Intake of Vegetables and Fruits and the Risk of Cataract Incidence in a Japanese Population: The Japan Public Health Center-Based Prospective Study

Sayaka Adachi¹, Norie Sawada², Kenya Yuki¹, Miki Uchino¹, Motoki Iwasaki², Kazuo Tsubota¹, and Shoichiro Tsugane²

¹Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan
²Epidemiology and Prevention Group, Center for Public Health Sciences, National Cancer Center, Tokyo, Japan

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ABSTRACT

Background: Although the consumption of vegetables and fruits is reported to influence the risk of cataract, no prospective study of this association from Asia has yet appeared. Here, we investigated the association between vegetable and fruit intake and cataract incidence in a large-scale population-based prospective cohort study in Japan.

Methods: This study included 32,387 men and 39,333 women aged 45–74 years who had no past history of cataract and had completed a dietary questionnaire of the Japan Public Health Center-based Prospective Cohort Study. The incidence of cataract was evaluated after 5-year follow-up. We used multiple logistic regression analyses to estimate the sex-specific odds ratios (ORs), with adjustment for confounding factors.

Results: We identified 1,836 incident cataracts in 594 men and 1,242 women. In men, the OR for cataract was decreased with higher intake of vegetables (ORQ5 vs Q1, 0.77; 95% confidence interval [CI], 0.59–1.01; PTrend across quartile categories = 0.03) and cruciferous vegetables (ORQ5 vs Q1, 0.74; 95% CI, 0.57–0.96; PTrend = 0.02). In contrast, the OR for cataract was increased with higher intake of vegetables among women (ORQ5 vs Q1, 1.28; 95% CI, 1.06–1.53; PTrend = 0.01). Green and yellow vegetable and fruit intake were not associated with cataract in either sex.

Conclusions: This study suggests that vegetables may reduce the risk of cataract in men, but not in women.

Key words: food intake; cataract risk; food frequency questionnaire; prospective cohort study

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INTRODUCTION

Age-related cataract is the leading cause of visual loss and blindness globally, with almost 20 million people affected.¹ Cataract incidence increases with age,² and since Japan leads the world in life expectancy,³ the incidence of cataract in Japan is also increasing. Visual impairment due to cataract increases the risk of falling⁴,⁵ and is associated with decreased cognitive function⁶,⁷ in elderly people. These findings warrant ongoing and focused epidemiological research on lifestyle prevention of cataract in the elderly.

Many studies have reported the association of cataract and foods, including vegetables.⁸–¹⁵ A meta-analysis indicated that higher consumption of vegetables might reduce cataract risk, mainly in American and European populations.¹⁵ Prospective cohort studies reported that the intake of vegetables and fruits, which include lutein, vitamin C, and vitamin E, may reduce the risk of cataracts.⁹,¹⁰,¹¹ and that vegetarians had lower risk of cataract than meat eaters among British residents.¹⁴

Lens opacities in cataracts may occur as a result of lens protein damage by oxidative stress due to smoking,¹⁶ ultraviolet (UV) radiation exposure,¹⁷ steroid,¹⁸ diabetes mellitus,¹⁹,²⁰ and high body mass index.²¹–²³ Accordingly, it has been speculated that high doses of antioxidants, such as vitamin A, vitamin C, vitamin E, and β-carotene, may help prevent age-related cataract formation. Indeed, recent meta-analyses reported that such antioxidant intake might be associated with reduced cataract risk.²⁴–²⁶ Moreover, a recent study reported that cruciferous vegetables containing isothiocyanates protect lens cells against oxidative stress.²⁷ Green and yellow vegetables are rich in carotenoids and lutein, and a number of studies have reported an association between lutein and carotene and cataract risk.⁸–¹⁰ To date, however, no prospective study has reported the relationship between vegetables and fruits and cataract risk in Asia, although a previous case-control study in India reported that mean vegetable and fruit intakes were lower in cataract patients than in controls (P < 0.001).²⁸

Here, we investigated the association between vegetable and fruit intake and incidence of cataract among middle-aged Japanese in a large-scale population-based prospective cohort study in Japan.
MATERIALS AND METHODS

Study cohort
The Japan Public Health Center-based Prospective (JPHC) Study was initiated in 1990 for cohort I and in 1993 for cohort II. Cohort I participants were residents aged 40–59 years in 1990 from five public health center areas (Iwate, Akita, Nagano, Okinawa-chubu, and Tokyo), while those of cohort II included residents aged 40–69 years in 1993 from six public health center areas (Ibaraki, Niigata, Kochi, Nagasaki, Okinawa-Miyako, and Osaka).

