent association between coffee intake and ED in prospective population-based studies, including our previous study (19), in which we found an inverse association. However, in that previous study, we used cross-sectional data and a smaller sample size ($n$ = 3,724). In a population-based prospective study of 202 patients with incident ED among Finnish men with 5 years of follow-up, Shiri et al. (9) found no association between coffee consumption and ED. No data were provided on decaffeinated coffee intake.

Some aspects of our prospective study merit discussion. Although we observed an increased risk for ED in men who consumed 4 cups/day or more of decaffeinated coffee compared with those who consumed 0 cups/day, we interpret these findings cautiously for the following reasons. First, only 0.9% of men consumed 4 of cups/day or more of decaffeinated coffee. Second, there is no strong biological plausibility between decaffeinated coffee intake and ED. During the process of decaffeination, some of the polyphenols and anti-inflammatory compounds may be removed (32–36), but we found no association between regular coffee consumption and ED. It is possible that deleterious chemical compounds may be added to the decaffeinated coffee in the process of decaffeination (34–39). Third, heavy drinkers of decaffeinated coffee had an unusual lifestyle, with comorbid characteristics such as higher BMI, more current and past smoking history, as well as more hypertension, high cholesterol and higher alcohol consumption, but they also had slightly better diets (Alternative Healthy Eating Index score). Interestingly, we observed an association between decaffeinated coffee intake and ED only among current smokers, suggesting that residual confounding may have accounted for the association.

Strengths of the present study include the large sample size, number of patients with incident ED, long follow-up data from participants, and detailed data on ED risk factors. These strengths increased our statistical power for the categorical

**Table 4.** Multivariable Associations of Cumulative Average Intakes of Total, Regular, and Decaffeinated Coffee With Erectile Dysfunction ($n$ = 21,403), Health Professionals Follow-up Study, 1998–2010

| Coffee Type and Consumption | No. of Person-Years | No. of ED Cases | Model 1[a] | | | Model 2[b] | | |
|---|---|---|---|---|---|---|---|---|
| | | | HR | 95% CI | *P* for Trend | HR | 95% CI | *P* for Trend |
| Total coffee, cups/day | | | | | 0.004 | | | 0.37 |
| None[c] | 24,630 | 829 | 1.00 | Referent | | 1.00 | Referent | |
| 0.01–0.50 | 23,167 | 764 | 0.92 | 0.83, 1.01 | | 0.93 | 0.84, 1.03 | |
| 0.50–0.99 | 19,705 | 738 | 0.94 | 0.85, 1.03 | | 0.92 | 0.83, 1.02 | |
| 1.00–3.99 | 103,629 | 4,242 | 1.04 | 0.96, 1.12 | | 0.99 | 0.92, 1.08 | |
| ≥4.00 | 18,861 | 725 | 1.08 | 0.97, 1.19 | | 1.00 | 0.90, 1.11 | |
| Regular coffee, cups/day | | | | | 0.09 | | | 0.90 |
| None[c] | 34,791 | 1,243 | 1.00 | Referent | | 1.00 | Referent | |
| 0.01–0.50 | 36,999 | 1,424 | 1.04 | 0.97, 1.12 | | 1.05 | 0.97, 1.13 | |
| 0.50–0.99 | 23,978 | 963 | 1.05 | 0.96, 1.14 | | 1.03 | 0.94, 1.12 | |
| 1.00–3.99 | 83,857 | 3,279 | 1.06 | 0.99, 1.13 | | 1.03 | 0.96, 1.10 | |
| ≥4.00 | 10,365 | 359 | 1.07 | 0.95, 1.20 | | 1.00 | 0.89, 1.13 | |
| Decaffeinated coffee, cups/day | | | | | 0.0005 | | | 0.02 |
| None[c] | 58,716 | 2,069 | 1.00 | Referent | | 1.00 | Referent | |
| 0.01–0.50 | 69,458 | 2,515 | 0.99 | 0.93, 1.05 | | 1.00 | 0.94, 1.06 | |
| 0.50–0.99 | 26,540 | 1,074 | 1.03 | 0.96, 1.11 | | 1.02 | 0.95, 1.10 | |
| 1.00–3.99 | 34,000 | 1,566 | 1.09 | 1.02, 1.17 | | 1.06 | 0.99, 1.13 | |
| ≥4.00 | 1,278 | 74 | 1.54 | 1.22, 1.95 | | 1.37 | 1.08, 1.73 | |

Abbreviations: CI, confidence interval; ED, erectile dysfunction; HR, hazard ratio.

