

## Consumption of coffee, green tea, oolong tea, black tea, chocolate snacks and the caffeine content in relation to risk of diabetes in Japanese men and women

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Although the inverse association between coffee consumption and risk of diabetes has been reported numerous times, the role of caffeine intake in this association has remained unclear. We evaluated the consumption of coffee and other beverages and food containing caffeine in relation to the incidence of diabetes. The study participants were 5897 men and 7643 women in a community-based cohort in Takayama, Japan. Consumption of coffee, green tea, oolong tea, black tea and chocolate snacks were measured with a semi-quantitative FFQ in 1992. At the follow-up survey in 2002, the development of diabetes and the time of diagnosis were reported. To assess the association, age, smoking status, BMI, physical activity, education in years, alcohol consumption, total energy intake, fat intake and women's menopausal status were adjusted. Among men who consumed one cup per month to six cups per week and among those who consumed one cup per d or more, the associated hazard ratios were 0.69 (95% CI 0.50, 0.97) and 0.69 (95% CI 0.49, 0.98) compared with those who drank little to no coffee, with a *P* value for trend of 0.32. The hazard ratios for women with the same coffee consumption patterns were 1.08 (95% CI 0.74, 1.60) and 0.70 (95% CI 0.44, 1.12), with a *P* value for trend of 0.03. The association between estimated total caffeine intake and risk of diabetes was insignificant both among men and among women. The results imply that coffee consumption decreased the risk of developing diabetes. The protective effect may exist aside from the influence of caffeine intake.

### Coffee: Diabetes mellitus: Caffeine: Japanese

The protective effect of heavy consumption of coffee on the development of diabetes has been reported in many epidemiological studies, substantially from European countries and the USA, where coffee is widely consumed<sup>(1–8)</sup>. Because caffeine is one of the biologically active components in coffee, its role in the association with diabetes has also been investigated as described below. Several clinical studies have shown that oral administration of caffeine increases thermogenesis and metabolism<sup>(9–11)</sup>. These results may support the protective effect of caffeine intake over the risk of diabetes through reducing the risk of obesity, although the studies have expressed a rather short-term effect. On the other hand, several other studies have shown that caffeine intake causes the reduction of glucose disposal and increases insulin resistance<sup>(12–14)</sup>. To assess the long-term effects of caffeine intake, observational studies have been conducted to examine the relationship between caffeine intake and the development of diabetes. The results of some of the studies indicated a lowered risk of diabetes with increased caffeine intake<sup>(15–19)</sup>. On the contrary, several studies showed that decaffeinated coffee also decreased the risk of diabetes<sup>(18–20)</sup>.

Caffeine is also contained in other dietary items such as tea and chocolate. In contrast to people in several European

countries and the USA, tea is commonly consumed in Japan, and, hence, it should also be considered as its source to evaluate caffeine intake among Japanese subjects. Three previous studies among Japanese people evaluated green tea consumption with the risk of diabetes, but the results were inconsistent<sup>(15,16,21)</sup>. Studies in the USA implied a protective effect of tea consumption on diabetes risk, although the upper 95% CI was at the null value; the hazard ratio was 0.77 (95% CI 0.59, 1.00) for a two cups per d increment in intake in one study<sup>(17)</sup>, and it was 0.88 (95% CI 0.64, 1.23) for four or more *v.* no cups per d in the other study<sup>(19)</sup>. Another study in the USA failed to show the association between tea consumption and risk of diabetes<sup>(18)</sup>. Chocolate snacks are relatively common in Japan, although the reported per capita consumption has been found to be lower than that in most Western countries: 23% of the consumption in the UK, and 37% of the consumption in the USA<sup>(22)</sup>.

We assessed the association between coffee consumption and risk of developing diabetes in a prospective cohort study among men and women in a general Japanese population. We further evaluated the consumption of beverages and foods containing caffeine. Total caffeine intake was estimated and discussed in relation to the risk of diabetes.

