Original Article

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Dietary Patterns and Breast Cancer Risk: A KCPS-II Cohort Study

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ABSTRACT

Objective: There have been inconsistencies in the evidence for a role of dietary patterns in the development of breast cancer. In this study, we used a large-scale cohort [Korean Cancer Prevention Study-II (KCPS-II)] to examine the association between dietary patterns and breast cancer risk in Korean women.

Materials and Methods: The dietary patterns of 14,807 women from the KCPS-II were derived by factor analysis and 135 cases of breast cancer were diagnosed during the follow-up period. Cox proportional models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of breast cancer.

Results: The following three major dietary patterns were identified: "Korean dietary pattern" (high intake of Kimchi, vegetables, and rice); "sweet dietary pattern" (high intake of soda and sugar); and "new (Western-like) dietary pattern" (high intake of dairy products, eggs, oil, fruits, and bread). After adjusting for potential confounders, neither the Korean (HR for the highest compared with the lowest tertile, 1.04; 95% CI 0.53–2.06) nor the sweet dietary patterns were associated with the risk of breast cancer. In contrast, the new (Western-like) dietary pattern was found to be significantly associated with an increased risk of breast cancer with an HR (95% CI) of 1.01 (0.65–1.60) for the second tertile and 1.61 (1.04–2.50) for the third tertile as compared with the lowest tertile. After stratifying by menopausal status, these effects were only statistically significant among premenopausal women for the third tertile, compared with those in the bottom tertile (HR 1.69; 95% CI 1.06–2.68; p = 0.028). No significant association was observed between the Korean or sweet dietary pattern and breast cancer among either pre- or postmenopausal women.

Conclusion: Our findings revealed that a greater consumption of a new (Western-like) diet was associated with an increased breast cancer risk and consequently offer a potential prevention strategy for Korean women.

Keywords: Dietary pattern; breast cancer; KCPS-II cohort; Korean women

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Key Points

- Dietary patterns of 14,807 women from Korean Cancer Prevention Study-II were derived using factor analysis, and 135 cases of breast cancer were diagnosed during the follow-up period.
- Three major dietary patterns were identified: "Korean dietary pattern" (high intake of kimchi, vegetables, and rice), "sweet dietary pattern" (high intake of soda and sugar), and "new (Western) dietary pattern" (high intake of dairy products, eggs, oil, fruits, and bread).
- The Western diet was associated with an increased breast cancer risk, and reducing the consumption of Western diet may be a potential prevention strategy for Korean women.

Introduction

Breast cancer is one of the leading causes of death in women globally (1). It was among the most commonly diagnosed types of cancer in Korean women: 22,300 new cases were reported by the Korea Central Cancer Registry in 2017 (2). The age-specific incidence rate has been steadily increasing from 21.4 per 100,000 in 1999 to 55.6 per 100,000 in 2017 (2). Although several epidemiologic studies have examined the association between nutrient intake and breast cancer risk (3), their results have been inconsistent (4-6). Therefore, researchers have recently recognized the importance of identifying dietary patterns, following a holistic approach, rather than individual nutrients, in their contribution to chronic disease (7). Not only are such patterns practical tools for developing dietary recommendations but also a valuable method to determine risk factors and prevent disease simultaneously (8). Recently, prospective epidemiologic studies have examined associations

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between certain dietary patterns and breast cancer risk (9-13). However, most studies have been conducted in European populations, and only a few studies have investigated this relationship in Asian populations (14, 15). In addition, Zhang et al. (16) reported that a diet high in vegetables, fruits, and soy could decrease breast cancer risk, while Cui et al. (17) reported that this was not true for a vegetable-soy pattern, suggesting an inconsistency in results. Thus, this study aimed to identify dietary patterns and examine their association with the risk of developing breast cancer using a large-scale cohort study [Korean Cancer Prevention Study-II (KCPS-II)].

Materials and Methods

Study Population

The KCPS-II is a prospective cohort study initiated in April 2004 supported by the Seoul city government as a part of the Korean Metabolic Syndrome Research Initiative study (18). Participants received routine health assessments at 18 health promotion centers across South Korea. The number of retrospectively enrolled KCPS-II participants based on health examination records between 1994 and 2005 is 270,514; data from 192,358 participants was prospectively collected between 2004 and 2013. After excluding participants with missing information on lifestyle and dietary habits, as well as those who were male or had a history of breast cancer, a total of 14,807 participants were included for final analyses (Figure 1). Of 67,271 female cohort member with data collection from 2004–2013, a very large proportion (78%) had missing dietary data because only surveys in institutions with professional dietitians were available.