[a] Model 1 was adjusted for age in months and calendar time.

[b] Model 2 was adjusted for the variables in model 1 and smoking (never, past, or current, categorized as 1–14, 15–24, ≥25 cigarettes/day), body mass index (weight in kilometers divided by height in meters squared; <25.0, 25.0–29.9, or ≥30.0), alcohol consumption (grams/day; 0, 0.1–4.9, 5.0–14.9, 15.0–29.9, or ≥30.0), total physical activity (metabolic equivalent of tasks per week; quintiles), history of diabetes (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), history of cardiovascular disease (yes vs. no), energy intake (kcal/day; quintiles), Alternative Healthy Eating Index score (quintiles), marital status (married, divorced, separated, widowed, or never married), race (white, African-American, Asian-American, or other), difficulty of falling into sleep (yes vs. no), waking during the night (yes vs. no), not feeling rested upon waking (yes vs. no), and use of cholesterol-lowering, blood pressure–lowering, or sleep-enhancing medication (yes vs. no).

[c] Included men who drank no regular or decaffeinated coffee.

**Table 5.** Four-Year Latent Period in the Multivariable Associations[a] of Total, Regular, and Decaffeinated Coffee Intakes With Erectile Dysfunction, Health Professionals Follow-up Study, 2002–2010

| Type of Coffee | Coffee Intake, cups/day | | | | | | | | | | *P* for Trend |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | No Coffee[b] | | 0.01–0.50 | | 0.50–0.99 | | 1.00–3.99 | | ≥4.00 | | |
| | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | |
| Total | 1.00 | Referent | 0.87 | 0.77, 0.98 | 0.86 | 0.76, 0.97 | 0.93 | 0.85, 1.02 | 0.92 | 0.81, 1.04 | 0.63 |
| Regular | 1.00 | Referent | 0.93 | 0.84, 1.02 | 0.98 | 0.88, 1.09 | 0.98 | 0.91, 1.07 | 0.89 | 0.77, 1.02 | 0.74 |
| Decaffeinated | 1.00 | Referent | 0.95 | 0.89, 1.03 | 0.95 | 0.87, 1.05 | 0.99 | 0.91, 1.08 | 1.43 | 1.10, 1.87 | 0.64 |

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Models were adjusted for age in months, calendar time, smoking (never, past, or current, categorized as 1–14, 15–24, ≥25 cigarettes/day), body mass index (weight in kilometers divided by height in meters squared; <25.0, 25.0–29.9, or ≥30.0), alcohol consumption (grams/day; 0, 0.1–4.9, 5.0–14.9, 15.0–29.9, or ≥30.0), total physical activity (metabolic equivalent of tasks per week; quintiles), history of diabetes (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), history of cardiovascular disease (yes vs. no), energy intake (kcal/day; quintiles), Alternative Healthy Eating Index score (quintiles), marital status (married, divorced, separated, widowed, or never married), race (white, African-American, Asian-American, or other), difficulty of falling into sleep (yes vs. no), waking during the night (yes vs. no), not feeling rested upon waking (yes vs. no), and use of cholesterol-lowering, blood pressure–lowering, or sleep-enhancing medication (yes vs. no).

[b] Included men who drank no regular or decaffeinated coffee.

