Statistical analysis

Inclusion criteria for this analysis

In this report, we examined the effects of dietary intervention using data from the first half of the study, that is, the group receiving dietary intervention in the first year as the intervention group and the other group as the control group. Because durations of the intervention effects were not clear, we did not include the data from the second half of the study to assess simply the effects of dietary intervention. Subjects were excluded from the analysis of dietary and serum data if they met either of the following criteria: (1) DHQ and blood samples were incomplete in both 1998 and 1999, and (2) estimated energy intake was less than 50% of the energy requirement for a sedentary lifestyle or greater than 150% of the energy requirement for a vigorous lifestyle. Furthermore, for the analysis of urine data, we excluded subjects with (3) a creatinine (mg)/body weight (kg) ratio less than 14.4 or greater than 33.6 in men, and less than 10.8 or greater than 25.2 in women [33], (4) urine volume differences between 1998 and 1999 in the highest or lowest fifth percentile.

Outcomes and statistical analysis

Primary study outcomes were intervention effect in the first year, i.e., the differences in changes between the intervention and control groups. We computed mean daily intakes of energy, targeted nutrients and mean values of the corresponding biomarkers (i.e., urinary sodium, serum alpha- and beta-carotene, and serum ascorbic acid) at pre- and post-intervention (baseline and Year 1). Total carotene was defined as the sum of the alpha- and beta-carotene levels that were quantified in the serum and diet. As for vegetable intakes we also computed intakes of carotene- and vitamin C-rich vegetables ("green and yellow vegetables") and others ("other vegetables") separately. Definitions of this classification refer to guidelines established by the Ministry of Health and Welfare, Japan, 1983. Dark-green leafy vegetables, carrots, pumpkin, broccoli, tomatoes, sweet peppers, tomato juice, and vegetable juice were included in the "green and yellow vegetables" category. We also computed intakes of major salted foods such as miso, salted fish, salted vegetable pickles, and seasonings. Because the distribution was skewed to the right for carotenes and vitamin C, for both intakes and serum concentrations, the values at each point were transformed by the natural logarithm before computation. Intakes of fruit, vegetables, and salted foods were also transformed by the natural logarithm before computation. Differences from baseline to Year 1 within groups are presented with 95% confidence intervals (95% CI). Multiple regression analysis was used to examine the differences between changes from baseline to Year 1 between groups. Results were adjusted for baseline values, but not for other characteristics (smoking, sex, age, BMI, plasma cholesterol concentration), since these made no material difference to the results. All analyses were done with SAS statistical software (SAS Institute Inc, Cary NC, version 8.0).

Results

At baseline, among 550 respondents who completed the DHQ, we obtained 506 blood, and 292 urine samples (Fig. 2). At Year 1, among 534 subjects who completed the DHQ, we obtained 477 blood, and 240 urine samples. For the analysis of dietary and serum data, 470 subjects were included, while 191 subjects were included in the analysis of dietary and urine data.

Table 1 shows the demographic and health-related characteristics of subjects at baseline with dietary assessment and blood samplings for the intervention and control groups. We did not observe statistically significant differences in listed variables between the two groups. We also compared these variables between the subjects included and excluded in the DHQ and blood analysis (n = 470 and 80, respectively). No remarkable differences were observed between respondents and non-respondents (data not shown).

Table 2 gives the daily intakes of energy and nutrients assessed by DHQ. At Year 1, energy intakes were not significantly different in the two groups. Sodium intake in the intervention group decreased by 384 mg/day (95% CI: −683 to −129 mg/day), while increased by 255 mg/day (+8 to +502 mg/day) in the control group. This change constituted a statistically significant difference between the two groups ($p < 0.001$). At baseline, mean carotene values differed statistically significant or there were borderline differences between the two groups (p = 0.005–0.072). Vitamin C intakes at baseline were slightly but not significantly higher in the intervention group than in the control group (p = 0.185). At Year 1, the intervention group showed greater increases in carotene (+418, 95% CI: +124 to +712 μg/day) and vitamin C (+13, +2 to +24 mg/day), than the controls (+220, −26 to +469, and +2, −8 to +13 mg/day, respectively) ($p < 0.05$ for all). No statistically significant changes were observed in other nutrients between the two groups.