Cancer information was ascertained by linkages to the Korea Central Cancer Registry, until 31 December 2018. Cancer incidence was identified based on the 10th revision of International Classification of Disease. Our health examinations included questions on lifestyle, family, and personal medical history in addition to an assessment of anthropometric and clinical factors. General demographic and lifestyle variables including age, sex, education level, smoking status, and alcohol intake were collected by a standardized questionnaire; we also deployed a short version of the food-frequency questionnaire (FFQ). The Yonsei University Health System Institutional Review Board approved the study (decision no: Y-2020-0142, date: 05.10.2020), and all participants provided written, informed consent prior to participation.

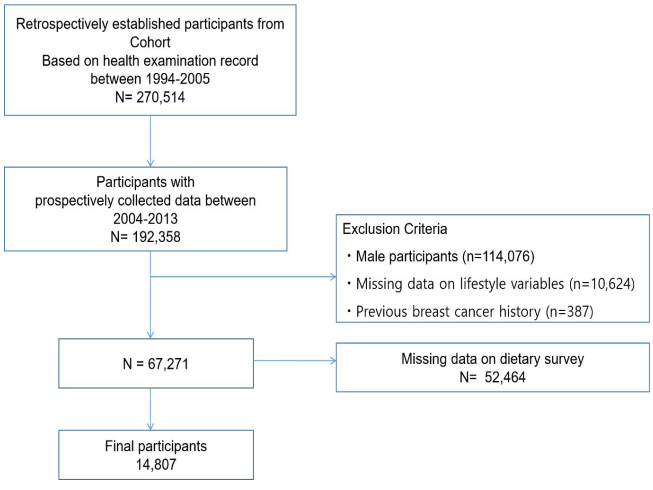

Figure 1. Flow diagram for study participants

Assessment of Dietary Intake and Risk Factors

A brief dietary assessment evaluated and validated in a previous study was used for estimating dietary patterns (19). This assessment comprised a short version of the FFQ, which is suitable to identify relationships between dietary intake and disease risk (20). It consists of 17 food items based on seven food groups: (1) fish, meat, eggs, and soybean products; (2) milk and dairy products; (3) vegetables; (4) fruits; (5) cereals and potatoes; (6) sugars and candies; and (7) fats and oil. Daily nutrient intakes were calculated based on food consumption: Participants were asked to fill out the frequency of their current intake of each food item according to four categories (0: never, 0.5: often, 1.0: regular, 1.5: always sufficient). Well trained dietitians asked participants how often they had consumed 17 food items in the morning, afternoon, and evening. Study participants were informed that the frequency of dietary intake in categories of always sufficient was assigned in reference to a regular frequency according to dietitian's instruction. The amounts of each food consumed are estimated in reference to a common size container (e.g., bowls, cups, and glasses), standard measuring cups and spoons such as photographs. Study participants were interviewed by a trained dietitian, who used instruments for estimating portion sizes according to the list of food exchanges for Korea. The third edition of food exchange lists was revised in 2010 by the Korean Diabetes Association, the Korean Nutrition Society, the Korean Society of Community Nutrition, the Korean Dietetic Association and the Korean Association of Diabetes Dietetic. Each participant's age, regular exercise habit (yes, no), alcohol intake (never, ex-drinkers, current drinkers), smoking status (never, ex-smokers, current smokers), menopausal status (pre-menopausal or postmenopausal), age at menarche, and the presence of family history of cancer (no, yes) were obtained using the questionnaire. We obtained information on the participant's height (cm) and weight (kg) directly measured by the medical staff. The body mass index (BMI) (kg/m^2) was calculated by dividing the body weight (kg) by the square of height (m).

