The official journal of the Japan Atherosclerosis Society and
the Asian Pacific Society of Atherosclerosis and Vascular Diseases

Original Article

J Atheroscler Thromb, 2024; 31: 000-000. http://doi.org/10.5551/jat.65049

Dairy Intake and All-Cause, Cancer, and Cardiovascular Disease Mortality Risk in A Large Japanese Population: A 12-Year Follow-Up of the J-MICC Study

Naoko Miyagawa[1,2], Naoyuki Takashima[3,4], Akiko Harada[4], Aya Kadota[2,4], Keiko Kondo[2,4], Katsuyuki Miura[2,4], Nahomi Imaeda[5], Chiho Goto[6], Jun Otonari[7], Hiroaki Ikezaki[8], Keitaro Tanaka[9], Chisato Shimanoe[10], Mako Nagayoshi[11], Takashi Tamura[11], Yoko Kubo[11], Yasufumi Kato[11], Yuriko N. Koyanagi[12], Hidemi Ito[13,14], Nobuaki Michihata[15], Yohko Nakamura[15], Shiroh Tanoue[16], Rie Ibusuki[17], Sadao Suzuki[18], Takeshi Nishiyama[18], Etsuko Ozaki[3], Isao Watanabe[3], Kiyonori Kuriki[19], Takeshi Watanabe[20], Masashi Ishizu[20], Asahi Hishida[21], Yoshikuni Kita[2,22], Kenji Wakai[11], Keitaro Matsuo[12,23] and J-MICC Study Group

[1] Department of Preventive Medicine and Public Health, Keio University School of Medicine, Tokyo, Japan
[2] Department of Public Health, Shiga University of Medical Science, Shiga, Japan
[3] Department of Epidemiology for Community Health and Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan
[4] NCD Epidemiology Research Center, Shiga University of Medical Science, Shiga, Japan
[5] Department of Nutrition, Faculty of Wellness, Shigakkan University, Aichi, Japan
[6] Department of Health and Nutrition, School of Health and Human Life, Nagoya Bunri University, Aichi, Japan
[7] Department of Psychosomatic Medicine Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[8] Department of General Internal Medicine, Kyushu University Hospital, Fukuoka, Japan
[9] Department of Preventive Medicine, Faculty of Medicine, Saga University, Saga, Japan
[10] Department of Pharmacy, Saga University Hospital, Saga, Japan
[11] Department of Preventive Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan
[12] Division of Cancer Epidemiology and Prevention, Aichi Cancer Center Research Institute, Nagoya, Japan
[13] Division of Cancer Information and Control, Aichi Cancer Center Research Institute, Nagoya, Japan
[14] Department of Descriptive Cancer Epidemiology, Nagoya University Graduate School of Medicine, Nagoya, Japan
[15] Cancer Prevention Center, Chiba Cancer Center Research Institute, Chiba, Japan
[16] Department of Epidemiology and Preventive Medicine, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan
[17] Department of International Island and Community Medicine, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan
[18] Department of Public Health, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan
[19] Laboratory of Public Health, Division of Nutritional Sciences, School of Food and Nutritional Sciences, University of Shizuoka, Shizuoka, Japan
[20] Department of Preventive Medicine, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan
[21] Department of Public Health, Aichi Medical University School of Medicine, Aichi, Japan
[22] Faculty of Nursing Science, Tsuruga Nursing University, Fukui, Japan
[23] Department of Cancer Epidemiology, Nagoya University Graduate School of Medicine, Nagoya, Japan

Aim: We examined the association between dairy intake and all-cause, cancer, and cardiovascular disease mortality in a cohort of the general population followed up for 12 years across Japan.

Methods: We conducted a longitudinal cohort study of 79,715 participants from the Japan Multi-Institutional Collaborative Cohort study (57.2% women, mean age 54.7 years old). The amount of dairy (milk and yogurt) intake was determined using a validated short-food frequency questionnaire. The hazard ratio for mortality according to sex-specific tertile of dairy intake was calculated using Cox proportional hazards regression models with adjustment for potential confounding factors and dietary factors by sex.

Results: During the follow-up period (932,738 person-years), 3,723 participants died, including 2,088 cancer and 530 cardiovascular disease deaths. The highest tertile of total dairy intake (versus the lowest tertile) was

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

associated with a 19% lower all-cause mortality risk (hazard ratio = 0.81, 95% confidence interval: 0.70-0.92; *P* for trend = 0.001) in women. Similarly, we observed inverse associations between milk intake and all-cause and cancer mortality risk in women, yogurt intake and cardiovascular disease risk in women, and yogurt intake and all-cause mortality risk in both sexes.

Conclusion: A higher total dairy and milk intakes in women and yogurt intake in both sexes were associated with a reduced risk of all-cause mortality in the general population across Japan during the 12-year follow-up period.

Key words: Dairy products, Milk, Yogurt, Mortality, Cohort study

Abbreviations: NCD: non-communicable disease, CVD: cardiovascular disease, J-MICC: Japan Multi-Institutional Collaborative Cohort, BMI: body mass index, FFQ: food frequency questionnaire, CI: confidence interval

Introduction

A suboptimal diet is a major contributor to the global burden of non-communicable disease (NCD) mortality and morbidity[1] but is also a preventable risk factor for NCDs. Dietary choices are associated with culture, climate, and socioeconomic status. The development of NCDs is defined by genetic and environmental factors, including dietary habits. Therefore, identifying the dietary factors that reduce the risk of developing NCDs and death in each ethnic group remains a primary concern.

Dairy intake is a recommended component of a healthy diet in dietary patterns, such as Dietary Approaches to Stop Hypertension (DASH) dietary patterns[2] and dietary recommendations from various countries[3-5]. However, recent meta-analyses of prospective cohorts examining the association between dairy intake and mortality risk in mainly Western populations have reported inverse[6, 7], positive[6, 8], or no association[6, 8-10], with inconsistent associations based on cause of death, dairy product type, and participant background. In addition, as dairy products are not part of the traditional Japanese diet[11], dairy intake in the Japanese population is much lower than that in Western populations[12, 13].

Reports from large cohorts across Japan have revealed an inverse association between dairy intake and all-cause or cardiovascular disease (CVD) mortality in men only[14, 15]. However, in another cohort study, an inverse association between dairy intake and CVD mortality was observed in women only[16]. In other words, the association between dairy intake and total and NCD mortality in the Japanese population, who consume far fewer dairy products than Western populations, is not consistent across studies, especially by sex.

Study Aim

We examined the association between dairy intake and all-cause, cancer, and CVD mortality in a cohort of the general population followed up for 12 years across Japan.

Methods

Study Population

A total of 92,514 Japanese individuals 35–69 years old from 14 regions in various parts of Japan participated in the baseline survey of the Japan Multi-Institutional Collaborative Cohort (J-MICC) study from 2005 to 2014 (the dataset used in this study was fixed on October 16, 2023). The J-MICC study methods have been reported previously[17, 18]. We included 79,715 participants (57.2% women, mean age 54.7 years old) in the analysis, excluding those with a history of cancer (*n*=6,482) and CVD (*n*=3,545), those with missing information regarding dairy intake (*n*=678) at baseline, those with total energy intake at baseline deviating from the sex-specific mean by ±3 standard deviations (*n*=921), and those who died within a year from the baseline (*n*=1,173) **(Fig. 1)**.