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## Materials and methods

Subjects in the present study were from a community-based cohort study conducted in Takayama City (Gifu, Japan). The rationale and design of the Takayama study have been described in detail elsewhere<sup>(23–25)</sup>. In 1992, 31 152 individuals aged 35 years and over completed a baseline self-administered questionnaire which included a semi-quantitative FFQ for 169 food items consumed in the previous year, and other questions asking about physical and demographic characteristics such as age, height, weight, marital status and length of education. Women's health issues including menopausal status and use of hormone replacement therapy were also asked. The questionnaire also asked about smoking status, previous diagnosis of diabetes and other medical and reproductive histories. To assess the amount of regular physical activity, the average time (in hours) spent for listed physical activities was sought, and the metabolic equivalents were estimated. The list contained vigorous sports (such as jogging, bicycling on hills, tennis, racquet ball, swimming laps, or aerobics), vigorous work requiring muscle strength and endurance (such as moving heavy furniture, loading or unloading trucks, shovelling, or other equivalent manual labour) and moderate sports or work (such as housework, brisk walking, golfing, bowling, bicycling on level ground, or gardening). Further details and the validity information of the physical activity questionnaire have been previously reported<sup>(26,27)</sup>. The participation rate for the questionnaire administered at baseline was 85.3%. In the cohort, participants who were younger than 70 years at baseline (*n* 26 546) were followed for the present study. Among them, 1120 participants died and 1058 participants moved out of Takayama between September 1992 and March 2000, as confirmed by the residential registry. For the remainder of the follow-up until July 2002, we did not have access to the residential registry, but we identified an additional 404 deaths using the obituaries issued by Takayama city. After excluding the deaths and relocations, we sent 23 964 participants a follow-up questionnaire in 2002. In response to sending out the questionnaire, we learned that an additional 1460 participants had moved out of Takayama, eighteen had died and fifty-one were physically unable to complete the questionnaire. Of the remaining subjects, 14 975 completed the questionnaire, which yielded the response rate of 66.7%. Compared with the 14 975 subjects, the 11 571 subjects without follow-up data were slightly younger (aged 50.3 v. 52.3 years among men and 50.8 v. 52.0 years among women), less likely to be educated 12 years or longer (43.9 v. 46.9% among men and 35.5 v. 39.4% among women), more likely to have high caffeine intake (139 v. 132 mg among men and 144 v. 138 mg among women), but were similar in terms of BMI.

For the present analysis, participants who reported a diagnosis of diabetes (*n* 541), cancer (*n* 274), or either myocardial infarction, angina or stroke (*n* 535) at baseline were excluded. We further excluded participants who were newly identified having diabetes at baseline from the follow-up questionnaire (*n* 85). After these exclusions, 5897 men and 7643 women were included in the present analysis.

The information on baseline consumption of coffee and other beverages and foods among the participants was derived from the FFQ administered at baseline. The validity

and reliability of the questionnaire and other detailed information have been described previously<sup>(24)</sup>. In the present study, we evaluated the following drinks: coffee, decaffeinated coffee, green tea, oolong tea and black tea. We also examined the consumption of chocolate snacks, since chocolate is also a source of caffeine<sup>(28,29)</sup>. Chocolate truffles and solid chocolate bars are common chocolate snacks in Japan. Since there were separate questions for cookies/biscuits and cake, chocolate cookies, chocolate-covered cookies and chocolate cake were not likely to be classified as chocolate snacks by many participants. The content of caffeine from coffee and tea was estimated by using data from the Standard Tables of Food Composition in Japan, 5th edition, published by the Science and Technology Agency of Japan. In the questionnaire, one serving was defined as 150 g for coffee and decaffeinated coffee, 100 g was defined as one serving for green tea and black tea, and 250 g was defined as one serving for oolong tea. The estimated content of caffeine per serving was 90 mg for coffee, 20 mg for green tea, 30 mg for black tea and 50 mg for oolong tea. The consumption of decaffeinated coffee was asked separately from the consumption of coffee, and, hence, estimated consumption of coffee and that of decaffeinated coffee were mutually exclusive. The caffeine content in chocolate snacks was defined as 12.5 mg per 100 g according to a literature review<sup>(28)</sup>. We estimated the intake of caffeine from each beverage and chocolate snack by totaling a weight proportional to the frequency of consumption in the questionnaire, and multiplying that total by the above caffeine content. We also estimated the intake of other nutrients based on the FFQ by referring to the same standard table. The intake of each nutrient was adjusted for total energy after log-transformation by using the residual method proposed by Willett<sup>(30)</sup>.