Table 3 presents the intakes of salted foods, and fruits and vegetables. At baseline, intakes of these foods did not differ between the two groups. At Year 1, except for salted pickles made of green and yellow vegetables and seasonings, salted foods decreased significantly more in the intervention group ($p < 0.01$). Total vegetable intake increased slightly in the intervention group, but the difference did not reach statistical significance (p = 0.081). Among total vegetables, consumption of green and yellow vegetables increased in the intervention group, and this change was statistically significant (p = 0.010).

Table 4 shows the mean urinary excretions of sodium and potassium and the corresponding daily intakes. In the intervention group, at Year 1, urinary excretion and intake of sodium decreased by 1003 mg/day (95% CI: −1282 to

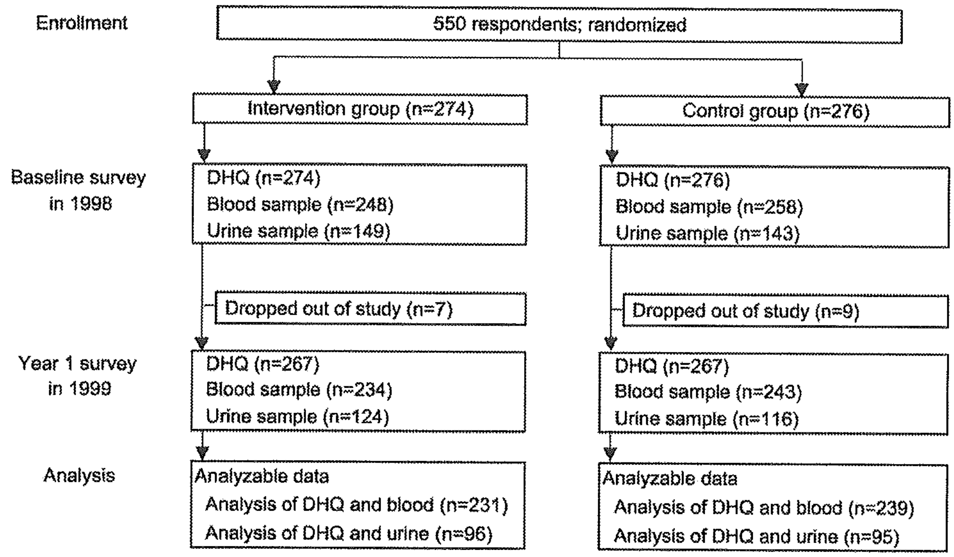

Fig. 2. The number of subjects in the trial.

−724 mg/day) and 406 mg/day (−764 to −47 mg/day), respectively. Differences in changes between the two groups were also statistically significant ($p < 0.001$). No statistically significant change was observed for potassium in either urinary excretion or intake.

Table 5 presents the mean serum concentrations of carotenes and ascorbic acid. Serum concentrations of carotenes and ascorbic acid in the two groups were similar at baseline ($p = 0.534–0.888$). At Year 1, the intervention group showed increases in carotenes and vitamin C as compared to controls. However, the only statistically significant difference between the intervention and control groups was in alpha-carotene levels. (+10, 95% CI: +2 to +18 and, −3, −9 to +2 mg/L, respectively, p for difference < 0.01).

Among the intervention subjects, 84% received dietary counseling, and the remaining 16% were mailed feedback sheets. The subjects who received dietary counseling were older than their counterparts, and changed remarkably their sodium intakes, but not carotene or vitamin C intakes, remarkably.