Written informed consent was obtained from all participants after a thorough explanation of the outline and purpose of the study. The present study

Address for correspondence: Naoko Miyagawa, Department of Preventive Medicine and Public Health, Keio University School of Medicine, Tokyo, Japan 35 Shinanomachi Shinjuku-ku, Tokyo, 160-8582 Japan E-mail: naocom@belle.shiga-med.ac.jp

Received: April 17, 2024 Accepted for publication: September 23, 2024

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

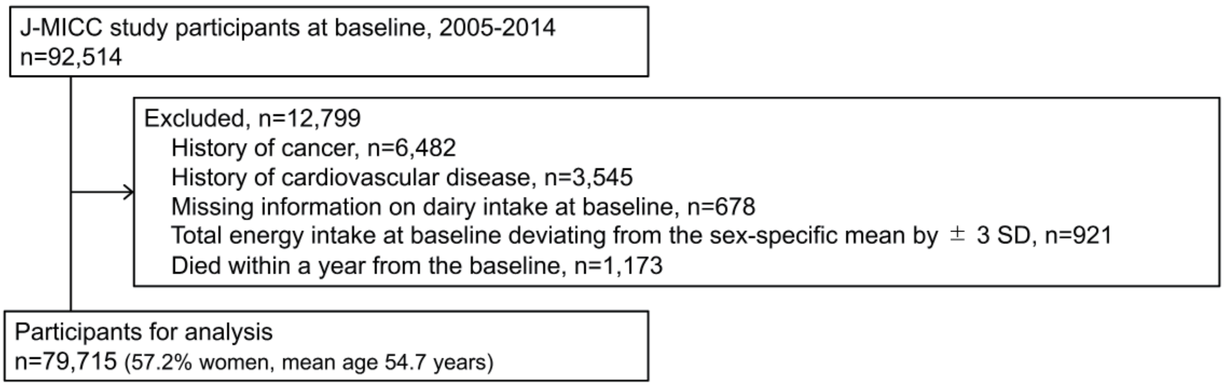

Fig. 1. Flow chart of the participant selection process in the present study. J-MICC, Japan Multi-Institutional Collaborative Cohort; SD, standard deviation

was conducted according to the guidelines laid down in the Declaration of Helsinki, and the study protocol was approved by the Institutional Review Boards of the Aichi Cancer Center (IRB No. 2022-0-306), Shiga University of Medical Science (IRB No. G2005-103), and all other study centers.

Mortality Surveillance

The participants were followed up until December 31, 2020 (Chiba, Aichi Cancer Center, Okazaki, Shizuoka, Daiko, Takashima, Kyoto, Fukuoka, Saga, Tokushima, Kyushu and Okinawa Population Study [KOPS], and Iga) or December 31, 2021 (Kagoshima and Shizuoka-Sakuragaoka), providing 12 years of follow up. The vital status of the participants was monitored using registration records from the local governments where they lived. During the follow-up period, 4,577 participants (5.7%) moved out of the study sites, and 309 participants (0.4%) could not be followed up for other reasons. These individuals were censored at the last date when they were known to reside at the study sites. National Vital Statistics were utilized to identify the causes of death with permission from the Japanese Ministry of Health, Labour and Welfare, Government of Japan. The underlying causes of death in the National Vital Statistics were coded according to the 10th International Classification of Disease (ICD10). The classification details have been described previously[19]. The corresponding ICD10 codes are as follows: cancer mortality, C00–C97; and CVD mortality, I00–I99.

Baseline Examinations

The height and weight of the participants were measured during the survey at 12 study sites and self-reported for participants at the remaining two sites. The body mass index (BMI) was calculated by dividing the body weight (kg) by the height (m^2). A self-administered questionnaire was used to obtain information on behavioral factors, such as smoking and drinking habits, leisure-time physical activity, and the medical history at baseline. Physical activity during leisure time (metabolic equivalent of task hours per day) was calculated from three different intensity levels of exercise and hours of these activities[20]. Smoking and drinking statuses were categorized as never, past, or current.

Dietary Assessments

A validated short-food frequency questionnaire (FFQ) was used to assess eating habits. The details of the short FFQ have been described elsewhere[21-24]. In brief, participants reported how often they consumed 47 foods and beverages in the past year at baseline from among 8 options (rarely, 1–3 times/month, 1–2 times/week, 3–4 times/week, 5–6 times/week, 1 time/day, 2 times/day, and 3 or more times/day). The total intake of food and beverages was calculated by multiplying the frequency of consumption by portion size. We combined milk and yogurt intake into the total dairy intake. Similarly, multiple foods were grouped as follows: red meat, for beef, pork, processed meat, and liver; fish and shellfish, for fish, small fish, canned tuna, shellfish, roe, and fish cake; vegetables, for pumpkin, carrot, broccoli, green leafy vegetables, cabbage, Japanese radish, dried radish, burdock root, bamboo shoot, and other vegetables; and fruits, for citrus fruits and other fruits.

Validity has been reported elsewhere[21] by assessing the short FFQ and 12-day (4 seasons of 3 non-consecutive days) weighed dietary records of 288 men and women. Spearman's correlation coefficient between the energy-adjusted dairy, milk, and yogurt intake questionnaire and the dietary record were 0.77, 0.89, and 0.84 for men; and 0.55, 0.73, and 0.69 for women[21].

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

Statistical Approaches

The baseline characteristics and nutritional parameters of the participants were presented as means and standard deviations or medians and interquartile ranges for continuous variables and as percentages for categorical variables. Differences in baseline characteristics among sex-specific tertiles of dairy intake were assessed using trend analyses or the Cochran-Armitage test.

Cox proportional hazards regression models were used to estimate the multivariate-adjusted hazard ratio (HR) and 95% confidence interval (CI) of all-cause, cancer, and CVD mortality according to sex-specific tertiles of dairy intake by sex. Model 1 was adjusted for age and study site. Model 2 was adjusted for the variables in Model 1 plus a history of hypertension (yes or no), diabetes (yes or no), dyslipidemia (yes or no), and BMI categories (<18.5, 18.5–to <25, ≥ 25 kg/m^2). Model 3 was adjusted for the variables in Model 2 plus the smoking status (never, past, and current), drinking status (never, past, and current), physical activity during leisure time (MET-hour/day), and intake of red meat, fish, vegetables, and fruits. Food intake was used in the analysis as intake per 1,000 kcal of daily energy intake. Physical activity and food intake were analyzed in sex-specific tertiles. We created a category for the missing values for each covariate. Corresponding analyses were conducted separately for milk intake and yogurt intake, instead of dairy intake as a whole. *P*-values for linear trends across tertiles were calculated using variables 0, 1, and 2 assigned to successive tertiles.

All statistical analyses were performed using the SAS software program, version 9.4 for Windows (SAS Institute Inc., Cary, NC, USA). Analysis items with a two-tailed *P*-value of <0.05 were considered statistically significant.