The participants who developed diabetes between the time of the baseline study and at the time of follow-up were identified in the questionnaire. All participants were asked if they had ever been diagnosed with diabetes, and, if so, how old they were at the time of the diagnosis. Using the information on their age at baseline and age at diagnosis, the time from baseline to diagnosis was estimated. Because thirty-one men and ten women who developed diabetes during the follow-up period did not provide the information regarding the time of diagnosis, we assigned median values of length to the diagnosis among participants for men and women separately.

### Statistical analysis

Participants were placed into categories based on the frequency of consumption of coffee, tea and chocolate snacks, roughly based on the distribution of consumption of each item in the current population. Three categories for frequency of coffee and oolong tea consumption were created: never or almost never, once per month to six times per week, and once per d or more. Four categories for frequency of green tea consumption were created: never or almost never, once per month to six times per week, once per d, and twice per d or more. For the consumption of decaffeinated coffee and black tea, two categories were created: never or almost never and once per month or more. The amount of chocolate snacks consumed was multiplied by the frequency of consumption, and put into three categories: never or almost never, one piece

per month to two or three pieces per month, and one piece per week or more. Caffeine intake was analysed in tertile groups. Cox proportional hazards models were used to assess the contributions of coffee, tea, chocolate consumption, and caffeine intake respectively, to the subsequent risk of developing diabetes. The age-adjusted model and multivariate model adjusted for potential confounders, age, smoking status, BMI, physical activity, education in years, alcohol consumption, total energy intake, fat intake and women's menopausal status were examined for each beverage and chocolate snacks respectively. To test for linear trends across categories, we modelled the median of each category of coffee, tea and chocolate consumption, and caffeine intake as a continuous variable.

All statistical analyses were performed by using SAS statistical software (version 9.1; SAS Institute, Inc., Cary, NC, USA). Statistical significance was considered to be  $P < 0.05$ . The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethics Committee at Gifu University Graduate School of Medicine. Written informed consent was obtained from all subjects.

## Results

Of the 5897 men and 7643 women participating in the study, 278 men and 175 women reported the development of diabetes during the follow-up. Baseline characteristics of the study participants across sex-specific categories of coffee consumption are presented in Table 1. Higher coffee consumption was associated with younger age, 12 years or more of education, and cigarette smoking. Total energy intake and carbohydrate intake were higher with an increased level of coffee consumption. Consumption of soda was also higher with the increased level. Correlation coefficient analysis between caffeine intake and BMI showed no clear correlation both among men and among women (data not shown).

With the multivariate model, hazard ratios among men showed that participants who consumed coffee once per month to six times per week and who consumed coffee daily had a significantly decreased risk of diabetes compared with those who never or almost never consumed coffee, with no significance in analysis of trend (Table 2). Among women, although hazard ratios did not show a significant association, an analysis for linear trend after multivariate adjustment showed a statistically significant decrease in the development of diabetes (Table 2).

Consumption of decaffeinated coffee tended to be associated with a decreasing risk of diabetes among women, but the association was not statistically significant (Table 2). Green tea consumption and black tea consumption were not significantly associated with a risk of diabetes either. Consumption of oolong tea was insignificantly positively associated with a risk of diabetes among men, and the trend analysis showed the risk increased significantly with higher consumption among women (Table 2). Although the association with consumption of oolong tea was attenuated after multivariate adjustment among men, it remained significant after the adjustment among women. We observed a weak but significant inverse association between the consumption of chocolate snacks and the risk of diabetes among men in

the trend analysis. The lowered risk was also observed among women, although not all the decreases in hazard ratios were statistically significant, and no significance was observed in the trend analysis (Table 2).