Statistical Analysis

General characteristics of study participants stratified by breast cancer incidence outcome were compared using Student's t-test and chi-square test. Cox proportional hazards model with person-years was used to evaluate the hazard ratio (HR) and 95% confidence interval (CI) of breast cancer risk for each three dietary patterns. Multivariable HRs were adjusted for age (continuous), total energy intake (kcal/day, continuous), educational level (middle school or less, high school or college, undergraduate or more), exercise (yes, no), smoking status (never, ex-smokers, current smokers), alcohol intake (never, ever, current), and the menopausal status (pre-menopausal, postmenopausal). We used multivariable Cox proportional hazards regression models to examine the HRs and 95% CI for breast cancer risk across the tertile categories of each dietary pattern score, taking the lowest tertile category as reference. Principal factor analysis was used to cluster factors, followed by orthogonal (Varimax) rotation to assist in interpretation of the factors (PROC FACTOR and Varimax options). The principal factor analysis requires the number of clusters to be specified in advance and generates mutually exclusive clusters by comparing Euclidean distances between each subject and each cluster center in an interactive process using a K-means method (20). The SAS statistical package for Windows (version 9.4, SAS) was used for all statistical analyses. P<0.05 was considered significant. Food groups with an absolute loading greater than 0.3 on a given factor were considered to contribute importantly to that factor. We determined

three factors by eigenvalues of >1.1 and a scree plot and interpretability of the derived factors. We presented the distributions of each food item for the three dietary patterns (Supplementary Table 1). The final number of clusters was selected as 3-cluster by comparing between cluster variance and within-cluster variance ratios.

Results

The results derived from the factor loading matrix for major dietary patterns are depicted in Table 1. We extracted three major dietary patterns from the KCPS-II cohort. Based on the predominant food groups, we labeled these three patterns the "Korean dietary pattern", the "sweet dietary pattern", and the "New (Western-like) dietary pattern". The Korean pattern comprised a high content of meat, fish, tofu, herbs, vegetables, kimchi, rice, bread, and noodles; the sweet dietary pattern contained two food groups that consisted of sugar (honey) and soda; the new pattern featured a high load of eggs, milk, dairy products, oil, bread, snacks, and fruits. The total variances of the Korean, sweet, and new dietary patterns were 1.9%, 1.6%, and 1.6%, respectively.

Table 2 summarizes the general characteristics of study participants stratified by breast cancer incidence. Among the total of 14,807 women included for final analysis, 135 were diagnosed with breast cancer

Table 1. Factor loading matrix for the three major dietary patterns (*n* = 14,807)

Food group	Korean	Sweet	New (Western-like)
Meat, fish, tofu	0.62407		
Eggs			0.68750
Milk and dairy products			0.47546
Herbs and vegetables	0.65056		
Kimchi	0.73593		
Rice, bread, noodles	0.69294		
Oil			0.66155
Sugar and honey		0.83046	
Soda		0.82371	
Bread and snacks			0.40228
Fruits			0.43916
Variance explained by each factor	1.9108947	1.6446474	1.5862974

Factor loading scores less than 0.3 are not shown

Table 2. General characteristics of study participants

	No breast cancer *n* = 14,672	Incident breast cancer *n* = 135	*p*-value
	Mean (SD)	Mean (SD)	
Age (year)	46.39 (11.07)	46.97 (8.96)	0.46
Education (year)	13.2 (3.51)	14.0 (3.25)	0.00
Height (cm)	157.93 (5.49)	158.91 (5.66)	0.04
Body mass index (kg/m^2)	23.04 (3.09)	22.79 (2.88)	0.36
Family history of breast cancer (%)	3.21	0.00	0.59
Age in years at menarche (year)	14.90 (1.86)	14.74 (1.99)	0.46
Menopausal status (%)			
Pre-menopausal	93.30	91.85	
Postmenopausal	6.70	8.15	0.50
Amount of alcohol drinking (g/day)	5.16 (19.92)	7.79 (24.92)	0.26
Smoking status (yes/no, %)	4.58	8.15	0.04
Alcohol drinking (yes/no, %)	38.92	40.74	0.65
Use of oral contraceptives (%)	17.77	22.81	0.32
Total energy intake (kcal)	1.728 (311)	1.718 (303)	0.71
Follow-up (years)	8.43 (4.73)	6.69 (4.51)	<0.0001

SD: Standard deviation

during a mean follow-up of 8.15 years. Education, height, and smoking status showed statistically significant differences between non-breast cancer and breast cancer patients. Table 3 shows HRs between the three dietary patterns and breast cancer risk in multivariable analysis. The new dietary pattern was significantly associated with an increased risk of breast cancer by HR (95% CI), which was 1.01 (0.65–1.60) for the second tertile and 1.61 (1.04–2.50) for the third tertile compared with the bottom tertile. However, the Korean and sweet dietary patterns showed no statistically significant association with breast cancer risk in multivariable analysis.