A questionnaire survey was carried out at baseline and at 5- and 10-year follow-up. The questionnaire was self-administered and included information on medical history and lifestyle, such as smoking and drinking habits and diet and vitamin supplement use at the time of the survey. We used the 5-year follow-up survey in place of the baseline survey as starting point for the present analysis because it provided more comprehensive information on dietary intake.

Ethics approval was obtained from the Institutional Review Board of the National Cancer Center and Keio University.

Study population
Participant numbers were 103,880 in the 5-year (starting point) and 99,512 in the 10-year follow-up survey. Of these, 87,290 were 103,880 in the 5-year (starting point) and 100% apple juice.

Each food item was given nine options of consumption frequency, ranging from rarely (less than once a month) to seven or more times a day. Standard portion sizes for each food item were divided into the three options of small (less than half the standard serving size), medium (standard serving size), or large (more than one and half times the standard size). The daily intake of each food was calculated by multiplying the daily consumption frequency and relative portion size for each food item.

The intake of each food item was adjusted for total energy intake using the residual method. Food intakes were divided into quintiles. For the validity of food intake measurements from the FFQ and 28-day dietary records, Spearman’s rank correlation coefficients were 0.22 in men and 0.32 in women for vegetable intake and 0.41 in men and 0.23 in women for fruit intake in cohort I and 0.35 in men and 0.43 in women for vegetable intake and 0.50 in men and 0.30 in women for fruit intake in cohort II. These results reveal that the FFQ can be used to rank individuals according to food intake in the JPHC Study.

Statistical analysis
Multiple logistic-regression analyses were used to calculate the sex-specific odds ratios (ORs) and 95% confidence intervals (CIs) of cataract incidence according to quartiles of total vegetables, cruciferous vegetables, green and yellow vegetables, and fruits. Multivariate adjustment used covariates with risk factors known or suspected to affect cataract incidence. These were adjusted for age, area, and the following potential confounding factors: body-mass index (BMI), calculated as weight (kg)/height squared (m²) and grouped into four categories (<21.0, 21.0–22.9, 23.0–24.9, and ≥25.0 kg/m²); smoking status (non-smokers who did not have a history of smoking, and smokers who smoked currently or had smoked in the past); weekly alcohol intake (g/week), using four levels of consumption in men (non- and occasional drinkers, and drinkers of 1–149 g/week, 150–299 g/week, 300–499 g/week, and ≥500 g/week) and in women (non- and occasional drinkers, and drinkers of ≥1 g/week); total fruit intake, which was an adjustment factor in the analysis of total vegetable, cruciferous vegetable, and green and yellow vegetable intake (otherwise, total vegetable intake was used as an adjustment factor in the analysis of total fruit intake); vitamin supplement intake (yes or no); and fundus...
photographic examination (yes or no). Furthermore, we calculated $P$ interaction values using a likelihood-ratio test to compare logistic models with and without cross-product terms for smoking (non-smokers or smokers) and age (<60 or ≥60 years).

All statistical analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Table 1 shows the baseline characteristics of participants according to quartile of vegetable intake by sex. Intake of vegetables, cruciferous vegetables, green and yellow vegetables, and fruits tended to be higher in older people; in those with higher BMI, those who never or only occasionally drank alcohol, and non-smokers; and in those who underwent fundus photographic examinations.

Table 2 shows the age- and area-adjusted ORs and multivariate ORs with 95% CIs for cataract incidence according to energy-adjusted total vegetable and cruciferous vegetable intake were 0.77 (95% CI, 0.59–1.01) ($P$ for trend = 0.03) and 0.74 (95% CI, 0.57–0.96) ($P$ for trend = 0.02), respectively. The multivariate ORs for the highest versus lowest quartile of green and yellow vegetable and total fruit intake were 0.85 (95% CI, 0.66–1.11) and 1.13 (95% CI, 0.85–1.49), respectively. In women, in contrast, the results for total vegetable and cruciferous vegetable intakes showed the opposite results, with a multivariate OR for the highest quartile of energy-adjusted total vegetable intake compared with the lowest of 1.28 (95% CI, 1.06–1.53) ($P$ for trend = 0.01). Further, the multivariate OR of cruciferous vegetables was positively associated with cataract risk, albeit without significant difference in trend analysis. A multivariate OR for the highest quartile of green and yellow vegetable intake was positively associated with cataract, but without statistical significance. Total fruit intake also tended to be positively associated, at 1.15 (95% CI, 0.96–1.39), but without statistical significance. Furthermore, we adjusted for vitamin C intake of vegetables, cruciferous vegetables, green and yellow vegetable, and fruit intake by quartile. In men, the multivariate ORs for the highest versus lowest quartile of total vegetable and cruciferous vegetable intake were 0.77 (95% CI, 0.59–1.01) ($P$ for trend = 0.03) and 0.74 (95% CI, 0.57–0.96) ($P$ for trend = 0.02), respectively.