Results

Table 1 presents the baseline characteristics of the study participants according to sex-specific tertiles of dairy intake. The median dairy intake was 34.6 g/1,000 kcal energy intake (66.0 g/day) in men and 79.7 g/1,000 kcal energy intake (127.5 g/day) in women. As dairy intake increased, the age, prevalence of dyslipidemia, physical activity, and dietary intake of fish, vegetables, and fruits increased. In contrast, the prevalence of current smokers and drinkers decreased in both sexes. The relationships between milk and yogurt intake and age, history of cardiometabolic diseases, behavioral factors, and eating habits were also generally similar to those of dairy products **(Supplemental Tables 1 and 2)**.

The observed total person-years were 932,738, and the median follow-up period was 12.4 years. During the follow-up, 3,723 participants died. Of the all-cause mortality, 2,088 died from cancer and 530 from CVD.

Table 2 presents multivariate-adjusted HRs and 95% CIs according to sex-specific tertiles of dairy intake. In women, the HRs of all-cause mortality were significantly lower in the highest tertiles of dairy intake (T3) (HR 0.81 [95% CI 0.70–0.92]) than in the lowest tertile (T1) in Model 3, and its inverse linear trend was significant in Model 3 (*P*=0.001). The trends of HRs in relation to the dairy intake were similar for cancer and CVD mortality in women but not significant. In men, dairy intake and all-cause and cancer mortality were inversely associated when adjusted for the age, study site, histories of cardiometabolic diseases, and BMI in Models 1 and 2 but were no longer associated when behavioral factors and eating habits were further adjusted in Model 3. No statistically significant associations were observed between dairy intake and CVD mortality risk in men.

Table 3 presents the multivariate-adjusted HRs and 95% CIs according to sex-specific tertiles of milk intake. In women, on comparing the highest tertile of milk intake with the lowest, the multivariate-adjusted HR for all-cause mortality risk was 0.84 (95% CI 0.73–0.95; *P* for trend=0.007), and that for cancer mortality was 0.82 (95% CI 0.69–0.99; *P* for trend=0.034). In men, milk intake was inversely associated with all-cause and cancer mortality risks in Models 1 and 2; however, it was no longer associated with the final model. In contrast, no significant associations were observed between milk intake and CVD mortality risk in either sex.

Table 4 presents multivariate-adjusted HRs and 95% CIs according to sex-specific tertiles of yogurt intake. On comparing the highest tertile of yogurt intake with the lowest, the multivariate-adjusted HR for all-cause mortality risk was 0.90 (95% CI 0.82-0.999; *P* for trend=0.034) in men and 0.87 (95% CI 0.76-0.997; *P* for trend=0.046) in women, respectively. Furthermore, the multivariate-adjusted HR of CVD mortality was significantly lower in the highest tertiles of yogurt intake (HR 0.64 [95% CI 0.46-0.90]; *P* for trend=0.007) than the lowest tertile in women. For men, in Models 1 and 2, yogurt intake was inversely associated with cancer mortality risk and marginally associated with CVD mortality in Models 1 and 2; however, they were no longer associated in the final model. No significant associations were observed between yogurt intake and cancer mortality risk in women.

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

Table 1. Baseline characteristics of participants in the J-MICC according to the sex-specific tertiles of dairy intake

	Men			Women		
	Dairy intake, g/1,000 kcal			Dairy intake, g/1,000 kcal		
	T1 (low)	T2	T3 (high)	T1 (low)	T2	T3 (high)
Range of dairy intake (median), g/1,000kcal	0 – 15.0 (4.7)	15.0-63.6 (34.6)	63.6-515.9 (94.1)	0-49.7 (18.9)	49.7-107.1 (79.7)	107.1-801.1 (149.0)
Median intake of dairy (IQR), g/day	10 (0, 16)	66 (42, 96)	170 (160, 260)	26 (10, 50)	128 (98, 155)	235 (178, 255)
Number at risk	11,364	11,365	11,364	15,207	15,208	15,207
Age, years	54.3 (9.3)	55 (9.3)	56.7 (9.2)*	53.4 (9.4)	54.7 (9.3)	54.8 (9.5)*
Body mass index, kg/m^2	23.8 (3.2)	23.9 (3.1)	23.6 (2.8)*	22.5 (3.5)	22.3 (3.3)	22.1 (3.2)*
History of hypertension, %	22.5	22.3	21.8	15.2	15.1	14.0*
History of diabetes, %	6.9	8.7	9.2*	3.0	3.1	3.1
History of dyslipidemia, %	13.4	15.5	16.0*	13.2	14.6	15.9*
Drinking status, %			*			*
Never	18.4	19.4	22.9	58.6	61.2	62.1
Past	2.7	2.9	3.5	1.9	1.6	1.9
Current	78.8	77.7	73.5	39.4	37.1	35.9
Missing	0.1	0.1	0.1	0.1	0.1	0.1
Smoking status, %			*			*
Never	23.2	29.8	35.1	81.2	87.5	86.8
Past	37.2	40.4	41.9	7.9	6.5	6.9
Current	39.2	29.5	22.8	10.4	5.5	5.6
Missing	0.3	0.3	0.2	0.5	0.5	0.6
Physical activity in leisure time, MET-hours/day	0.8 (0, 2.2)	1.1 (0.2, 2.8)	1.4 (0.3, 3.6)*	0.5 (0, 2.2)	0.8 (0.1, 2.6)	1.1 (0.2, 2.7)*
Dietary intake						
Energy, kcal/day	1914.5 (356.7)	1907.1 (335.4)	1893.4 (302.6)*	1496.3 (235.4)	1554.2 (214.4)	1532.4 (238.8)*
Milk, g/1,000kcal	0 (0, 7.7)	16.8 (9.4, 34.9)	79.2 (65.4, 91.2)*	9.8 (0, 18.9)	50.0 (20.2, 78.2)	101.8 (89.6, 125.5)*
Yogurt, g/1,000kcal	0 (0, 4.6)	8.4 (3.5, 24.6)	13.7 (4.3, 49.8)*	7.1 (0, 13.3)	21.9 (6.7, 54.3)	49.5 (15.1, 64.5)*
Red meat, g/1,000kcal	9.7 (6.9, 16.5)	10.2 (7.6, 16.8)	10.0 (7.4, 16.7)	13.6 (9.3, 21.8)	14.7 (9.5, 21.9)	13.8 (9.4, 21.4)
Fish, g/1,000kcal	23.7 (15.8, 34.6)	25.2 (17.2, 34.9)	25.7 (17.0, 35.4)*	29.1 (19.5, 39.9)	30.5 (21.0, 40.5)	30.4 (20.7, 41.4)*
Vegetable, g/1,000kcal	45.8 (30.8, 67.7)	51.0 (35.4, 73.6)	56.7 (38.6, 81.5)*	84.8 (59.3, 117.6)	92.5 (67.1, 125.1)	96.2 (68.4, 133.5)*
Fruits, g/1,000kcal	11.2 (7.0, 20.6)	16.2 (9.6, 31.7)	19.3 (10.6, 43.6)*	23.7 (12.7, 54.2)	37.2 (17.9, 64.1)	44.6 (20.2, 73.3)*

All variables were expressed as mean (standard deviation) or median (IQR) for continuous variables or as percentages for categorical variables. $^{*}p<0.05$: differences among sex-specific tertiles of dairy intake were assessed using trend analysis or the Cochran-Armitage test.
J-MICC, Japan Multi-Institutional Collaborative Cohort; T, tertile; IQR, interquartile range; MET, metabolic equivalent of task.