Table 1
Subject characteristics at baseline

	Intervention group (n = 231)	Control group (n = 239)	P^a
Age (yr)	56.3 ± 7.7	56.6 ± 8.0	0.723
Sex (% female)	67.4	66.1	0.669
Height (cm)	154.9 ± 7.3	155.2 ± 8.1	0.671
Weight (kg)	57.0 ± 8.5	56.2 ± 8.5	0.310
Body mass index (kg/m^2)	23.7 ± 2.8	23.3 ± 2.7	0.101
Smoking (% current)	8.7	11.3	0.226
Alcohol drinker (% current)	48.9	49.1	0.847
Status of disease (on medication)			
Hypertension (%)	12.1	9.6	0.384
Liver dysfunction (%)	1.3	1.3	0.967
Diabetes (%)	3.5	2.9	0.742
Hyperlipidemia (%)	6.1	9.6	0.152
Gastritis (%)	0.9	0.8	0.973
Gastric ulcer (%)	0.4	2.1	0.109

[a] P value for comparison between groups.

Discussion

The Hiraka Dietary Intervention Study is a large-scale community-based randomized cross-over trial designed to modify multiple nutrient intakes.

At the time of planning this study, in 1997, carotene and vitamin C were the most reliable nutrients as protective factors of stomach cancer [5]. But the question has arisen by the results of some large-scale randomized trials of antioxidant vitamins, such as beta-carotene and alpha-tocopherol [34]. It should be noted that to increase carotene and vitamin C intake, we aimed at increasing fruits and vegetables as daily diet rather than supplementation of carotene and vitamin C. Fruits and vegetables contains various possibly beneficial components like polyphenols and other antioxidant as well as vitamin C and carotene. Three recent prospective cohort studies found inverse associations between fruit and vegetable intake and stomach cancer [35–37]. Protective effect of fruit and vegetable intake was also supported by recent report from the joint WHO/FAO experts consultation [6]. We believe that increase of fruit and vegetable intake is no doubt as a beneficial recommendation in the general public, such as "Five a Day" program that conducted in many countries.

We observed a significant net change, due to dietary intervention, in all targeted nutrients. Above all, mean intakes of sodium decreased dramatically, as a consequence of decreased intake of salted foods. For decades, excess intake

Table 2
Intakes of energy, protein, fat, dietary fiber, and targeted nutrients assessed with self-administered diet history questionnaire

	Intervention group (n = 231)			Control group (n = 239)			Between-group difference in change
	Baseline	Year 1	Change (95% CI)[c]	Baseline	Year 1	Change (95% CI)[c]	P[d]
	Mean (95% CI)	Mean (95% CI)		Mean (95% CI)	Mean (95% CI)		
Energy (kJ)	8.51 (3.46, 13.55)	8.36 (3.44, 13.28)	−0.15 (−0.40, 0.11)	8.19 (3.40, 12.97)	8.40 (3.43, 13.38)	0.22 (−0.06, 0.49)	0.146
Protein (% of energy)	15.1 (9.6, 20.7)	15.3 (10.2, 20.4)	0.1 (−0.2, 0.5)	15.2 (9.2, 21.2)	15.3 (9.6, 21)	0.1 (−0.2, 0.4)	0.805
Carbohydrates (% of energy)	57.3 (43.2, 71.4)	57.0 (42.3, 71.7)	−0.3 (−1.2, 0.6)	57.6 (43.4, 71.8)	56.7 (43, 70.4)	−0.9 (−1.6, −0.1)	0.350
Fat (% of energy)	22.5 (10.9, 34.1)	23.4 (12, 34.8)	0.9 (0.2, 1.5)	22.0 (9.8, 34.2)	23.3 (11.0, 35.7)	1.3 (0.7, 2.0)	0.519
P/S ratio[a]	1.05 (0.05, 1.64)	1.09 (0.50, 1.68)	0.04 (0.01, 0.08)	1.05 (0.46, 1.65)	1.06 (0.46, 1.66)	0.01 (−0.02, 0.04)	0.170
Dietary fiber (g/day)	15.5 (3.0, 27.9)	15.9 (3.9, 27.9)	0.4 (−0.4, 1.2)	14.4 (3.2, 25.6)	14.9 (4.2, 25.5)	0.5 (−0.2, 1.1)	0.280
Soluble dietary fiber	2.3 (0.1, 4.5)	2.5 (0.2, 1.9)	0.2 (0.0, 0.4)	2.2 (0.2, 4.1)	2.3 (0.4, 4.2)	0.1 (0.0, 0.2)	0.058
Insoluble dietary fiber	12.1 (2.8, 21.4)	12.2 (3.2, 21.3)	0.1 (−0.5, 0.8)	11.3 (2.7, 19.9)	11.6 (3.5, 19.7)	0.3 (−0.2, 0.8)	0.513
Sodium (mg/day)	5432 (1753, 9112)	5049 (1214, 8884)	−384 (−638, −129)	5305 (1571, 9039)	5560 (1402, 9717)	255 (8, 502)	<0.001
Potassium (mg/day)	2738 (709, 4768)	2810 (654, 4966)	72 (−66, 210)	2569 (712, 4426)	2632 (765, 4499)	63 (−48, 173)	0.298
Carotene (μg/day)[b]	2128 (491, 9228)	2549 (650, 9986)	418 (124, 712)	1840 (349, 9696)	2033 (407, 10165)	220 (−26, 469)	0.032
Alpha-carotene (μg/day)[b]	203 (28, 1494)	255 (29, 2204)	78 (35, 121)	156 (20, 1224)	168 (16, 1724)	41 (3, 78)	0.013
Beta-carotene (μg/day)[b]	1861 (420, 8237)	2219 (563, 8750)	340 (75, 604)	1624 (296, 8907)	1798 (356, 9092)	178 (−45, 402)	0.048
Vitamin C (mg/day)[b]	105 (31, 355)	120 (40, 357)	13 (2, 24)	97 (26, 365)	102 (29, 365)	2 (−8, 13)	0.023