Table 1. Baseline characteristics of participants according to quartile of vegetable intake by sex

|                | Vegetable intake by quartile | P value |
|----------------|------------------------------|---------|
|                | Quartile 1 (0–110.7) & Quartile 2 (110.7–166.4) & Quartile 3 (166.4–242.7) & Quartile 4 (≥241.7) |
| Participants   | 8,096                        | 8,097   | 8,097 | 8,097 |
| Age, years, mean (SD) | 49.7 (7.4)                     | 50.3 (7.4) | 51.3 (7.6) | 52.5 (7.6) |
| BMI, kg/m², mean (SD)  | 23.4 (2.9)                     | 23.5 (2.7) | 23.6 (2.8) | 23.7 (2.9) |
| Total energy intake, kcal/day, mean (SD) | 2,166.9 (647.4) | 2,235.1 (629.1) | 2,214.9 (620.0) | 2,157.8 (630.4) |
| Vegetable intake, g/day, mean (SD) | 78.5 (39.4) | 150.2 (52.6) | 215.9 (74.6) | 367.1 (190.9) |
| Cruciferous vegetable intake, g/day, mean (SD) | 33.4 (21.0) | 61.4 (30.8) | 86.3 (42.2) | 145.2 (99.0) |
| Green and yellow vegetable intake, g/day, mean (SD) | 30.8 (17.3) | 60.8 (22.9) | 90.2 (30.7) | 161.5 (86.0) |
| Fruit intake, g/day, mean (SD) | 121.3 (143.4) | 167.3 (147.8) | 207.5 (169.5) | 245.7 (207.6) |
| Smoking status, % | Non-smokers: 30.7 | 33.6 | 37.2 | 41.9 |
|                | Smokers: 69.3 | 66.4 | 62.8 | 58.1 |
| Alcohol consumption, % | Non and occasional drinkers: 20.1 | 21.1 | 24.6 | 29.9 |
|                | 1–149 g/week: 19.7 | 23.8 | 26.8 | 29.5 |
|                | 150–299 g/week: 17.6 | 19.6 | 20.5 | 19.8 |
|                | 300–449 g/week: 17.7 | 17 | 14.9 | 12.1 |
|                | ≥450 g/week: 25 | 18.5 | 13.2 | 8.7 |
| Supplement intake, % | 9 | 9.8 | 10.4 | 11.2 |
| Fundus photographic examination, % | 39.5 | 43.1 | 45.3 | 46.4 |

Table 2. Age- and area-adjusted ORs and multivariate ORs with 95% CIs for cataract incidence according to energy-adjusted total vegetable intake by quartile.

|                | Vegetable intake by quartile | P value |
|----------------|------------------------------|---------|
|                | Quartile 1 (0–139.9) & Quartile 2 (139.9–199.7) & Quartile 3 (199.7–278.8) & Quartile 4 (≥278.8) |
| Participants   | 9,833                        | 9,833   | 9,834 | 9,833 |
| Age, years, mean (SD) | 50.4 (7.7)                     | 50.7 (7.6) | 51.3 (7.5) | 52.2 (7.5) |
| BMI, kg/m², mean (SD)  | 23.4 (3.2)                     | 23.4 (3.1) | 23.5 (3.1) | 23.6 (3.1) |
| Total energy intake, kcal/day, mean (SD) | 1,882.2 (603.1) | 1,902.7 (554.3) | 1,881.5 (531.2) | 1,851.7 (542.4) |
| Vegetable intake, g/day, mean (SD) | 107.9 (53.1) | 183.7 (67.7) | 251.5 (89.1) | 411.4 (209.5) |
| Cruciferous vegetable intake, g/day, mean (SD) | 44.3 (27.0) | 74.6 (37.0) | 100.7 (47.9) | 166.4 (109.3) |
| Green and yellow vegetable intake, g/day, mean (SD) | 42.9 (19.7) | 74.4 (24.7) | 105.7 (33.0) | 178.4 (86.3) |
| Fruit intake, g/day, mean (SD) | 203.9 (193.9) | 249.1 (199.1) | 272.4 (202.6) | 303.9 (233.9) |
| Smoking status, % | Non-smokers: 92.3 | 93.5 | 94.4 | 95.5 |
|                | Smokers: 7.7 | 6.5 | 5.6 | 4.5 |
| Alcohol consumption, % | Non and occasional drinkers: 78.2 | 78.7 | 80.7 | 84.0 |
|                | ≥1 g/week: 21.8 | 21.3 | 19.4 | 16.0 |
| Supplement intake, % | 13.7 | 15.2 | 15.2 | 15.0 |
| Fundus photographic examination, % | 39.7 | 45.4 | 47.9 | 50.2 |