Discussion

In this 12-year general population prospective cohort study across Japan, we observed that total dairy and milk intake in women and yogurt intake in both sexes were inversely associated with total mortality risk after adjusting for potential confounding factors and dietary factors. Similarly, milk intake was inversely associated with cancer mortality risk and yogurt intake with CVD mortality risk in women.

Several prospective cohort meta-analyses have examined the association between dairy product intake and mortality risk in recent years. These studies were conducted in cohorts consisting primarily of Western populations, and dose-response analyses have shown associations with outcomes for each increase of approximately 200 g/day in total dairy products. Previous meta-analyses have revealed inverse associations between one additional serving of yogurt and the risk of all-cause mortality[7] and between fermented dairy and total cancer mortality in women[6]. Another meta-analysis reported a positive association between the total mortality and cancer risk associated with milk intake in women[6]. A non-linear dose-response relationship also exists between dairy products and all-cause mortality, with no adverse effects observed for an intake of up to 750 g/day, while a 15% increased risk of death was observed at intakes below 1000 g/day[8]. Conversely, some meta-analyses have reported that dairy products were not associated with total or cancer mortality[6, 8, 10], and the addition of 200 mL/day of dairy or milk intake was

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

Table 2. Adjusted hazard ratios and 95% CIs for the mortality from all cause, cancer, cardiovascular disease according to sex-specific tertiles of dairy intake: J-MICC study

	Men				Women			
	Dairy intake, g/1000 kcal energy intake				Dairy intake, g/1000 kcal energy intake			
	T1 (low)	T2	T3 (high)	*P* for trend	T1 (low)	T2	T3 (high)	*P* for trend
Median dairy (IQR) intake g/1,000kcal	4.7 (0, 9.4)	34.6 (21.5, 49.5)	94.1 (78.2, 127.2)		18.9 (7.5, 31.4)	79.7 (64.6, 93.8)	149.0 (123.5, 184.4)	
Person years	129,751	131,560	130,717		180,258	180,611	179,842	
Total mortality								
Number of deaths	802	751	826		504	423	417	
Rate/1000 person years	6.18	5.71	6.32		2.80	2.34	2.32	
Hazard ratio (95% CI)								
Model 1	1.00	0.89 (0.80-0.98)	0.84 (0.77-0.93)	0.001	1.00	0.78 (0.69-0.89)	0.75 (0.66-0.85)	<0.001
Model 2	1.00	0.88 (0.80-0.97)	0.85 (0.77-0.94)	0.001	1.00	0.79 (0.70-0.90)	0.77 (0.68-0.88)	<0.001
Model 3	1.00	0.98 (0.88-1.08)	0.99 (0.90-1.10)	0.895	1.00	0.83 (0.73-0.95)	0.81 (0.70-0.92)	0.001
Cancer mortality								
Number of deaths	465	438	460		257	245	223	
Rate/1000 person years	3.58	3.33	3.52		1.43	1.36	1.24	
Hazard ratio (95% CI)								
Model 1	1.00	0.89 (0.78-1.01)	0.80 (0.71-0.91)	0.001	1.00	0.90 (0.76-1.08)	0.80 (0.67-0.96)	0.018
Model 2	1.00	0.90 (0.79-1.02)	0.81 (0.71-0.92)	0.002	1.00	0.93 (0.78-1.10)	0.83 (0.70-0.999)	0.049
Model 3	1.00	0.98 (0.86-1.12)	0.94 (0.82-1.07)	0.342	1.00	0.97 (0.81-1.16)	0.85 (0.71-1.03)	0.093
Cardiovascular disease mortality								
Number of deaths	99	91	117		84	73	66	
Rate/1000 person years	0.76	0.69	0.90		0.47	0.40	0.37	
Hazard ratio (95% CI)								
Model 1	1.00	0.87 (0.65-1.15)	0.99 (0.76-1.30)	0.995	1.00	0.79 (0.58-1.08)	0.69 (0.50-0.96)	0.025
Model 2	1.00	0.85 (0.64-1.14)	0.99 (0.76-1.30)	0.998	1.00	0.79 (0.58-1.09)	0.73 (0.52-1.004)	0.051
Model 3	1.00	0.98 (0.73-1.31)	1.22 (0.92-1.62)	0.156	1.00	0.86 (0.62-1.18)	0.80 (0.58-1.12)	0.193

Model 1 was adjusted for age and study site. Model 2 was adjusted for the variables in Model 1 plus a history of hypertension, diabetes, and dyslipidemia. Model 3 was adjusted for the variables in Model 2 plus the body mass index, smoking status, drinking status, physical activity during leisure time (MET-hours/day), intake of red meat (g/1,000 kcal), fish (g/1,000 kcal), vegetables (g/1,000 kcal), and fruits (g/1,000 kcal).
T, tertile; IQR, interquartile range; CI, confidence interval.

not associated with the risk of all-cause mortality[6, 9]. The present study observed inverse associations between total dairy products and total mortality, milk and all-cause/cancer mortality and between yogurt and CVD mortality in women as well as inverse associations between yogurt and total mortality in both sexes. The total daily intake of participants in the present study, even in the highest third quintile, was a median of 170 g/day for men and 235 g/day for women, which indicates a significant difference in the distribution of intake. This is one of the main reasons for the difference in results from the meta-analyses conducted primarily on Western populations. However, even among the Western cohort and the EPIC-Italy cohort[25], examining associations in a relatively low milk intake range similar to the Japanese population (120–160 g/day vs. no intake) revealed a 25% reduction in all-cause mortality risk with dairy intake, which was consistent with the association in our study. Similar levels of dairy intake may explain why the present study and the report by EPIC-Italy[25] showed similar associations.

In the present study, the dairy intake was inversely associated with mortality risk in women, and only yogurt intake was inversely associated with the risk of all-cause mortality in men after adjusting for potential confounding factors. A large Japanese cohort[16] reported that dairy intake was inversely associated with CVD mortality risk only in women, and we observed a similar association in women in our cohort. However, in other large Japanese cohorts[14, 15], total dairy and milk intake was inversely associated with all-cause and CVD mortality risks, and yogurt intake was inversely associated with all-cause, cancer, and CVD mortality risks only in men. Among men in our cohort, we only found an inverse association

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

Table 3. Adjusted hazard ratios and 95% CIs for the mortality from all cause, cancer, cardiovascular disease according to sex-specific tertiles of milk intake: J-MICC study