**Table 6.** Associations[a] of Cumulative Average Intakes of Total Coffee, Regular Coffee, and Decaffeinated Coffee With Erectile Dysfunction, Stratified by Smoking Status, Health Professionals Follow-up Study, 1998–2010

| Type of Coffee and Smoking Status | Coffee Intake, cups/day | | | | | | | | | | *P* for Trend | *P* for Interaction |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No Coffee[b] | | 0.01–0.50 | | 0.50–0.99 | | 1.00–3.99 | | ≥4.00 | | | |
| | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | | |
| Total coffee | | | | | | | | | | | | 0.11 |
| Never smoker | 1.00 | Referent | 0.98 | 0.87, 1.10 | 0.91 | 0.80, 1.04 | 0.98 | 0.89, 1.08 | 0.99 | 0.84, 1.15 | 0.78 | |
| Past smoker | 1.00 | Referent | 0.90 | 0.74, 1.09 | 0.97 | 0.80, 1.17 | 1.01 | 0.86, 1.17 | 1.02 | 0.85, 1.22 | 0.23 | |
| Current smoker | 1.00 | Referent | 0.72 | 0.27, 1.93 | 0.72 | 0.26, 2.02 | 1.45 | 0.72, 2.95 | 1.23 | 0.59, 2.56 | 0.14 | |
| Regular coffee | | | | | | | | | | | | 0.80 |
| Never smoker | 1.00 | Referent | 1.01 | 0.92, 1.12 | 0.98 | 0.87, 1.10 | 1.00 | 0.92, 1.10 | 1.06 | 0.87, 1.29 | 0.86 | |
| Past smoker | 1.00 | Referent | 1.11 | 0.97, 1.26 | 1.09 | 0.95, 1.25 | 1.07 | 0.95, 1.20 | 1.05 | 0.88, 1.25 | 0.76 | |
| Current smoker | 1.00 | Referent | 1.23 | 0.62, 2.44 | 1.85 | 0.93, 3.70 | 1.50 | 0.84, 2.67 | 1.20 | 0.63, 2.27 | 0.55 | |
| Decaffeinated coffee | | | | | | | | | | | | 0.06 |
| Never smoker | 1.00 | Referent | 1.00 | 0.92, 1.09 | 0.97 | 0.87, 1.08 | 1.02 | 0.92, 1.13 | 1.30 | 0.82, 2.06 | 0.72 | |
| Past smoker | 1.00 | Referent | 0.94 | 0.86, 1.03 | 1.00 | 0.89, 1.11 | 1.00 | 0.91, 1.10 | 1.31 | 0.98, 1.74 | 0.34 | |
| Current smoker | 1.00 | Referent | 1.54 | 1.07, 2.21 | 1.54 | 0.98, 2.40 | 1.63 | 1.13, 2.35 | 2.64 | 0.88, 7.87 | 0.005 | |

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Included men who drank no regular or decaffeinated coffee.

[b] Models were adjusted for age in months, calendar time, smoking (never, past, or current, categorized as 1–14, 15–24, ≥25 cigarettes/day), body mass index (weight in kilometers divided by height in meters squared; <25.0, 25.0–29.9, or ≥30.0), alcohol consumption (grams/day; 0, 0.1–4.9, 5.0–14.9, 15.0–29.9, or ≥30.0), total physical activity (metabolic equivalent of tasks per week; quintiles), history of diabetes (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), history of cardiovascular disease (yes vs. no), energy intake (kcal/day; quintiles), Alternative Healthy Eating Index score (quintiles), marital status (married, divorced, separated, widowed, or never married), race (white, African-American, Asian-American, or other), difficulty of falling into sleep (yes vs. no), waking during the night (yes vs. no), not feeling rested upon waking (yes vs. no), and use of cholesterol-lowering, blood pressure–lowering, or sleep-enhancing medication (yes vs. no).

comparison groups and generalizability for studies with similar study populations, and also reduced residual confounding because of our well-characterized risk factors. We used repeated measurements and assessed cumulative dietary intake to more accurately assess long-term coffee intake and reduce measurement error. Yet, the present study has some limitations as well. First, definition of ED was self-reported by participants, which will inevitably be imperfect. However, health professionals tend to report medical conditions with high accuracy, and we have previously reported on classic risk factors for ED such as BMI and physical activity (12) which have been confirmed in other populations with more detailed assessments of patients with incident ED. Although we adjusted for several potential confounders, there is still the possibility of confounding from additional unmeasured factors. However, due to our detailed and updated adjustment for confounders, it is unlikely that these would fully account for the observed findings. Second, although detailed assessment of coffee intake was conducted, this was done every 4 years, therefore, any shorter-term (<4 years) fluctuation of the intake could have been missed. However, coffee intake is consistent over time. Third, no data were available on the preparation methods of coffee, information which can provide insight on the alteration of the chemical composition of coffee. Fourth, it is possible that coffee consumption over a longer time period could have influenced risk. Yet, it is notable that coffee consumption is relatively consistent over time and drinking habits during the study period correlated with prior coffee drinking. Fifth, future studies should focus on investigating a nonlinear association between coffee intake and ED. Finally, reverse causation did not seem to play a role in our findings, but it is possible that subtle alterations in health could have influenced coffee consumption even after including a 4-year lag in our sensitivity analyses.