The association between coffee consumption and risk of diabetes remained in an analysis which included the categorical variables of coffee consumption and caffeine intake simultaneously in the multivariate model. The hazard ratios for diabetes according to coffee consumption categories of never or almost never, once per month to six times per week, and once per d or more were 1.00, 0.70 (95% CI 0.50, 0.99) and 0.66 (95% CI 0.43, 1.03), and the  $P$  value for trend was 0.33 among men. The corresponding hazard ratios for women were 1.00, 1.00 (95% CI 0.67, 1.49) and 0.60 (95% CI 0.36, 1.01), with the  $P$  value for trend of 0.02. In the same model, no significant association between caffeine intake and risk of diabetes was observed (data not shown).

To minimise a potential effect of subclinical disease, we conducted additional analyses by excluding thirty-eight men and nineteen women who reported the diagnosis of diabetes during the first 2 years of the follow-up period. The results did not alter our original findings. Because we needed to assign the median length of follow-up to forty-one participants who developed diabetes, we conducted a separate analysis using logistic regression, but these results also did not alter our findings; the multivariate OR for diabetes according to the coffee consumption categories of never or almost never, once per month to six times per week, and once per d or more were 1.00, 0.70 (95% CI 0.50, 0.98) and 0.69 (95% CI 0.48, 0.99), and the  $P$  value for trend was 0.31 among men. Among women, the same results were 1.00, 1.00 (95% CI 0.67, 1.48) and 0.60 (95% CI 0.37, 0.96), with a  $P$  value for trend of 0.01.

## Discussion

Higher coffee consumption modestly decreased the risk of development of diabetes both among men and women even though consumption of coffee is relatively low in the current Japanese population compared with that in Western countries. In contrast, caffeine intake estimated from coffee, green tea and other caffeinated beverages and chocolate snacks was not associated with risk. The results suggest that a beneficial effect of coffee consumption exists aside from its caffeine content. Studies conducted in the USA showed that a higher caffeine intake significantly lowered the risk of diabetes, but in some of the studies, the association between caffeine intake and risk of diabetes was diminished after further adjustment for coffee consumption<sup>(17–19)</sup>. In the same studies, it was reported that the consumption of decaffeinated coffee was also inversely associated with the risk of diabetes<sup>(17–19)</sup>. The consumption of coffee may increase the intake of antioxidants other than caffeine. It has been reported that chlorogenic acid, a polyphenol abundant in coffee, is probably responsible for the substantial part of antioxidants<sup>(31–33)</sup>.

The present study failed to observe any association between decaffeinated coffee and diabetes risk, which may have been caused by a lack of power since a very small number of the participants, less than one-tenth of them, reported consumption of decaffeinated coffee in some frequency. The significant

**Table 1.** Baseline characteristics of the study population according to level of coffee consumption  
(Mean values and standard deviations or percentages)