[a] Ratio of polyunsaturated to saturated fat.
[b] Values at each point were transformed by the natural logarithm before computation because of the skewed distributions. They were back-transformed to show means and 95% CIs.
[c] Difference between baseline and Year 1.
[d] P-values for comparison between intervention group and control group by t-test after adjustment for baseline intake.

of sodium has been a concern in Japan. Several public health comments have long focused on reduction of salt intake in this study area, mainly because of the link between very high salt intake and a high prevalence of hypertension [24]. Thus, subjects in this area were presumably more receptive to the message to decrease sodium.

As a result of this intervention which emphasized carotene- and vitamin C-rich vegetables, while consumption of other vegetables decreased slightly, that of green and yellow vegetables increased significantly. Subjects in the intervention group replaced other vegetables with those of the green and yellow vegetables, rather than increasing total vegetable intake. Green and yellow vegetables were the primary source of dietary carotenes (contribution rate, 94%) and vitamin C (44%). This change produced significant changes in dietary carotenes and vitamin C.

Short-questionnaires with a limited number of food items, assessed as "servings per day" rather than "grams per day", have been used in most large-scale dietary intervention studies with free-living people and which aimed at increasing fruit and vegetable intakes [13,22,23]. In contrast, DHQ was used in this study, because we targeted certain nutrients as well as foods, such that detailed information, on specific foods and nutrients derived from this DHQ, was needed. With this detailed information, we were able to consider more suitable and practical intervention strategies for individual subjects. As a consequences, we ascertained the effects of dietary intervention only on targeted nutrients without the undesirable effects of other nutrients. Moreover, the concept of "servings" has not been established in Japan, because information on the contribution of individual components to composite dishes is scarce, though most vegetables are often eaten as mixed dishes. In addition, the components and portions of mixed dishes tend to vary widely.