In summary, we did not find an association, either positive or negative, between total or regular coffee intake and ED. However, decaffeinated-coffee intake seemed to be associated with ED, possibly because of residual confounding. None of the modifiable lifestyles factors influenced the association of coffee intake with ED.

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## REFERENCES

1. O'Keefe JH, Bhatti SK, Patil HR, et al. Effects of habitual coffee consumption on cardiometabolic disease, cardiovascular health, and all-cause mortality. *J Am Coll Cardiol*. 2013; 62(12):1043–1051.
2. León-Carmona JR, Galano A. Is caffeine a good scavenger of oxygenated free radicals? *J Phys Chem B*. 2011;115(15): 4538–4546.
3. Wilson KM, Kasperzyk JL, Rider JR, et al. Coffee consumption and prostate cancer risk and progression in the Health Professionals Follow-up Study. *J Natl Cancer Inst*. 2011;103(11):876–884.
4. Freedman ND, Park Y, Abnet CC, et al. Association of coffee drinking with total and cause-specific mortality. *N Engl J Med*. 2012;366(20):1891–1904.
5. Ferraro PM, Taylor EN, Gambaro G, et al. Caffeine intake and the risk of kidney stones. *Am J Clin Nutr*. 2014;100(6): 1596–1603.
6. Diokno AC, Brown MB, Herzog AR. Sexual function in the elderly. *Arch Intern Med*. 1990;150(1):197–200.
7. Akkus E, Kadioglu A, Esen A, et al. Prevalence and correlates of erectile dysfunction in Turkey: a population-based study. *Eur Urol*. 2002;41(3):298–304.
8. Berrada S, Kadri N, Mechakra-Tahiri S, et al. Prevalence of erectile dysfunction and its correlates: a population-based study in Morocco. *Int J Impot Res*. 2003;15(suppl 1):S3–S7.
9. Shiri R, Koskimäki J, Hakama M, et al. Effect of life-style factors on incidence of erectile dysfunction. *Int J Impot Res*. 2004;16(5):389–394.
10. Lue TF. Erectile dysfunction. *N Engl J Med*. 2000;342(24): 1802–1813.
11. Selvin E, Burnett AL, Platz EA. Prevalence and risk factors for erectile dysfunction in the US. *Am J Med*. 2007;120(2): 151–157.
12. Bacon CG, Mittleman MA, Kawachi I, et al. A prospective study of risk factors for erectile dysfunction. *J Urol*. 2006; 176(1):217–221.
13. Francis ME, Kusek JW, Nyberg LM, et al. The contribution of common medical conditions and drug exposures to erectile dysfunction in adult males. *J Urol*. 2007;178(2):591–596.
14. Guay AT, Spark RF, Bansal S, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of male sexual dysfunction: a couple's problem–2003 update. *Endocr Pract*. 2003;9(1):77–95.
15. Sansone A, Romanelli F, Gianfrilli D, et al. Endocrine evaluation of erectile dysfunction. *Endocrine*. 2014;46(3): 423–430.
16. Paton CD, Lowe T, Irvine A. Caffeinated chewing gum increases repeated sprint performance and augments increases in testosterone in competitive cyclists. *Eur J Appl Physiol*. 2010;110(6):1243–1250.
17. Kelly DM, Jones TH. Testosterone: a vascular hormone in health and disease. *J Endocrinol*. 2013;217(3):R47–R71.
18. Adebiyi A, Adaikan PG. Effect of caffeine on response of rabbit isolated corpus cavernosum to high K+ solution, noradrenaline and transmural electrical stimulation. *Clin Exp Pharmacol Physiol*. 2004;31(1–2):82–85.
19. Lopez DS, Wang R, Tsilidis KK, et al. Role of caffeine intake on erectile dysfunction in US men: results from NHANES 2001–2004. *PLoS One* 2015;10(4):e0123547.