	Men				Women			
	Milk intake, g/1000 kcal energy intake				Milk intake, g/1000 kcal energy intake			
	T1 (low)	T2	T3 (high)	*P* for trend	T1 (low)	T2	T3 (high)	*P* for trend
Median milk (IQR) intake	0 (0, 0)	16 (9.9, 20.3)	79.2 (65.4, 91.2)		0 (0, 10.7)	48.4 (23.1, 64.5)	102.2 (94.3, 125.5)	
Person years	128,099	132,412	131,517		177,771	181,952	180,988	
Total mortality								
Number of deaths	770	761	848		492	420	432	
Rate/1000 person years	5.93	5.78	6.49		2.73	2.33	2.40	
Hazard ratio (95% CI)								
Model 1	1.00	0.92 (0.83-1.01)	0.90 (0.82-0.99)	0.040	1.00	0.80 (0.70-0.91)	0.80 (0.70-0.91)	0.001
Model 2	1.00	0.91 (0.83-1.01)	0.90 (0.82-0.99)	0.040	1.00	0.80 (0.70-0.91)	0.81 (0.71-0.92)	0.001
Model 3	1.00	0.97 (0.88-1.07)	1.01 (0.92-1.12)	0.779	1.00	0.84 (0.73-0.95)	0.84 (0.73-0.95)	0.007
Cancer mortality								
Number of deaths	454	440	469		265	239	221	
Rate/1000 person years	3.50	3.34	3.59		1.47	1.32	1.23	
Hazard ratio (95% CI)								
Model 1	1.00	0.92 (0.81-1.05)	0.86 (0.75-0.98)	0.021	1.00	0.87 (0.73-1.03)	0.79 (0.66-0.95)	0.010
Model 2	1.00	0.92 (0.81-1.05)	0.86 (0.76-0.98)	0.025	1.00	0.87 (0.73-1.04)	0.80 (0.67-0.96)	0.015
Model 3	1.00	0.97 (0.85-1.11)	0.96 (0.85-1.1)	0.592	1.00	0.9 (0.76-1.08)	0.82 (0.69-0.99)	0.034
Cardiovascular disease mortality								
Number of deaths	92	99	116		80	65	78	
Rate/1000 person years	0.71	0.75	0.89		0.44	0.36	0.43	
Hazard ratio (95% CI)								
Model 1	1.00	0.98 (0.74-1.30)	1.04 (0.79-1.36)	0.793	1.00	0.74 (0.53-1.03)	0.84 (0.62-1.15)	0.291
Model 2	1.00	0.95 (0.72-1.27)	1.02 (0.77-1.34)	0.871	1.00	0.74 (0.53-1.03)	0.86 (0.63-1.17)	0.343
Model 3	1.00	1.04 (0.78-1.39)	1.18 (0.89-1.56)	0.256	1.00	0.78 (0.56-1.09)	0.91 (0.66-1.25)	0.557

Model 1 was adjusted for the age and study site. Model 2 was adjusted for the variables in Model 1 plus a history of hypertension, diabetes, and dyslipidemia. Model 3 was adjusted for the variables in Model 2 plus the body mass index, smoking status, drinking status, physical activity during leisure time (MET-hours/day), intake of red meat (g/1,000 kcal), fish (g/1,000 kcal), vegetables (g/1,000 kcal), and fruits (g/1,000 kcal).
T, tertile; IQR, interquartile range; CI, confidence interval.

between yogurt intake and risk of total mortality. Possible reasons for the inverse association between dairy intake and risk of mortality in men observed in the previous two reports[14, 15] from Japanese large cohorts were less pronounced among men in our study because men consume approximately half as much dairy as women, and our study had a shorter follow-up period than the previous reports. Furthermore, our study cohort started after 2000, which may have been associated with differences in the disease structure. For example, the mortality rate from CVD has decreased in recent years[26, 27]. These may make the association between dairy products and mortality risk less visible due to the lower mortality rates compared to previous reports. Therefore, we wish to continue to follow-up on sex differences in dairy intake and mortality risk.

We observed an inverse association between milk intake and cancer mortality risk in women but not with yogurt intake. Although this difference may be related to differences in the association between fermented and non-fermented milk with site-specific cancer mortality risk, the small number of events in the present study precludes site-specific examination. We also observed an inverse association between yogurt intake and the risk of CVD mortality in women but not with milk intake. Previous reports have shown that the intake of dairy products, including milk and yogurt, has a protective effect on hypertension[28], a major risk factor for CVD. We did not find a statistically significant inverse association between milk intake and the risk of CVD mortality because the number of mortalities was small in this study. Further large cohort studies of people with genetic backgrounds similar to the present study population are needed to clarify these differences.

Several limitations associated with the present study warrant mention. First, we analyzed the intake

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

Table 4. Adjusted hazard ratios and 95% CIs for the mortality from all cause, cancer, cardiovascular disease according to sex-specific tertiles of yogurt intake: J-MICC study

	Men				Women			
	Yogurt intake, g/1000 kcal energy intake				Yogurt intake, g/1000 kcal energy intake			
	T1 (low)	T2	T3 (high)	*P* for trend	T1 (low)	T2	T3 (high)	*P* for trend
Median (IQR) intake	0 (0, 0)	5.6 (5, 7.4)	40.2 (22.5, 53.2)		5.5 (0, 6.6)	14.1 (12.4, 29)	61.6 (51.6, 69.9)	
Person years	155,822	107,731	128,475		181,759	182,204	176,748	
Total mortality								
Number of deaths	1122	534	723		492	435	417	
Rate/1000 person years	8.65	4.06	5.53		2.73	2.41	2.32	
Hazard ratio (95% CI)								
Model 1	1.00	0.82 (0.74-0.91)	0.76 (0.69-0.84)	<0.001	1.00	0.89 (0.78-1.01)	0.79 (0.69-0.90)	0.001
Model 2	1.00	0.82 (0.74-0.91)	0.77 (0.7-0.85)	<0.001	1.00	0.91 (0.80-1.03)	0.83 (0.73-0.95)	0.005
Model 3	1.00	0.90 (0.81-0.998)	0.90 (0.82-0.999)	0.034	1.00	0.95 (0.84-1.09)	0.87 (0.76-0.997)	0.046
Cancer mortality								
Number of deaths	619	308	436		238	240	247	
Rate/1000 person years	4.77	2.34	3.34		1.32	1.33	1.37	
Hazard ratio (95% CI)								
Model 1	1.00	0.86 (0.75-0.98)	0.79 (0.69-0.89)	<0.001	1.00	1.02 (0.85-1.22)	0.95 (0.80-1.14)	0.595
Model 2	1.00	0.86 (0.75-0.98)	0.80 (0.70-0.90)	<0.001	1.00	1.04 (0.87-1.24)	1.01 (0.84-1.21)	0.943
Model 3	1.00	0.94 (0.82-1.08)	0.93 (0.81-1.06)	0.251	1.00	1.08 (0.90-1.30)	1.03 (0.85-1.24)	0.793
Cardiovascular disease mortality								
Number of deaths	143	74	90		103	63	57	
Rate/1000 person years	1.10	0.56	0.69		0.57	0.35	0.32	
Hazard ratio (95% CI)								
Model 1	1.00	0.86 (0.65-1.15)	0.77 (0.59-1.01)	0.054	1.00	0.62 (0.45-0.84)	0.53 (0.38-0.73)	<0.001
Model 2	1.00	0.86 (0.65-1.14)	0.77 (0.59-1.01)	0.057	1.00	0.65 (0.47-0.89)	0.57 (0.41-0.79)	0.001
Model 3	1.00	0.95 (0.71-1.27)	0.96 (0.73-1.28)	0.772	1.00	0.69 (0.50-0.95)	0.64 (0.46-0.90)	0.007