Multivariable HRs of breast cancer according to menopausal status are shown in Table 4. In premenopausal women, multivariable HRs for the new pattern were significantly associated with an increased risk of breast cancer; when comparing the highest with the lowest tertile of the new dietary pattern, the HR was 1.69 (95% CI 1.06–2.68).

Table 3. Breast cancer risk with multivariable Cox proportional hazard model

Variables		HR (95% CI)*	*p*-value	*p*-trend
	Tertile 1	1.0		
Korean dietary patterns	Tertile 2	1.17 (0.73–1.89)	0.51	
	Tertile 3	1.04 (0.53–2.06)	0.90	0.51
	Tertile 1	1.0		
Sweet dietary patterns	Tertile 2	1.11 (0.72–1.71)	0.62	
	Tertile 3	1.13 (0.73–1.75)	0.58	0.45
	Tertile 1	1.0	0.95	
New (Western-like) dietary patterns	Tertile 2	1.01 (0.65–1.60)		
	Tertile 3	1.61 (1.04–2.50)	0.01	0.01

*HR (95% CI) adjusted for age (continuous), total energy intake (kcal/day, continuous), educational duration (years), exercise (yes, no), alcohol intake (never, ever, current), smoking status (never, ex-smokers, current smokers), and the menopausal status (pre-menopausal, postmenopausal); HR: Hazard ratio; CI: Confidence interval

Table 4. Hazard ratio of breast cancer risk by menopausal status

Variables		HR (95% CI)*	*p*-value
Pre-menoposal			
	Tertile 1	1.0	
Korean dietary patterns	Tertile 2	1.12 (0.68–1.83)	0.66
	Tertile 3	0.98 (0.48–1.98)	0.95
	Tertile 1	1.0	
Sweet dietary patterns	Tertile 2	1.01 (0.64–1.59)	0.96
	Tertile 3	1.13 (0.72–1.78)	0.59
	Tertile 1	1.0	
New (Western-like) dietary patterns	Tertile 2	1.09 (0.67–1.75)	0.74
	Tertile 3	1.69 (1.06–2.68)	0.03
Postmenopausal			
	Tertile 1	1.0	
Korean dietary patterns	Tertile 2	4.35 (0.42–44.90)	0.22
	Tertile 3	3.61 (0.21–63.34)	0.38
	Tertile 1	1.0	
Sweet dietary patterns	Tertile 2	2.68 (0.64–11.27)	0.18
	Tertile 3	0.87 (0.14–5.65)	0.89
	Tertile 1	1.0	
New (Western-like) dietary patterns	Tertile 2	0.68 (0.13–3.56)	0.64
	Tertile 3	1.34 (0.33–5.42)	0.68

*HR (95% CI) adjusted for age (continuous), total energy intake (100 kcal/day, continuous), educational duration (years), exercise (yes, no), alcohol intake (never, ever, current), smoking status (never, ex-smokers, current smokers); HR: Hazard ratio; CI: Confidence interval

However, this pattern showed no statistically significant association with breast cancer risk among postmenopausal women.

In addition, the Korean and sweet dietary patterns were not associated with the risk of breast cancer after adjusting for lifestyle factors (smoking status, exercise, and alcohol drinking), total calorie intake, and age among either pre- or postmenopausal women.

Discussion and Conclusion

In the present study we identified three major dietary patterns: Korean, sweet, and new (Western-like). We found that a higher consumption of a new diet was significantly associated with an increased risk of developing breast cancer. This study confirms the international concept that Western diet, along with other sociocultural habits, is associated with an increase incidence of breast cancer in Eastern populations, particularly among young women. However, there were no associations between the Korean or the sweet dietary pattern and breast cancer risk among Korean women.