|  | Men (n 5897)                  |      |                                       |      |                         |      | Women (n 7643)                 |      |                                       |      |                         |      |
|--|-------------------------------|------|---------------------------------------|------|-------------------------|------|--------------------------------|------|---------------------------------------|------|-------------------------|------|
|  | Never or almost never (n 931) |      | Once/month to six times/week (n 2402) |      | Once/d or more (n 2564) |      | Never or almost never (n 1398) |      | Once/month to six times/week (n 3312) |      | Once/d or more (n 2933) |      |
|  | Mean                          | SD   | Mean                                  | SD   | Mean                    | SD   | Mean                           | SD   | Mean                                  | SD   | Mean                    | SD   |
| Age (years)  | 56.7                          | 8.0  | 53.1                                  | 8.7  | 48.9                    | 8.6  | 56.4                           | 8.7  | 52.5                                  | 8.9  | 48.0                    | 8.1  |
| BMI (kg/m <sup>2</sup> )*                              | 22.3                          | 2.6  | 22.7                                  | 2.6  | 22.6                    | 2.7  | 21.9                           | 2.9  | 22.3                                  | 2.7  | 22.0                    | 2.7  |
| Smoking status (%)†                                    |                               |      |                                       |      |                         |      |                                |      |                                       |      |                         |      |
| Never  | 23.4                          |      | 21.9                                  |      | 11.7                    |      | 79.8                           |      | 84.4                                  |      | 76.1                    |      |
| Current  | 39.0                          |      | 44.0                                  |      | 65.5                    |      | 5.9                            |      | 5.3                                   |      | 15.5                    |      |
| Past   | 34.8                          |      | 32.7                                  |      | 21.4                    |      | 2.4                            |      | 3.1                                   |      | 3.7                     |      |
| Currently married (%)                                  | 95.0                          |      | 93.9                                  |      | 94.5                    |      | 81.9                           |      | 86.8                                  |      | 85.9                    |      |
| Education 12 years or longer (%)                       | 30.9                          |      | 44.9                                  |      | 57.3                    |      | 24.2                           |      | 37.7                                  |      | 51.1                    |      |
| Physical activity (metabolic equivalents/h per week)   | 26.6                          | 39.8 | 31.1                                  | 43.3 | 28.0                    | 42.1 | 18.0                           | 26.8 | 22.6                                  | 33.1 | 22.0                    | 30.4 |
| Postmenopausal (%)                                     |                               |      |                                       |      |                         |      | 74.3                           |      | 58.5                                  |      | 38.4                    |      |
| Current use of hormone replacement therapy (%)         |                               |      |                                       |      |                         |      | 2.2                            |      | 1.7                                   |      | 1.4                     |      |
| Daily dietary intake                                   |                               |      |                                       |      |                         |      |                                |      |                                       |      |                         |      |
| Total energy (kJ)                                      | 10 820                        | 3438 | 11 059                                | 3375 | 11 408                  | 3640 | 8570                           | 3160 | 9154                                  | 3058 | 9391                    | 3232 |
| Fat (g)  | 56.9                          | 28.0 | 60.2                                  | 26.5 | 63.7                    | 29.2 | 51.5                           | 25.5 | 57.5                                  | 25.9 | 60.7                    | 26.6 |
| Carbohydrate (g)                                       | 349                           | 105  | 366                                   | 107  | 388                     | 118  | 304                            | 108  | 321                                   | 102  | 327                     | 111  |
| Dietary fibre (g)                                      | 16.1                          | 9.0  | 16.0                                  | 7.9  | 16.4                    | 8.9  | 16.7                           | 9.5  | 17.2                                  | 8.5  | 17.1                    | 8.5  |
| Mg (mg)  | 400                           | 171  | 401                                   | 154  | 415                     | 166  | 360                            | 163  | 374                                   | 146  | 383                     | 152  |
| Caffeine (mg)  | 42                            | 48   | 79                                    | 57   | 218                     | 100  | 60                             | 56   | 97                                    | 66   | 226                     | 103  |
| Alcohol (g)  | 50.7                          | 44.1 | 44.5                                  | 40.5 | 41.0                    | 39.1 | 6.2                            | 13.9 | 6.8                                   | 14.1 | 9.5                     | 17.5 |
| Soda (servings)  | 0.08                          | 0.21 | 0.15                                  | 0.28 | 0.22                    | 0.39 | 0.08                           | 0.24 | 0.10                                  | 0.23 | 0.13                    | 0.28 |
| Coffee, tea and chocolate consumption per d (servings) |                               |      |                                       |      |                         |      |                                |      |                                       |      |                         |      |
| Coffee   | 0.0                           | 0.0  | 0.3                                   | 0.3  | 1.8                     | 0.9  | 0.0                            | 0.0  | 0.3                                   | 0.2  | 1.6                     | 0.8  |
| Decaffeinated coffee                                   | 0.01                          | 0.1  | 0.02                                  | 0.1  | 0.06                    | 0.3  | 0.02                           | 0.2  | 0.02                                  | 0.1  | 0.07                    | 0.4  |
| Green tea  | 1.2                           | 1.4  | 1.3                                   | 1.4  | 1.3                     | 1.3  | 1.7                            | 1.4  | 1.8                                   | 1.4  | 1.6                     | 1.3  |
| Black tea  | 0.03                          | 0.2  | 0.06                                  | 0.2  | 0.06                    | 0.2  | 0.04                           | 0.2  | 0.07                                  | 0.2  | 0.08                    | 0.3  |
| Oolong tea   | 0.2                           | 0.6  | 0.3                                   | 0.6  | 0.3                     | 0.7  | 0.3                            | 0.8  | 0.4                                   | 0.8  | 0.5                     | 0.9  |
| Chocolate snack pieces                                 | 0.05                          | 0.2  | 0.10                                  | 0.2  | 0.12                    | 0.3  | 0.08                           | 0.2  | 0.15                                  | 0.3  | 0.19                    | 0.4  |

\* For men, n 5677; for women, n 7416.  
† Values do not add to 100% because of missing data.