The self-administered semiquantitative dietary assess-

Table 3
Daily food intakes at two points[a]

	Intervention group (n = 231)			Control group (n = 239)			Between-group difference in change
	Baseline	Year 1	Change[e] (95% CI)	Baseline	Year 1	Change[e] (95% CI)	
	Mean (95% CI)	Mean (95% CI)		Mean (95% CI)	Mean (95% CI)		P^f
Salted foods							
Miso[b]	22.6 (6.0, 79.3)	18.7 (4.8, 66.0)	−4.0 (−5.8, −2.2)	22.9 (6.2, 78.1)	23.5 (5.5, 90.9)	1.2 (−0.6, 2.9)	<0.001
Salted pickles	36.8 (4.6, 254.1)	28.9 (3.9, 179.4)	−13.6 (−19.0, −8.2)	34.4 (3.8, 258.4)	35.6 (4.0, 266.7)	2.1 (−3.8, 8.0)	<0.001
Green & yellow vegetables[c]	3.8 (−0.7, 67.0)	3.4 (−0.7, 55.4)	−2.4 (−4.8, −0.1)	3.0 (−0.7, 54.8)	4.0 (−0.7, 83.2)	2.2 (−0.8, 5.2)	0.193
Other vegetables	28.8 (3.3, 206.6)	21.9 (2.6, 145.7)	−11.2 (−15.5, −6.9)	27.3 (2.7, 212.8)	27.5 (2.9, 208.4)	−0.1 (−4.6, 4.3)	<0.001
Salted fish	27.4 (5.2, 129.9)	23.6 (4.3, 113.2)	−4.6 (−8.9, −0.4)	24.9 (3.7, 140.3)	27.0 (3.9, 160.5)	4.3 (−0.4, 9.1)	0.005
Seasonings	26.4 (4.9, 142.6)	27.7 (5.5, 139.0)	−0.4 (−6.5, 5.6)	28.1 (4.7, 167.8)	29.5 (4.8, 181.6)	1.3 (−5.6, 8.2)	0.214
Fruits and Vegetables							
Vegetables	247.5 (70.3, 864.7)	261.2 (80.8, 839.7)	13.1 (−14.0, 40.2)	232.7 (69.1, 777.5)	231.4 (66.7, 796.2)	−0.1 (−17.6, 17.4)	0.081
Green & yellow vegetables[d]	97.1 (19.4, 471.6)	117.9 (25.2, 539.5)	27.7 (8.2, 47.2)	91.1 (17.8, 450.7)	95.7 (18.2, 485.2)	5.3 (−5.8, 16.3)	0.010
Other vegetables	138.5 (38.9, 487)	128.6 (38.4, 425.5)	−14.6 (−28.4, −0.7)	128.2 (35.9, 451.5)	122.7 (33.1, 447.3)	−5.4 (−16.4, 5.5)	0.846
Fruits	65.0 (8.4, 464.4)	83.5 (12.4, 530.6)	20.0 (6.8, 33.1)	57.9 (5.8, 512.4)	64.2 (7.7, 488.3)	2.9 (−8.7, 14.5)	0.009

[a] Values at each point were transformed by the natural logarithm before computation because of the skewed distributions. They were back-transformed to show means and 95% CIs.
[b] Fermented and salted soy-bean paste.
[c] Includes salted pickles made of dark-green leafy vegetables or carrots.
[d] Includes dark-green leafy vegetables, carrots, pumpkin, tomatoes, broccoli, sweet peppers, tomato juice, and vegetable juice.
[e] Difference between baseline and Year 1.
[f] P-values for comparison between intervention group and control group by t-test after adjustment for baseline intake.

ment questionnaire [27–29] was used in this study. We also examined the validity of the DHQ employing a one-month dietary intervention with 39 middle aged (35–56 year old) healthy female volunteers. The Pearson correlation coefficient was 0.27 for the change in dietary and 48-hour urinary excretion of salt between pre-intervention and post-intervention points. Those between intakes and serum concentrations of carotene and vitamin C were 0.26 and 0.14, respectively. The results should therefore be interpreted cautiously, considering the imperfect measurements.