Model 1 was adjusted for the age and study site. Model 2 was adjusted for the variables in Model 1 plus a history of hypertension, diabetes, and dyslipidemia. Model 3 was adjusted for the variables in Model 2 plus the body mass index, smoking status, drinking status, physical activity during leisure time (MET-hours/day), intake of red meat (g/1,000 kcal), fish (g/1,000 kcal), vegetables (g/1,000 kcal), and fruits (g/1,000 kcal).
T, tertile; IQR, interquartile range; CI, confidence interval.

of dairy products regardless of fat content because information on the fat content of dairy products was unavailable. Second, we did not have data on cheese intake and did not examine the association between cheese intake and the risk of mortality. However, the Japanese population[13] consumes over 90% of its dairy products from milk and yogurt, so this should not have significantly affected the results. Third, we could not perform a disease-specific analysis for cancer and CVD because of the insufficient number of events. Fourth, we could not consider salt intake as a covariate, because the short FFQ used in this study was not developed to assess salt intake. Fifth, we did not have information on the lactase gene polymorphisms. However, most Japanese populations are likely to have lactase non-persistence phenotypes[29], and in a multi-ethnic U.S. cohort including Asian Americans, dairy intake was estimated by ethnic background rather than gene polymorphism[30]. Sixth, there were some unadjusted confounding factors, such as socioeconomic status and salt intake, for which our cohort did not have sufficient data. Finally, as the study participants were middle-aged and older Japanese individuals, our results cannot be generalized to other populations.

Conclusion

A higher total dairy and milk intakes in women and yogurt intake in both sexes were associated with a reduced risk of all-cause mortality in the general population across Japan during a 12-year follow-up. The present study suggests that the consumption of dairy products, at least to the extent daily consumed by the Japanese population, is not inconsistent with recommendations for a healthy dietary component.

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

Acknowledgements

We are deeply grateful to Dr. Nobuyuki Hamajima and Dr. Hideo Tanaka for initiating and organizing the J-MICC Study as former principal investigators and to Dr. Hirotsugu Ueshima for initiating and organizing the Takashima Study as a former principal investigator for one site of the J-MICC Study.

Conflicts of Interest

Naoko Miyagawa received research funding from the Dairy Products Health Science Council and Japan Dairy Association. The other authors declare no conflicts of interest.

Funding Disclosure

This study was supported by Grants-in-Aid for Scientific Research for Priority Areas of Cancer (No.17015018), Innovative Areas (No.221S0001), and Platform of Supporting Cohort Study and Biospecimen Analysis (Japan Society for the Promotion of Science [JSPS] KAKENHI Grants No.16H06277 and 22H04923 [CoBiA]) from the Japanese Ministry of Education, Culture, Sports, Science, and Technology. This work was also supported in part by Grants-in-Aid from JSPS KAKENHI, Grant Numbers 19H03902, 24390165, 20390184, and 17390186.

References

1) Collaborators GBDD: Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet, 2019; 393: 1958-1972
2) Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH and Karanja N: A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med, 1997; 336: 1117-1124
3) Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. 2020;
4) Yoshiike N, Hayashi F, Takemi Y, Mizoguchi K and Seino F: A new food guide in Japan: the Japanese food guide Spinning Top. Nutr Rev, 2007; 65: 149-154
5) Rossi L, Berni Canani S, Censi L, Gennaro L, Leclercq C, Scognamiglio U, Sette S and Ghiselli A: The 2018 Revision of Italian Dietary Guidelines: Development Process, Novelties, Main Recommendations, and Policy Implications. Front Nutr, 2022; 9: 861526
6) Jin S and Je Y: Dairy Consumption and Total Cancer and Cancer-Specific Mortality: A Meta-Analysis of Prospective Cohort Studies. Adv Nutr, 2022; 13: 1063-1082
7) Tutunchi H, Naghshi S, Naemi M, Naeini F and Esmaillzadeh A: Yogurt consumption and risk of mortality from all causes, CVD and cancer: a comprehensive systematic review and dose-response meta-analysis of cohort studies. Public Health Nutr, 2023; 26: 1196-1209
8) Schwingshackl L, Schwedhelm C, Hoffmann G, Lampousi AM, Knuppel S, Iqbal K, Bechthold A, Schlesinger S and Boeing H: Food groups and risk of all-cause mortality: a systematic review and meta-analysis of prospective studies. Am J Clin Nutr, 2017; 105: 1462-1473
9) Mullie P, Pizot C and Autier P: Daily milk consumption and all-cause mortality, coronary heart disease and stroke: a systematic review and meta-analysis of observational cohort studies. BMC Public Health, 2016; 16: 1236
10) Guo J, Astrup A, Lovegrove JA, Gijsbers L, Givens DI and Soedamah-Muthu SS: Milk and dairy consumption and risk of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. Eur J Epidemiol, 2017; 32: 269-287
11) Saito A, Okada E, Tarui I, Matsumoto M and Takimoto H: The Association between Milk and Dairy Products Consumption and Nutrient Intake Adequacy among Japanese Adults: Analysis of the 2016 National Health and Nutrition Survey. Nutrients, 2019; 11:
12) Beydoun MA, Gary TL, Caballero BH, Lawrence RS, Cheskin LJ and Wang Y: Ethnic differences in dairy and related nutrient consumption among US adults and their association with obesity, central obesity, and the metabolic syndrome. Am J Clin Nutr, 2008; 87: 1914-1925
13) Ministry of Health, Labour and Welfare. The National Health and Nutrition Survey. https: //www.mhlw.go.jp/bunya/kenkou/kenkou_eiyou_chousa.html Accessed 23 June 2021
14) Ge S, Zha L, Sobue T, Kitamura T, Iso H, Ishihara J, Kito K, Iwasaki M, Inoue M, Yamaji T, Tsugane S and Sawada N: Associations between dairy intake and mortality due to all-cause and cardiovascular disease: the Japan Public Health Center-based prospective study. Eur J Nutr, 2023; 62: 2087-2104
15) Wang C, Yatsuya H, Tamakoshi K, Iso H and Tamakoshi A: Milk drinking and mortality: findings from the Japan collaborative cohort study. J Epidemiol, 2015; 25: 66-73
16) Kondo I, Ojima T, Nakamura M, Hayasaka S, Hozawa A, Saitoh S, Ohnishi H, Akasaka H, Hayakawa T, Murakami Y, Okuda N, Miura K, Okayama A, Ueshima H and Group NDR: Consumption of dairy products and death from cardiovascular disease in the Japanese general population: the NIPPON DATA80. J Epidemiol, 2013; 23: 47-54
17) Hamajima N and Group JMS: The Japan Multi-Institutional Collaborative Cohort Study (J-MICC Study) to detect gene-environment interactions for cancer. Asian Pac J Cancer Prev, 2007; 8: 317-323
18) Takeuchi K, Naito M, Kawai S, Tsukamoto M, Kadomatsu Y, Kubo Y, Okada R, Nagayoshi M, Tamura T, Hishida A, Nakatochi M, Sasakabe T, Hashimoto S, Eguchi H, Momozawa Y, Ikezaki H, Murata M, Furusyo N, Tanaka K, Hara M, Nishida Y, Matsuo K, Ito H, Oze