**Table 2.** Risk of diabetes incidence according to consumption of coffee and tea, and caffeine intake (Hazard ratios (HR) and 95 % confidence intervals)

|                                   | Men          |           |                       |            |                               |            | Women        |           |                       |            |                               |            |
|-----------------------------------|--------------|-----------|-----------------------|------------|-------------------------------|------------|--------------|-----------|-----------------------|------------|-------------------------------|------------|
|                                   | Subjects (n) | Cases (n) | HR (adjusted for age) | 95 % CI    | HR (multivariate adjustment)* | 95 % CI    | Subjects (n) | Cases (n) | HR (adjusted for age) | 95 % CI    | HR (multivariate adjustment)* | 95 % CI    |
| <b>Coffee</b>                     |              |           |                       |            |                               |            |              |           |                       |            |                               |            |
| Never or almost never             | 931          | 56        | 1.00                  | –          | 1.00                          | –          | 1398         | 39        | 1.00                  | –          | 1.00                          | –          |
| Once/month to six times/week      | 2402         | 107       | 0.74                  | 0.53, 1.03 | 0.69                          | 0.50, 0.97 | 3312         | 92        | 1.10                  | 0.75, 1.60 | 1.08                          | 0.74, 1.60 |
| Once/d or more                    | 2564         | 115       | 0.73                  | 0.52, 1.03 | 0.69                          | 0.49, 0.98 | 2933         | 44        | 0.73                  | 0.46, 1.15 | 0.70                          | 0.44, 1.12 |
| <i>P</i> value for trend          |              |           | 0.35                  |            | 0.32                          |            |              |           | 0.04                  |            | 0.03                          |            |
| <b>Caffeine intake</b>            |              |           |                       |            |                               |            |              |           |                       |            |                               |            |
| 1st tertile                       | 1966         | 98        | 1.00                  | –          | 1.00                          | –          | 2553         | 58        | 1.00                  | –          | 1.00                          | –          |
| 2nd tertile                       | 1967         | 81        | 0.81                  | 0.60, 1.09 | 0.81                          | 0.60, 1.10 | 2547         | 66        | 1.35                  | 0.94, 1.94 | 1.26                          | 0.88, 1.82 |
| 3rd tertile                       | 1964         | 99        | 1.00                  | 0.75, 1.35 | 0.95                          | 0.69, 1.30 | 2543         | 51        | 1.18                  | 0.79, 1.75 | 0.95                          | 0.63, 1.43 |
| <i>P</i> value for trend          |              |           | 0.77                  |            | 0.94                          |            |              |           | 0.55                  |            | 0.53                          |            |
| <b>Green tea</b>                  |              |           |                       |            |                               |            |              |           |                       |            |                               |            |
| Never or almost never             | 2131         | 104       | 1.00                  | –          | 1.00                          | –          | 1539         | 32        | 1.00                  | –          | 1.00                          | –          |
| Once/month to six times/week      | 801          | 48        | 1.30                  | 0.92, 1.84 | 1.23                          | 0.87, 1.76 | 1075         | 24        | 0.92                  | 0.54, 1.58 | 0.90                          | 0.52, 1.54 |
| Once/d                            | 616          | 28        | 0.94                  | 0.61, 1.43 | 0.97                          | 0.63, 1.49 | 778          | 14        | 0.94                  | 0.50, 1.77 | 1.00                          | 0.53, 1.89 |
| Twice/d or more                   | 2349         | 98        | 0.91                  | 0.69, 1.20 | 0.94                          | 0.71, 1.26 | 4251         | 105       | 1.07                  | 0.72, 1.60 | 1.03                          | 0.69, 1.55 |
| <i>P</i> value for trend          |              |           | 0.20                  |            | 0.38                          |            |              |           | 0.51                  |            | 0.64                          |            |