BMI, body mass index; SD, standard deviation.
Table 2. Age- and area-adjusted odds ratios and multivariate odds ratios for cataract incidence according to total vegetable, cruciferous vegetable, green and yellow vegetable and fruit intake category in men and women

| Quartile category | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | P for trend | Per 50 g/day increment |
|-------------------|-------------|-------------|-------------|-------------|------------|------------------------|
| **Men**           |             |             |             |             |            |                        |
| **Total vegetable intake** |             |             |             |             |            |                        |
| Range, g          | 0–110.66    | 110.7–166.4 | 166.4–242.7 | >241.7      | >0.0001    | 1.02 (0.99–1.05)       |
| Number of participants | 8,096     | 8,097       | 8,097       | 8,097       |            |                        |
| Number of cases    | 128         | 146         | 151         | 169         |            |                        |
| Model 1            | 1.00        | 1.07 (0.84–1.36) | 0.98 (0.77–1.25) | 0.97 (0.77–1.24) | 0.64      |                        |
| Model 2            | 1.00        | 0.98 (0.76–1.27) | 0.85 (0.65–1.10) | 0.77 (0.59–1.01) | 0.03      | 0.95 (0.91–0.99)       |
| **Cruciferous vegetable intake** |             |             |             |             |            |                        |
| Range, g          | 0–39.3      | 39.3–63.7   | 63.7–96.8   | >96.8       | >0.0001    | 1.02 (0.99–1.05)       |
| Number of participants | 8,096     | 8,097       | 8,097       | 8,097       |            |                        |
| Number of cases    | 139         | 136         | 152         | 167         |            |                        |
| Model 1            | 1.00        | 0.92 (0.72–1.17) | 0.93 (0.73–1.18) | 0.87 (0.68–1.10) | 0.27      |                        |
| Model 2            | 1.00        | 0.89 (0.69–1.14) | 0.83 (0.64–1.07) | 0.74 (0.57–0.96) | 0.02      | 0.89 (0.82–0.97)       |
| **Green and yellow vegetable intake** |             |             |             |             |            |                        |
| Range, g          | 0–40.9      | 40.9–71.2   | 71.2–111.6  | >116        | >0.0001    | 1.02 (0.99–1.05)       |
| Number of participants | 8,096     | 8,097       | 8,097       | 8,097       |            |                        |
| Number of cases    | 137         | 142         | 147         | 168         |            |                        |
| Model 1            | 1.00        | 1.01 (0.79–1.28) | 0.99 (0.78–1.26) | 1.02 (0.81–1.29) | 0.89      |                        |
| Model 2            | 1.00        | 0.95 (0.74–1.22) | 0.90 (0.70–1.17) | 0.85 (0.66–1.11) | 0.21      | 0.95 (0.89–1.02)       |
| **Total fruit intake** |             |             |             |             |            |                        |
| Range, g          | 0–72.9      | 72.9–140.4  | 140.4–230.3 | >230.3      | >0.0001    | 1.02 (0.99–1.05)       |
| Number of participants | 8,096     | 8,097       | 8,097       | 8,097       |            |                        |
| Number of cases    | 126         | 126         | 172         | 170         |            |                        |
| Model 1            | 1.00        | 0.95 (0.74–1.22) | 1.21 (0.95–1.53) | 1.08 (0.85–1.37) | 0.24      |                        |
| Model 2            | 1.00        | 0.93 (0.71–1.22) | 1.22 (0.94–1.59) | 1.13 (0.85–1.49) | 0.17      | 1.02 (0.99–1.05)       |
and vitamin E intake in the same model, but the results did not change. Additionally, we further adjusted for energy intake in the same model, and the results were not substantially changed.