Previous cohort studies on the association between dietary patterns and breast cancer risk have been predominantly conducted in European populations (9, 21, 22) and the results have been inconsistent. A recent meta-analysis suggested that a Western-like diet may be associated with an increased risk of breast cancer, whereas a prudent dietary pattern was associated with a reduced risk of breast cancer (23). Dietary patterns are likely to vary among different populations due to cultural preferences, geographic characterization, socioeconomic status, and food accessibility (24). Besides, heterogeneity in components of dietary patterns and deviations in measurement methods between studies could have contributed to these inconsistent findings. In our study, we identified a new dietary pattern, characterized by a high intake of dairy products, oil, bread, and fruit in Korean women, and high consumption according to this pattern was significantly associated with the risk of breast cancer. Based on our previous cohort study (19), the consumption of Korean traditional foods, such as vegetables and cereals, has decreased, whereas a new dietary pattern has emerged among Korean adults, whereby the intake of dairy products and fruits has increased. According to the statistics of Korea National Health and Nutrition Examination Survey (2010) (25), less than 40% of the protein intake is derived from animal sources, while in the past, less than 10% of protein intake came from animal sources. It is important to note that the new (Western-like) dietary pattern identified in our study differs from that in others in several aspects. Although among European populations this diet is characterized by a high intake of red and processed meats (26, 27), which may contain pro-carcinogenic factors, such as heterocyclic amines and N-nitroso compounds, the major components of the new (Western-like) dietary pattern in this study were eggs, oil, bread, and dairy products. This pattern is consistent with that found in our previous study, in that the Western and "New" diets were characterized by a high consumption of eggs, oil, soda, fruits,dairy products, and potatoes using factor analysis in Korean women (19). Thus, the current Korean diet has dramatically shifted from the traditional foods to a New dietary pattern, which along with the economic development and globalization supports our observations (28).

In addition, most prospective studies found significant associations between Western dietary patterns and breast cancer risk among postmenopausal (9, 10, 15, 29), but not premenopausal women, although the etiology is still unclear. In contrast, in the current study, stratified-analyses showed that the positive association between a new (Western-like) dietary pattern and breast cancer risk was statistically significant among pre-menopausal, but not postmenopausal women. Given one of the obvious differences between pre- and postmenopausal women, the elevated levels of estrogen may be one plausible explanation for the impact a new (Western-like) dietary pattern has on the risk of developing breast cancer. One potential biological mechanism that the new (Western-like) dietary pattern, characterized by high intakes of energy, animal fat, and refined carbohydrates is through increased BMI and thereby increased levels of estrogen (23). A migration study of Asian-American women suggested that the dietary habits in early adult life may strongly affect breast cancer risk (30). Dietary fat intake was reported to affect endogenous hormones, which regulates ductal morphogenesis (31, 32). Previous studies on mammographic density have also shown the possible importance of early-life diet (saturated fat intake) in breast cancer risk (33).

A new (Western-like) dietary pattern is associated with increased breast cancer risk that needs further study in order to clarify the underlying mechanisms. Although many epidemiologic studies investigating the association between vegetable intake and breast cancer risk yielded inconsistent results, prudent dietary patterns characterized by an intake of vegetables and fruits have been assumed to decrease the breast cancer risk due to anti-oxidative effects (34, 35). However, in this study, we found no significant association between the Korean dietary pattern, which was mainly characterized by high intake of kimchi (spicy cabbage), rice, and vegetables, and breast cancer risk among pre- and postmenopausal women. This is in line with a prospective study among Japanese women, which identified three dietary patterns: "vegetable pattern" (vegetables, potatoes, seaweed, tofu, fruits, fresh fish, eggs, and miso soup); "animal food pattern" (meat, deep-fried foods, fried vegetables, fish paste, and salt-preserved fish); and "dairy product pattern" (milk, dairy products, fruits, coffee, and tea) (15). The authors found that the animal food pattern was significantly associated with a decreased risk of breast cancer morbidity, whereas no significant association was observed between the vegetable and dairy product dietary patterns and breast cancer risk (15).

Furthermore, the World Cancer Research Fund also reported that no statistically significant association was found between vegetables (including fruits) and breast cancer (36). However, a study examining Singapore Chinese women demonstrated that there was a dose-dependent trend of decreasing breast cancer risk for the vegetable-fruit-soy dietary pattern only among postmenopausal women (14).

Kimchi is a traditional Korean food manufactured by fermenting vegetables with probiotic lactic acid bacteria. Kimchi can be considered a vegetable probiotic food that contributes health benefits in a similar manner as yogurt as a dairy probiotic food (37). Cancer preventive/anticarcinogenic activity of kimchi is associated with the type of ingredients and products formed during fermentation (38). Thoennissen et al. (39) demonstrated that capsaicin caused cell-cycle arrest and apoptosis in breast cancer cells by modulating the epidermal growth factor receptor/human epidermal growth factor receptor 2 pathway and inhibited the development of pre-neoplastic breast lesions by up to 80% without toxicity.