I, Mikami H, Nakamura Y, Kusakabe M, Takezaki T, Ibusuki R, Shimoshikiryo I, Suzuki S, Nishiyama T, Watanabe M, Koyama T, Ozaki E, Watanabe I, Kuriki K, Kita Y, Ueshima H, Matsui K, Arisawa K, Uemura H, Katsuura-Kamano S, Nakamura S, Narimatsu H, Hamajima N, Tanaka H and Wakai K: Study profile of the Japan Multi-institutional Collaborative Cohort (J-MICC) Study. J Epidemiol, 2020;
19) Koyama T, Ozaki E, Kuriyama N, Tomida S, Yoshida T, Uehara R, Tanaka K, Hara M, Hishida A, Okada R, Kubo Y, Oze I, Koyanagi YN, Mikami H, Nakamura Y, Shimoshikiryo I, Takezaki T, Suzuki S, Otani T, Kuriki K, Takashima N, Kadota A, Arisawa K, Katsuura-Kamano S, Ikezaki H, Murata M, Takeuchi K, Wakai K and Japan Multi-Institutional Collaborative Cohort Study G: Effect of Underlying Cardiometabolic Diseases on the Association Between Sedentary Time and All-Cause Mortality in a Large Japanese Population: A Cohort Analysis Based on the J-MICC Study. J Am Heart Assoc, 2021; 10: e018293
20) Hara M, Higaki Y, Taguchi N, Shinchi K, Morita E, Naito M, Hamajima N, Takashima N, Suzuki S, Nakamura A, Ohnaka K, Uemura H, Nishida H, Hosono S, Mikami H, Kubo M, Tanaka H and Japan Multi-Institutional Collaborative Cohort Study G: Effect of the PPARG2 Pro12Ala polymorphism and clinical risk factors for diabetes mellitus on HbA1c in the Japanese general population. J Epidemiol, 2012; 22: 523-531
21) Imaeda N, Goto C, Sasakabe T, Mikami H, Oze I, Hosono A, Naito M, Miyagawa N, Ozaki E, Ikezaki H, Nanri H, Nakahata NT, Kamano SK, Kuriki K, Yaguchi YT, Kayama T, Kurihara A, Harada S and Wakai K: Reproducibility and validity of food group intake in a short food frequency questionnaire for the middle-aged Japanese population. Environ Health Prev Med, 2021; 26: 28
22) Imaeda N, Goto C, Tokudome Y, Hirose K, Tajima K and Tokudome S: Reproducibility of a short food frequency questionnaire for Japanese general population. J Epidemiol, 2007; 17: 100-107
23) Tokudome Y, Goto C, Imaeda N, Hasegawa T, Kato R, Hirose K, Tajima K and Tokudome S: Relative validity of a short food frequency questionnaire for assessing nutrient intake versus three-day weighed diet records in middle-aged Japanese. J Epidemiol, 2005; 15: 135-145
24) Tokudome S, Goto C, Imaeda N, Tokudome Y, Ikeda M and Maki S: Development of a data-based short food frequency questionnaire for assessing nutrient intake by middle-aged Japanese. Asian Pac J Cancer Prev, 2004; 5: 40-43
25) Pala V, Sieri S, Chiodini P, Masala G, Palli D, Mattiello A, Panico S, Tumino R, Frasca G, Fasanelli F, Ricceri F, Agnoli C, Grioni S and Krogh V: Associations of dairy product consumption with mortality in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Italy cohort. Am J Clin Nutr, 2019; 110: 1220-1230
26) Kubo M, Kiyohara Y, Kato I, Tanizaki Y, Arima H, Tanaka K, Nakamura H, Okubo K and Iida M: Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community: the Hisayama study. Stroke, 2003; 34: 2349-2354
27) Sekikawa A, Miyamoto Y, Miura K, Nishimura K, Willcox BJ, Masaki KH, Rodriguez B, Tracy RP, Okamura T and Kuller LH: Continuous decline in mortality from coronary heart disease in Japan despite a continuous and marked rise in total cholesterol: Japanese experience after the Seven Countries Study. Int J Epidemiol, 2015; 44: 1614-1624
28) Soedamah-Muthu SS, Verberne LD, Ding EL, Engberink MF, Geleijnse JM: Dairy consumption and incidence of hypertension: a dose-response meta-analysis of prospective cohort studies. Hypertension, 2012; 60: 1131-1137
29) Kato K, Ishida S, Tanaka M, Mitsuyama E, Xiao JZ and Odamaki T: Association between functional lactase variants and a high abundance of Bifidobacterium in the gut of healthy Japanese people. PLoS One, 2018; 13: e0206189
30) Chin EL, Huang L, Bouzid YY, Kirschke CP, Durbin-Johnson B, Baldiviez LM, Bonnel EL, Keim NL, Korf I, Stephensen CB and Lemay DG: Association of Lactase Persistence Genotypes (rs4988235) and Ethnicity with Dairy Intake in a Healthy U.S. Population. Nutrients, 2019; 11: 1860

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

Supplemental Table 1. Baseline characteristics of participants in the J-MICC according to the sex-specific tertiles of milk intake