| <b>Oolong tea</b>                 |              |           |                       |            |                               |            |              |           |                       |            |                               |            |
| Never or almost never             | 2245         | 95        | 1.00                  | –          | 1.00                          | –          | 2702         | 52        | 1.00                  | –          | 1.00                          | –          |
| Once/month to six times/week      | 2997         | 142       | 1.17                  | 0.90, 1.52 | 1.05                          | 0.80, 1.37 | 3696         | 77        | 1.05                  | 0.74, 1.51 | 0.89                          | 0.62, 1.28 |
| Once/d or more                    | 655          | 41        | 1.39                  | 0.96, 2.02 | 1.12                          | 0.77, 1.64 | 1245         | 46        | 2.00                  | 1.34, 3.00 | 1.37                          | 0.90, 2.07 |
| <i>P</i> value for trend          |              |           | 0.12                  |            | 0.58                          |            |              |           | 0.0001                |            | 0.03                          |            |
| <b>Decaffeinated coffee</b>       |              |           |                       |            |                               |            |              |           |                       |            |                               |            |
| Never or almost never             | 5394         | 249       | 1.00                  | –          | 1.00                          | –          | 6931         |           | 1.00                  | –          | 1.00                          | –          |
| Once/month or more                | 503          | 29        | 1.21                  | 0.82, 1.78 | 1.09                          | 0.73, 1.61 | 712          | 164       | 0.74                  | 0.40, 1.36 | 0.66                          | 0.36, 1.23 |
| <i>P</i> value for trend          |              |           | 0.34                  |            | 0.69                          |            |              | 11        | 0.33                  |            | 0.19                          |            |
| <b>Black tea</b>                  |              |           |                       |            |                               |            |              |           |                       |            |                               |            |
| Never or almost never             | 4225         | 205       | 1.00                  | –          | 1.00                          | –          | 4586         | 98        | 1.00                  | –          | 1.00                          | –          |
| Once/month or more                | 1672         | 73        | 0.91                  | 0.70, 1.19 | 0.88                          | 0.67, 1.16 | 3057         | 77        | 1.29                  | 0.96, 1.74 | 1.30                          | 0.95, 1.77 |
| <i>P</i> value for trend          |              |           | 0.48                  |            | 0.37                          |            |              |           | 0.10                  |            | 0.11                          |            |
| <b>Chocolate snack pieces</b>     |              |           |                       |            |                               |            |              |           |                       |            |                               |            |
| Never or almost never             | 2825         | 149       | 1.00                  | –          | 1.00                          | –          | 2494         | 74        | 1.00                  | –          | 1.00                          | –          |
| Once/month to less than once/week | 2199         | 98        | 0.83                  | 0.64, 1.07 | 0.84                          | 0.65, 1.09 | 3546         | 67        | 0.68                  | 0.49, 0.94 | 0.70                          | 0.50, 0.98 |
| Once/week or more                 | 873          | 31        | 0.68                  | 0.46, 1.00 | 0.65                          | 0.43, 0.97 | 1603         | 34        | 0.79                  | 0.53, 1.19 | 0.73                          | 0.48, 1.13 |
| <i>P</i> value for trend          |              |           | 0.06                  |            | 0.04                          |            |              |           | 0.53                  |            | 0.32                          |            |

Coffee, caffeine and diabetes among Japanese

\* Adjusted for age, smoking status, BMI, physical activity, length of education in years, alcohol consumption, total energy intake, fat intake and women's menopausal status to examine beverage and chocolate snacks, respectively.

association between coffee consumption and risk of diabetes was present even after controlling for caffeine intake in the present study.