20. Rimm EB, Giovannucci EL, Willett WC, et al. Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet*. 1991;338(8765):464–468.
21. Bacon CG, Mittleman MA, Kawachi I, et al. Sexual function in men older than 50 years of age: results from the Health Professionals Follow-up Study. *Ann Intern Med*. 2003;139(3): 161–168.
22. Gao X, Schwarzschild MA, O'Reilly EJ, et al. Restless legs syndrome and erectile dysfunction. *Sleep*. 2010;33(1):75–79.
23. Feskanich D, Rimm EB, Giovannucci EL, et al. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. *J Am Diet Assoc*. 1993;93(7):790–796.
24. Hu FB, Stampfer MJ, Rimm E, et al. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. *Am J Epidemiol*. 1999;149(6):531–540.
25. Cassidy A, Franz M, Rimm EB. Dietary flavonoid intake and incidence of erectile dysfunction. *Am J Clin Nutr*. 2016;103(2): 534–541.
26. Zhang X, Zhang MJ, Fine J. A proportional hazards regression model for the subdistribution with right-censored and left-truncated competing risks data. *Stat Med*. 2011;30(16): 1933–1951.
27. Loftfield E, Freedman ND, Graubard BI, et al. Association of coffee consumption with overall and cause-specific mortality in a large US prospective cohort study. *Am J Epidemiol*. 2015; 182(12):1010–1022.
28. Crippa A, Discacciati A, Larsson SC, et al. Coffee consumption and mortality from all causes, cardiovascular disease, and cancer: a dose-response meta-analysis. *Am J Epidemiol*. 2014;180(8):763–775.
29. Lu Y, Zhai L, Zeng J, et al. Coffee consumption and prostate cancer risk: an updated meta-analysis. *Cancer Causes Control*. 2014;25(5):591–604.
30. Je Y, Giovannucci E. Coffee consumption and total mortality: a meta-analysis of twenty prospective cohort studies. *Br J Nutr*. 2014;111(7):1162–1173.
31. Lopez DS, Wang R, Tsilidis KK, et al. Role of caffeine intake on erectile dysfunction in US men: results from NHANES 2001-2004. *PLoS One*. 2015;10(4):e0123547.
32. Pehl C, Pfeiffer A, Wendl B, et al. The effect of decaffeination of coffee on gastro-oesophageal reflux in patients with reflux disease. *Aliment Pharmacol Ther*. 1997;11(3):483–486.
33. Spiller MA. The coffee plant and its processing. *Prog Clin Biol Res*. 1984;158:75–89.
34. Borrelli RC, Visconti A, Mennella C, et al. Chemical characterization and antioxidant properties of coffee melanoidins. *J Agric Food Chem*. 2002;50(22):6527–6533.

35. Yu EK. Novel decaffeination process using cyclodextrins. *Appl Microbiol Biotechnol*. 1988;28(6):546.
36. Chen Y, Brown PH, Hu K, et al. Supercritical CO2 decaffeination of unroasted coffee beans produces melanoidins with distinct NF-κB inhibitory activity. *J Food Sci*. 2011;76(7):H182–H186.
37. Superko HR, Bortz W Jr, Williams PT, et al. Caffeinated and decaffeinated coffee effects on plasma lipoprotein cholesterol, apolipoproteins, and lipase activity: a controlled, randomized trial. *Am J Clin Nutr*. 1991;54(3):599–605.
38. Centers for Disease Control and Prevention (CDC). Fatal exposure to methylene chloride among bathtub refinishers – United States, 2000–2011. *MMWR Morb Mortal Wkly Rep*. 2012;61(7):119–122.
39. Melnick RL, Ward JM, Huff J. War on Carcinogens: industry disputes human relevance of chemicals causing cancer in laboratory animals based on unproven hypotheses, using kidney tumors as an example. *Int J Occup Environ Health*. 2013;19(4):255–260.