Table 3 shows the multivariate ORs with 95% CIs by smoking status for cataract incidence according to energy-adjusted total vegetable, cruciferous vegetable, green and yellow vegetable, and fruit intake by quartile. The multivariate OR for the highest quartile of total vegetable intake compared with the lowest was further reduced in smoking compared with total men (OR 0.67; 95% CI, 0.48–0.96). For cruciferous vegetables in men, the multivariate OR for the highest quartile of cruciferous vegetable intake compared with the lowest was further reduced in smoking compared with total men (OR 0.71; 95% CI, 0.50–1.00). For intake of green and yellow vegetables in smoking men, the multivariate OR tended to be negatively associated (OR 0.74; 95% CI, 0.53–1.05), but without statistical significance. For total fruits, the multivariate OR for the highest quartile compared with the lowest was 1.32 (95% CI, 0.92–1.90) in smoking men. In contrast, the results for total vegetables in women showed the opposite results, with a multivariate OR for the highest quartile of total vegetable intake compared with the lowest quartile of 1.27 (95% CI, 1.06–1.54) in non-smoking women. For cruciferous vegetables in women, the OR in non-smoking women was positively associated with higher intake of cruciferous vegetables, with a cataract incidence of 1.23 (95% CI, 1.01–1.48), but this was not statistically significant in trend analysis. For intakes of green and yellow vegetables and fruits in women, the ORs for the highest quartile compared with the lowest were 1.08 (95% CI, 0.90–1.31) and 1.15 (95% CI, 0.95–1.39), respectively, in non-smoking women. The interaction P values were not statistically significant.

Table 4 shows the multivariate ORs with 95% CIs stratified by age for cataract incidence according to total vegetable, cruciferous vegetable, green and yellow vegetable, and fruit intake by quartile. The multivariate ORs of total vegetable and cruciferous vegetable intake compared with the lowest was further reduced for men in the ≥60 years age group than for those in the <60 years age group (ORQ5 vs Q1, 0.66; 95% CI, 0.48–0.92) for total vegetable, P for interaction = 0.04 and ORQ5 vs Q1, 0.63; 95% CI, 0.46–0.85) for cruciferous vegetable, P for interaction = 0.007). Meanwhile, no significant differences by age were found for green and yellow vegetable and total fruit intake in men (P for interaction = 0.71 for green and yellow vegetable intake and P for interaction = 0.86 for total fruit intake). Moreover, significant differences by age among women were also not found.

These results for men and women did not change following stratification by vitamin supplement intake (data not shown).

**DISCUSSION**

In this prospective cohort study of the relationship between vegetable and fruit intake and incidence of cataract, we found an inverse association between higher intake of total vegetables and cruciferous vegetables and cataract incidence in men, but not in women. Our findings also revealed that there was no association between green and yellow vegetable and fruit intake and cataract risk for Japanese. To our knowledge, this is the first study in an Asian population to report the association of vegetable, cruciferous vegetable, green and yellow vegetable, and fruit intake with cataract risk.

A meta-analysis of the association between vegetable consumption and risk of age-related cataract that included nine articles involving 6,464 cataract cases and 112,447 participants found that higher vegetable consumption decreased the risk of cataract. In stratified analysis by study design, cohort studies from America and Europe showed inverse associations between vegetable consumption and cataract risk (summary RR 0.871; 95% CI, 0.791–0.959). Previous studies reported that intake of broccoli and spinach, included in cruciferous vegetables, reduced cataract risk, including a case-control study in Italy that found higher intake of cruciferous vegetables associated with decreased risk of cataract (summary OR 0.5; 95% CI, 0.3–0.8). Our finding of an inverse association between vegetable and cruciferous vegetable intake and cataract in men is consistent with these previous findings. Vegetables contain antioxidants, including vitamins, carotene, phytoestrogens, folate and dietary fiber, which may prevent cataract progression. These components are involved in biological processes that may alter the structure of cataracts, such as DNA methylation, oxidative stress, and protection against DNA damage.

Previous studies showed an inverse or no association between carotene and lutein, which are abundant in green and yellow vegetables, and the risk of cataract.4–10 Furthermore, our results showed that green and yellow vegetable intake reduced cataract risk.8 In this study, there was no significant difference between higher intake of green and yellow vegetables and the incidence of cataract. Brown et al reported that a high frequency of carrot and tomato intake was not related to cataract risk, whereas Tavani et al reported that high intake of spinach and tomatoes decreased cataract risk. The Blue Mountains Eye Study showed that there was no association between intake of green and yellow vegetables and cataract risk. In other words, not all green and yellow vegetables appear to reduce the risk of cataract.