	Men			Women		
	Milk intake, g/1,000 kcal			Milk intake, g/1,000 kcal		
	T1 (low)	T2	T3 (high)	T1 (low)	T2	T3 (high)
Range of milk intake (median), g/1,000kcal	0 - 8 (0)	8 - 43 (16)	43 - 465 (79.2)	0 - 19 (0)	19 - 85 (48.4)	85 - 500 (102.2)
Median intake of milk (IQR), g/day	0 (0, 0)	32 (16, 32)	160 (128, 160)	0 (0, 15.5)	78 (31, 78)	155 (155, 155)
Number at risk	11,364	11,365	11,364	15,207	15,208	15,207
Age, years	54.5 (9.4)	55.0 (9.3)	56.6 (9.2)*	54.0 (9.3)	54.4 (9.3)	54.5 (9.6)*
Body mass index, kg/m^2	23.7 (3.2)	24.0 (3.1)	23.7 (2.9)	22.4 (3.4)	22.5 (3.3)	22.2 (3.2)*
History of hypertension, %	22.4	22.3	22.0	15.1	15.1	14.1*
History of diabetes, %	6.8	8.5	9.5*	3.0	3.1	3.2
History of dyslipidemia, %	13.6	15.6	15.7*	14.0	14.6	15.1*
Drinking status, %			*			*
Never	18.5	19.4	22.8	58.5	60.7	62.6
Past	2.9	2.8	3.4	1.9	1.7	1.8
Current	78.6	77.7	73.7	39.5	37.5	35.5
Missing	0.1	0.1	0.1	0.1	0.1	0.2
Smoking status, %			*			*
Never	24.6	29.0	34.6	81.8	87.4	86.5
Past	39.1	39.4	40.9	8.1	6.4	6.8
Current	36.0	31.2	24.3	9.6	5.8	6.1
Missing	0.4	0.3	0.2	0.5	0.5	0.6
Physical activity in leisure time, MET-hour/day	0.8 (0, 2.6)	1.0 (0.1, 2.6)	1.4 (0.3, 3.5)*	0.5 (0, 2.2)	0.8 (0.1, 2.5)	1.0 (0.1, 2.6)*
Dietary intake						
Energy, kcal/day	1916.2 (361.8)	1881.2 (318.3)	1917.6 (313.7)	1490.6 (242.3)	1544.2 (231.4)	1548.1 (214.0)*
Dairy, g/1,000kcal	4.7 (0, 12.3)	23.6 (15.7, 42.8)	92.5 (74.7, 126.1)*	18.9 (7.5, 48.5)	73.9 (50.4, 94.5)	145.0 (112.3, 181.8)*
Yogurt, g/1,000kcal	0 (0, 9.9)	5.7 (0, 12.1)	8.0 (0, 38.3)*	11.4 (5.6, 41.3)	14.8 (7.3, 41.7)	29.2 (7.4, 60.0)*
Red meat, g/1,000kcal	9.8 (7.0, 16.7)	10.1 (7.5, 16.9)	9.9 (7.3, 16.5)	13.7 (9.1, 21.9)	14.5 (9.7, 21.9)	13.9 (9.3, 21.4)
Fish, g/1,000kcal	24.3 (16.0, 35.1)	25.4 (17.1, 35.1)	25.1 (16.8, 34.7)	29.9 (20.0, 41.2)	30.7 (21.0, 40.4)	29.5 (20.0, 40.2)*
Vegetable, g/1,000kcal	48.0 (31.9, 71.0)	50.7 (35, 73.5)	54.6 (37.2, 78.6)*	88.2 (61.7, 123.4)	91.3 (65.8, 123.5)	94.0 (66.8, 129.7)*
Fruits, g/1,000kcal	12.5 (7.5, 26.5)	15.7 (9.4, 30.7)	18.4 (10.1, 41.2)*	27.8 (13.6, 61.1)	35.8 (17.6, 62.2)	39.8 (18.7, 68.5)*

All variables are expressed as mean (standard deviation) or median (IQR) for continuous variables or as percentages for categorical variables. *$p <$ 0.05: differences among sex-specific tertiles of dairy intake were assessed using trend analysis or Cochran-Armitage test.
J-MICC, Japan Multi-Institutional Collaborative Cohort; T, tertile; IQR, interquartile range; MET, metabolic equivalent of task.

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024

Supplemental Table 2. Baseline characteristics of participants in the J-MICC according to the sex-specific tertiles of yogurt intake

	Men			Women		
	Yogurt intake, g/1,000 kcal			Yogurt intake, g/1,000 kcal		
	T1 (low)	T2	T3 (high)	T1 (low)	T2	T3 (high)
Range of yogurt intake (median), g/1,000kcal	0 - 0 (0)	3 - 10 (5.6)	10 - 223 (40.2)	0 - 9 (5.5)	9 - 34 (14.1)	34 - 328 (61.6)
Median intake of yogurt (IQR), g/day	0 (0, 0)	10 (10, 10)	80 (50, 100)	10 (0, 10)	20 (20, 50)	100 (80, 100)
Number at risk	13,444	9,285	11,364	15,207	15,208	15,207
Age, years	55.8 (9.1)	53.7 (9.5)	56.1 (9.3)	53.5 (9.6)	53.8 (9.4)	55.6 (9.1)*
Body mass index, kg/m^2	23.8 (3.1)	23.9 (3.1)	23.6 (2.9)*	22.5 (3.5)	22.4 (3.3)	22.0 (3.1)*
History of hypertension, %	23.6	20.6	21.9*	14.9	14.3	15.1
History of diabetes, %	8.4	7.4	8.7	3.3	3.0	3.0
History of dyslipidemia, %	13.4	14.4	17.2*	12.6	14.1	17.0*
Drinking status, %			*			*
Never	18.3	19.8	22.9	59.3	61.1	61.4
Past	3.0	2.6	3.4	2.0	1.6	1.8
Current	78.7	77.5	73.6	38.6	37.2	36.7
Missing	0.1	0.1	0.1	0.1	0.1	0.1
Smoking status, %			*			*
Never	23.3	31.4	34.9	80.8	87.1	87.7
Past	37.5	37.7	44.2	8.1	6.2	7.0
Current	38.9	30.6	20.5	10.7	6.2	4.6
Missing	0.3	0.2	0.3	0.4	0.5	0.7
Physical activity in leisure time, MET-hour/day	0.8 (0, 2.4)	1.0 (0.1, 2.6)	1.5 (0.5, 3.6)*	0.5 (0, 2.2)	0.8 (0.1, 2.4)	1.2 (0.3, 2.8)*
Dietary intake						
Energy, kcal/day	1907.7 (347.4)	1975.8 (332.3)	1843.9 (301.2)*	1529.0 (221.2)	1558.2 (230.4)	1495.7 (236.9)*
Dairy, g/1,000kcal	8.9 (0, 45.3)	23.0 (13.2, 66.0)	69.1 (44.9, 115.4)*	26.0 (7.5, 91.4)	72.1 (33.4, 110.8)	127.5 (78.9, 164.2)*
Milk, g/1,000kcal	8.9 (0, 45.3)	16 (7.8, 59.8)	25.5 (8.3, 78.6)*	20.9 (0, 88.0)	49.4 (18.7, 92.0)	64.5 (12.8, 100.0)*
Red meat, g/1,000kcal	9.5 (6.8, 16.1)	10.2 (7.5, 17.0)	10.3 (7.7, 17.0)*	13.3 (9.0, 21.4)	15.3 (9.7, 22.0)	13.7 (9.4, 21.7)*
Fish, g/1,000kcal	24.3 (15.8, 34.9)	23.8 (16.5, 33.3)	26.5 (17.9, 36.3)*	27.9 (18.5, 38.4)	30.2 (21.0, 40.2)	32 (21.9, 42.9)*
Vegetable, g/1,000kcal	46.5 (31.1, 68.6)	49.8 (34.3, 71.8)	58.4 (39.8, 83.4)*	82.4 (57.6, 114.1)	91.5 (65.9, 123.7)	99.9 (71.7, 137.5)*
Fruits, g/1,000kcal	11.5 (6.9, 23.2)	15.1 (9.3, 29.1)	20.6 (11.9, 45.2)*	21.8 (11.7, 51.8)	36.0 (18.5, 60.6)	50.5 (22.3, 78.9)*

All variables are expressed as mean (standard deviation) or median (IQR) for continuous variables or as percentages for categorical variables. *$p <$ 0.05: differences among sex-specific tertiles of dairy intake were assessed using trend analysis or Cochran-Armitage test.
J-MICC, Japan Multi-Institutional Collaborative Cohort; T, tertile; IQR, interquartile range; MET, metabolic equivalent of task.

Advance Publication Journal of Atherosclerosis and Thrombosis
Accepted for publication: September 23, 2024 Published online: November 13, 2024