However, in the present study, we found there was no dose-dependent trend of breast cancer risk among Korean dietary patterns. Diversities exist among cooking methods or types of vegetables among each

country, which may account for the differences observed between the various studies. The major strengths of our study include its large sample size and prospective design, in which information was collected before the diagnosis of breast cancer, eliminating the potential recall bias that occur in case-control studies. In addition, we retrieved cancer diagnosis data that had high sensitivity and completeness from the Korean Central Cancer Registry. Our study has some limitations. First, breast cancer is a heterogeneous disease, and several studies have suggested that risk factors for breast cancer may differ in their association depending on tumor receptor status (13, 14). Nevertheless, we were unable to consider the hormone receptor status since we had no data on the participants' molecular subtype. Second, we used a shorter version of the FFQ at baseline, such that we could not consider the possibility that secular transitions in dietary patterns may have occurred during follow-up. Third, we could not exclude the possibility of errors in measuring dietary intake. The diet assessment tool included a limited number of food items, although the tool was validated and the correlation with 3-day diet records confirmed. Fourth, the number of participants in this cohort is relatively large, nevertheless, the number of breast cancer cases was limited in the final analysis (only 135 incident breast cancers). In addition, of 67,271 female cohort member with data collection from 2004–2013, a very large proportion (78%) had missing dietary data although the distributions of general characteristics did not differ between study participants with dietary data and without dietary data (Supplementary Table 2).

Our study found that a new dietary pattern, characterized by high consumption of eggs, oil, dairy products, fruits, and bread, was associated with an increased risk of breast cancer among pre-menopausal women. In contrast, the Korean and sweet dietary patterns were not associated with breast cancer risk. Large scale prospective studies in Asian women are needed to confirm our findings.

Ethics Committee Approval: The Yonsei University Health System Institutional Review Board approved the study (decision no: Y-2020-0142, date: 05.10.2020).

Informed Consent: All participants provided written, informed consent prior to participation.

Authorship Contributions

Concept: J.Y.L., H.I.C., H.K.; Design: J.Y.L., H.I.C., H.K.; Data Collection and/or Processing: J.Y.L., H.I.C., H.K.; Analysis and/or Interpretation: J.Y.L., H.I.C., H.K.; Literature Search: J.Y.L., H.I.C., H.K.; Writing: J.Y.L., H.I.C., H.K.

Conflict of Interest: The authors have no conflicts of interest to declare.

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Supplementary Table 1. Food items and food groups for dietary pattern analysis

No	Food items	Foods or food groups
Korean dietary pattern		
1	Fishes, processed meats, tofu, bean products	Meats, fishes, tofu
2	Herbs and vegetables	Herbs and vegetables
3	Kimchi (Korean cabbage)	Kimchi
4	Cooked rice, bread, cooked noodles	Rice, bread, noodles
5	Potatoes, sweet potatoes	Potatoes and sweet potatoes
Sweet dietary pattern		
6	Sugar, honey	Sugar and honey
7	Sugar on coffee or tea	Sugar and honey
8	Jam, honey	Sugar and honey
9	Coke, carbonated beverage	Soda
New (Western-like) dietary pattern		
10	Eggs	Eggs
11	Egg type (scramble eggs, fried eggs, scrolled eggs)	Oil
12	Milk	Milk and dairy products
13	Yogurt, ice cream, cheese, other products	Milk and dairy products
14	Bread and snacks	Bread and snacks
15	Butter, margarine	Oil
16	Mayonnaise dressing food, fried food, stir-fried food	Oil
17	Fruits	Fruits

Supplementary Table 2. General characteristics of study participants stratified by with and without dietary data

	Participants with diet data (*n* = 14,807)	**Participants without diet data (*n* = 52,464)**	**Total participants (*n* = 67,271)**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**
Age, year	46.39 (11.04)	39.93 (11.03)	41.35 (11.36)
Body mass index, kg/m^2	23.04 (3.09)	22.09 (3.12)	22.30 (3.14)
Smoking status			
Never	13461 (90.81)	46010 (87.60)	59471 (88.31)
Ex	680 (4.59)	4430 (8.43)	5110 (7.59)
Current	682 (4.60)	2080 (3.96)	2762 (4.10)
Exercise			
Yes	7383 (50.03)	24388 (46.65)	31771 (47.39)
No	7375 (49.97)	27890 (53.35)	35265 (52.61)
Alcohol drinking			
Never	8494 (57.30)	15961 (30.39)	24455 (36.31)
Ex	561 (3.78)	9233 (17.58)	9794 (14.54)
Current	5768 (38.91)	27326 (52.03)	33094 (49.14)

SD: Standard deviation