It has been reported that fruit intake might be associated with a decreased risk of cataract incidence. Theodoropoulou et al reported a significant inverse association between monthly frequency of fruit consumption and risk of cataract in a case-control study. Pastor-Valero et al and Christen et al reported that increasing quartiles of combined fruit and vegetable intake were related with a reduction in cataract risk. While these previous analyses of higher intake of all fruits or all vegetables separately were similarly shown to decrease the risk of cataract, albeit without significant differences, our present findings showed no obvious relation between total fruit intake and cataract incidence risk among subjects of either sex in our study, despite the relatively high antioxidant content of fruits. According to Food and Agriculture Organization of the United Nations data, fruit consumption in Japan (average 144.8 g/capita/day) is the lowest in developed countries, and one-third or less than that in the Netherlands (average 482.5 g/capita/day), the country with the highest fruit consumption. Since average Japanese fruit intake is low, there may have been no association between fruit intake and cataract incidence, although the average intake of fruits in our highest category was over 200 g.

Because previous reports showed that smoking has effects on cataracts and is a cause of oxidative stress, we stratified the results by smoking status. Results showed a clearer association between total cruciferous vegetable intake and cataract incidence among smoking men. Cruciferous vegetables, such as broccoli, are rich in carotenoids, vitamin C, vitamin E, vitamin K, folate, and minerals. A previous study showed that cruciferous vegetables contain isothiocyanates, such as sulforaphane, which protect lens cells against oxidative stress. Cruciferous vegetables contain isothiocyanates, which may prevent cataract progression. These components are involved in biological processes that may alter the structure of cataracts, such as DNA methylation, oxidative stress, and protection against DNA damage.
Table 3. Multivariate odds ratios for cataract incidence according to total vegetable, cruciferous vegetable, green and yellow vegetable, and fruit intake category in men and women by smoking status

| Men | Quartile category | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | P for trend | Interaction P-value |
|-----|------------------|-------------|-------------|-------------|-------------|------------|-------------------|
|     | Quartile 1        | Quartile 2   | Quartile 3   | Quartile 4   |             |            |                   |
|     | Number of participants |            |            |            |             |            |                   |
|     | Number of cases   | 2,360       | 2,597       | 2,875       | 3,212       |            |                   |
|     | Model 1           | 1.00        | 1.03 (0.68–1.58) | 1.06 (0.70–1.60) | 0.95 (0.62–1.45) | 0.31       |                   |
| Non-smokers | Cruciferous vegetable intake | Number of participants | 5,330       | 5,139       | 4,857       | 4,462       |            |                   |
| Smokers   | Number of cases   | 84          | 87          | 75          | 80          |            |                   |
| Cr 1     | Model 1           | 1.00        | 0.96 (0.70–1.32) | 0.73 (0.52–1.03) | 0.67 (0.48–0.96) | 0.01       |                   |
|     | Green and yellow vegetable intake | Number of participants | 2,337       | 2,588       | 2,830       | 3,289       |            |                   |
| Smokers   | Number of cases   | 41          | 53          | 67          | 73          |            |                   |
| Gr 1     | Model 1           | 1.00        | 0.96 (0.70–1.32) | 0.73 (0.52–1.03) | 0.67 (0.48–0.96) | 0.01       |                   |
|     | Total fruit intake | Number of participants | 2,150       | 2,608       | 2,973       | 3,212       |            |                   |
| Smokers   | Number of cases   | 42          | 43          | 77          | 72          |            |                   |
| Fr 1     | Model 1           | 1.00        | 0.92 (0.66–1.27) | 0.81 (0.58–1.13) | 0.71 (0.50–1.00) | 0.04       |                   |
|     | Women | Quartile category | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | P for trend | Interaction P-value |
|-----|------------------|-------------|-------------|-------------|-------------|------------|------------|-------------------|
|     | Quartile 1        | Quartile 2   | Quartile 3   | Quartile 4   |             |            |            |
|     | Number of participants |            |            |            |             |            |            |
|     | Number of cases   | 8,473       | 8,685       | 8,750       | 8,858       |            |            |
|     | Model 1           | 2,360       | 2,597       | 2,875       | 3,212       |            |            |
| Non-smokers | Cruciferous vegetable intake | Number of participants | 8,520       | 8,736       | 8,743       | 8,767       |            |            |
| Smokers   | Number of cases   | 80          | 77          | 86          | 89          |            |            |
| Cr 1     | Model 1           | 1.00        | 0.92 (0.66–1.27) | 0.81 (0.58–1.13) | 0.71 (0.50–1.00) | 0.04       |            |
|     | Green and yellow vegetable intake | Number of participants | 8,374       | 8,731       | 8,790       | 8,871       |            |            |
| Smokers   | Number of cases   | 74          | 77          | 86          | 89          |            |            |
| Gr 1     | Model 1           | 1.00        | 0.92 (0.66–1.27) | 0.81 (0.58–1.13) | 0.71 (0.50–1.00) | 0.04       |            |
|     | Total fruit intake | Number of participants | 8,375       | 8,754       | 8,813       | 8,824       |            |            |
| Smokers   | Number of cases   | 223         | 247         | 298         | 311         |            |            |
| Fr 1     | Model 1           | 1.00        | 0.92 (0.66–1.27) | 0.81 (0.58–1.13) | 0.71 (0.50–1.00) | 0.04       |            |