Green tea consumption was not associated with the risk of diabetes in the present study. A prospective study in Japan reported a significant inverse association between green tea consumption and diabetes risk, primarily among women<sup>(15)</sup>. Two other studies in Japan failed to find an association between green tea consumption and risk of diabetes<sup>(16,21)</sup>, although these studies were cross-sectionally conducted. In the present study, a higher consumption of oolong tea raised the risk of diabetes among women. In our data, an especially high incidence of diabetes was observed among women who reported consuming oolong tea twice per d or more. We speculated that participants who were at risk for diabetes may have chosen to drink oolong tea because of its reputed ability to cleanse the body of extra fat, although an additional analysis showed that the association between oolong tea consumption and risk of diabetes among women remained after the exclusion of participants who developed diabetes within the first 2 years during the follow-up. A previously conducted clinical trial reported that oolong tea consumption decreased the plasma glucose level among patients with type 2 diabetes<sup>(34)</sup>. More observational studies are needed to evaluate the association of consumption of oolong tea with the risk of diabetes.

The consumption of chocolate snacks was inversely associated with a risk of diabetes among men, and the association was also implied among women. Several previous studies included chocolate snacks to estimate total caffeine intake and assessed it with the risk of diabetes<sup>(17–19)</sup>, but to our knowledge, no previous observational study has shown an association between chocolate snacks alone and risk of diabetes. The finding must be, however, interpreted with caution and any benefit derived from a possible reduction in the risk might be outweighed by the increased health risks, such as obesity, caused by the regular consumption of the high-energy snacks. The finding still leaves room for further evaluation of their components such as polyphenols for possible protective effects, although the possible effect of caffeine content cannot be completely eliminated. A clinical trial testing the insulin response to an oral glucose tolerance test indicated that polyphenol-rich dark chocolate improved insulin sensitivity in healthy subjects, which may support our finding<sup>(35)</sup>.

The use of self-reported status of diabetes may be one of the limitations of the present study. A previous study conducted in Japan reported a substantial agreement between diabetes reported in a questionnaire and its diagnosis; 82% of cases of self-reported diabetes were confirmed by medical records<sup>(36)</sup>. Even so, we were not able to determine the proportion of the participants who had diabetes and did not report it. Those subjects have been classified as not having diabetes, and this may attenuate the true association, if it exists. There is a possibility that subjects whose socio-economic status was high and who were health conscious were more likely to respond to the follow-up questionnaire, having the fact that the respondents were more likely to have high education levels than non-respondents. Furthermore, other dietary items might have contributed to the caffeine intake. The present study did not discuss caffeine intake from the consumption of sodas, since the FFQ did

not allow us to distinguish sodas with caffeine from those without caffeine. The consumption of sodas was relatively low in the current population, and it slightly increased with the level of coffee consumption, and hence it would not have much impact on the results. There still exists a possibility that the study results are influenced by some residual confounders, such as family history of diabetes, on which information is not available, which prevents us from making a definitive conclusion.

The present study has several advantages. First, it was a community-based study, and the participants were men and women from a general Japanese population. The risk of diabetes in relation to the consumption of coffee and tea was prospectively evaluated after controlling for potential confounders in a multivariate model. The values of nutrient intake and physical activity included in the model were measured with a validated questionnaire. We evaluated the association not only with coffee but also with other kinds of tea and foods containing caffeine, including green tea, which is commonly consumed in Japan. Caffeine intake was estimated from coffee, tea and chocolate snacks and was evaluated separately from coffee consumption.

In summary, a modest inverse association between coffee consumption and risk of development of diabetes was observed among men and women in a community-based cohort from the general Japanese population. Green tea consumption and total caffeine intake appeared to have no relationship with the risk of diabetes. It was suggested that the association of coffee consumption with risk of diabetes was separate from the influence of caffeine intake on the risk. Further studies may be needed to investigate which substances in coffee play a role in the beneficial effect on the risk of diabetes, as well as the association of tea and chocolate snack consumption with the risk.

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H. S. and C. N. designed the study and directed the study implementation. C. N., H. S. and N. T. supervised the field activities and collected data. S. O. conducted the statistical analysis and all authors interpreted the analysis results. S. O. and C. N. initially drafted all the sections of the text, and K. N., K. F., T. K., N. T. and H. S. were responsible for critical revision of the manuscript. All authors contributed to and approved the final version of the manuscript.

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