CI, confidence interval; OR, odds ratio.
Model 1 was adjusted for age, area, alcohol consumption, body mass index, fruit intake, supplement intake, and fundus photographic examination.
Model 2 was adjusted for age, area, alcohol consumption, body mass index, vegetable intake, supplement intake, and fundus photographic examination.
## Table 4. Multivariate odds ratios for cataract incidence according to total vegetable, cruciferous vegetable, green and yellow vegetable, and fruit intake category in men and women stratified by age

|                          | Quartile category | Odds ratio (95% CI) | Interaction P-value | P for trend |
|--------------------------|-------------------|---------------------|---------------------|-------------|
|                          | Quartile 1 | Quartile 2 | Quartile 3 | Quartile 4 |
| Total vegetable intake   |            |            |            |            |
| Age <60 years            | Number of participants | 5,917 | 5,663 | 5,251 | 4,652 |
|                          | Number of cases | 42 | 44 | 45 | 50 |
|                          | Model 1 | 1.00 | 1.08 (0.70–1.68) | 1.11 (0.71–1.75) | 1.23 (0.77–1.95) |
|                          | Number of participants | 2,179 | 2,434 | 2,846 | 3,445 |
|                          | Number of cases | 86 | 102 | 106 | 119 |
|                          | Model 1 | 1.00 | 0.96 (0.71–1.31) | 0.79 (0.57–1.08) | 0.66 (0.48–0.92) |
| Age ≥60 years            | Number of participants | 1,000 | 1,080 (0.70–1.68) | 1.11 (0.71–1.75) | 1.23 (0.77–1.95) |
|                          | Number of cases | 43 | 43 | 52 | 43 |
|                          | Model 1 | 1.00 | 1.11 (0.72–1.71) | 1.34 (0.87–2.06) | 1.36 (0.86–2.16) |
|                          | Number of participants | 2,094 | 2,370 | 2,834 | 3,606 |
|                          | Number of cases | 96 | 93 | 100 | 124 |
|                          | Model 1 | 1.00 | 0.81 (0.59–1.10) | 0.68 (0.50–0.93) | 0.63 (0.46–0.85) |
| Cruciferous vegetable intake | Number of participants | 5,704 | 5,559 | 5,346 | 4,874 |
| Age <60 years            | Number of cases | 50 | 42 | 37 | 52 |
|                          | Model 1 | 1.00 | 0.78 (0.51–1.20) | 0.67 (0.43–1.06) | 0.89 (0.57–1.39) |
| Age ≥60 years            | Number of participants | 2,392 | 2,538 | 2,834 | 3,606 |
|                          | Number of cases | 87 | 100 | 110 | 80 |
|                          | Model 1 | 1.00 | 0.92 (0.67–1.27) | 0.77 (0.55–1.07) | 0.74 (0.53–1.05) |
| Green and yellow vegetable intake | Number of participants | 5,828 | 5,575 | 5,293 | 4,874 |
| Age <60 years            | Number of cases | 52 | 37 | 45 | 47 |
|                          | Model 2 | 1.00 | 0.74 (0.48–1.16) | 0.98 (0.63–1.51) | 1.14 (0.72–1.79) |
| Age ≥60 years            | Number of participants | 2,392 | 2,538 | 2,834 | 3,606 |
|                          | Number of cases | 74 | 89 | 127 | 123 |
|                          | Model 2 | 1.00 | 1.08 (0.77–1.53) | 1.41 (1.01–1.97) | 1.18 (0.83–1.68) |
| Total fruit intake       | Number of participants | 5,828 | 5,575 | 5,293 | 4,874 |
| Age <60 years            | Number of cases | 52 | 37 | 45 | 47 |
|                          | Model 2 | 1.00 | 0.74 (0.48–1.16) | 0.98 (0.63–1.51) | 1.14 (0.72–1.79) |
| Age ≥60 years            | Number of participants | 2,392 | 2,538 | 2,834 | 3,606 |
|                          | Number of cases | 74 | 89 | 127 | 123 |
|                          | Model 2 | 1.00 | 1.08 (0.77–1.53) | 1.41 (1.01–1.97) | 1.18 (0.83–1.68) |

CI, confidence interval; OR, odds ratio.
Model 1 was adjusted for age, area, smoking status, alcohol consumption, body mass index, fruit intake, supplement intake, and fundus photographic examination.
Model 2 was adjusted for age, area, smoking status, alcohol consumption, body mass index, vegetable intake, supplement intake, and fundus photographic examination.
Vegetable and Fruit Intake and Cataract Risk

Vegetables have antioxidant activity and may act to antagonize the oxidative action of smoking, and possibly to inhibit cataract incidence. However, the percentage of cataract incidence was lower in smokers (1.6% in men and 2.7% in women) than non-smokers (2.1% in men and 3.1% in women) in both sexes, as shown in Table 3. Smokers might be less likely to consult an ophthalmologist than non-smokers due to a lack of health consciousness. Therefore, we cannot rule out the possibility that the results in smokers were overestimated due to detection bias, and the results in non-smokers may be more certain.

Contrary to our expectations, we found a positive association between total vegetable and cruciferous vegetable intake and cataract in women. Given the higher incidence of cataract in women than men in this study, this might be partly explained by the difference between sexes in the percentage of participants receiving medical advice. There are few subjective symptoms in the early development of cataracts, and many cataracts progress and develop symptoms slowly. Further, cataracts are often not diagnosed without a doctor visit. The Japanese Ministry of Health, Labour and Welfare reported in a patient survey of eligible persons using medical facilities throughout the country that women are more likely to consult a doctor than men. This result is consistent with the report by Simon et al. Accordingly, if participants visit a doctor, early lens opacities are also likely to be diagnosed. Since we had no information from consultations with doctors, we used information from fundus photographic examination at health check-ups as surrogate information. Although we adjusted data and stratified subjects by the presence of fundus photographic examination, the positive association in women was not changed. Correspondingly, the positive association between total vegetable and cruciferous vegetable intake and cataract risk for men in the <60 years age group is similar to the results in women. Like women, relatively younger men with a higher intake of vegetables might be more likely to consult a doctor at a health check-up or comprehensive medical examination due to increased health consciousness. Therefore, the results in women and men aged <60 years might be overestimated due to detection bias. Since we could not adjust by the number of persons who actually consulted doctors, we cannot remove this detection bias. A second consideration is that women generally have a higher incidence of cataract than men in the same age group due to the decrease in estrogen which follows menopause, which causes cataract progression. In other words, the lens is protected in women by the antioxidant action of estrogen until menopause. In our study, higher consumption of vegetables and cruciferous vegetables was associated with older age. We were, therefore, unable to eliminate the potential biases and confounding factors arising from this difference. Further study of the cause of these sex differences in the influence of vegetable and cruciferous vegetable intake and cataract incidence is anticipated.

We agree that some randomized trials of antioxidant vitamin supplements have not shown protective effects against cataract, and further studies of antioxidant vitamins supplements have not been recommended. However, this study might be meaningful in revealing the relationship between vegetable and fruit intake and cataract risk in daily life.

The strengths of the present study include its large number of participants of both sexes; population-based prospective cohort design; limited localized bias, with inclusion of 11 public health center areas nationwide; use of a validated FFQ; and adjustment or stratification for potentially important confounding factors. However, the study also has several limitations. First, we had no source of information for cataract diagnosis other than the questionnaire, and might therefore have underestimated cataract incidence due to false-negative cases who had not visited an ophthalmology clinic and were not diagnosed with cataract. These sources of detection bias may have led to an underestimation of the overall incidence of age-related cataract. At the same time, this detection bias may have affected our results as mentioned above. In previous studies in which information on cataract was obtained using medical records or evaluation via ophthalmic examination, and not from self-report data, some reports showed an inverse association in women. We might not be able to remove this detection bias. Second, evaluation of dietary intake occurred at only one time point: the second survey, which was the baseline of this study. Repeated assessment of long-term dietary intake before disease onset is more likely to predict exposure conditions. Third, the follow-up period of 5 years was relatively short for a disease with such a protracted natural history. Fourth, we analyzed the data after excluding subjects with a history of diabetes mellitus; however, we did not exclude cases having diabetic mellitus during follow-up, and did not adjust for glucose/HbAlc level because data on these variables was not available. Finally, we were unable to remove the possibility of unmeasured and residual confounding factors.

In conclusion, the results of this prospective large-cohort study suggested that the intake of vegetables and cruciferous vegetables may reduce the risk of cataract incidence among Japanese men.

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