In most dietary intervention studies in free-living healthy adults, the evaluation methods have been limited to self-reports, such as dietary records, 24-hour dietary recall, food frequency questionnaires, DHQ, or a combination of these assessments. Because dietary intervention cannot be blinded, results of these dietary assessments may not accurately represent habitual diets, due to intentional exaggeration of adherence to assigned diets. The use of objective biological markers that are responsive to change in the quantity and variety of foods consumed is necessary to establish adherence to the intervention. This study is unique among those published to date, because dietary intervention effects were assessed not only with responses to a self-administered questionnaire but also with the corresponding biomarkers, in large-scale study of free-living subjects. This made it possible to assess intervention effects more accurately than in most previous studies. In regard to sodium, changes observed in the self-administered dietary questionnaire and those observed in the corresponding biomarkers were concordant. For total-carotene and beta-carotene, however, we did not observe significant changes in serum concentrations, whereas dietary changes were significant. These results indicate that subjects in the intervention group did not report entirely accurately what they ate over the long term. These phenomenon have already been observed in previous intervention trials [38]. Very limited food sources of carotene, i.e., about 80% derived from dark-green leafy vegetables and carrots, might be more likely to be overestimated than those of other nutrients.

Biomarkers have several limitations, despite being the gold standard. Serum carotene reflects relatively long-term intake, such as several weeks [39], making it a reasonable

Table 4
Dietary intakes and 48-hour urinary excretions of sodium and potassium among subjects who completed urine collection at two points

	Intervention group (n = 96)			Control group (n = 95)			Between-group difference in change
	Baseline	Year 1	Change (95% CI)	Baseline	Year 1	Change (95% CI)	
	Mean (95% CI)	Mean (95% CI)		Mean (95% CI)	Mean (95% CI)		P[b]
Sodium (mg/day)							
Dietary intake	5551 (1976, 9127)	5146 (1616, 8675)	−406 (−764, −47)	5253 (1810, 8696)	5836 (1481, 10191)	583 (202, 964)	<0.001
Urinary excretion[a]	5625 (2339, 8911)	4622 (1599, 7644)	−1003 (−1282, −724)	5830 (2366, 9294)	5746 (1665, 9826)	−84 (−392, 224)	<0.001
Potassium (mg/day)							
Dietary intake	2807 (861, 4753)	2934 (929, 4939)	127 (−78, 332)	2624 (842, 4405)	2733 (888, 4577)	109 (−67, 285)	0.407
Urinary excretion[a]	2570 (1125, 4016)	2402 (874, 3929)	−169 (−329, −8)	2674 (1170, 4179)	2499 (937, 4060)	−176 (−324, −28)	0.679
Urinary creatinine (mg/day)	950 (443, 1458)	871 (457, 1285)	−79 (−107, −51)	927 (504, 1350)	882 (469, 1294)	−45 (−72, −19)	0.109
Urine volume (mL/day)	1425 (653, 2197)	1343 (583, 2104)	−82 (−146, −18)	1418 (597, 2238)	1469 (605, 2333)	51 (−21, 123)	0.010

[a] Expected intake was considered to be observed urinary excretion divided by 0.86 for sodium and 0.77 for potassium. See text for details.
[b] P-values for comparison between intervention group and control group by t-test after adjustment for baseline value.

marker for the purpose of this study. In contrast, urinary excretions of sodium and serum ascorbic acid reflect much shorter intake periods of intakes such as a few days [39]. Forty-eight hour urinary collection would be difficult to keep compliance in ordinary daily life. This difficulty may have lead to the decrease in urine volume in the second year in both groups. We did the sub-analysis on the assumption that the total urine volume did not change. Because the results were materially unchanged, the effect of the decrease may be negligible at least for comparison of changes between groups. Also, for the same reason, the participants who collected their urine would have been more motivated than non-collectors. We examined differences in intervention effects between the collectors and the non-collectors. We did not observe statistically significant differences between them in daily sodium as reduction assessed with the DHQ (data not shown).

A major strength of our study was the use of a randomized controlled design, involvement of a relatively large number of free-living participants, focus on middle-aged and older subjects, using biological measures as well as a self-reported dietary assessment, and a high rate of follow-up. The intervention method tested in this study involving only two face-to-face counseling sessions, two newsletters,

Table 5
Serum carotene and vitamin C concentrations at two points[a]

	Intervention group (n = 231)			Control group (n = 239)			Between-group difference in change
	Baseline	Year 1	Change[b] (95% CI)	Baseline	Year 1	Change[b] (95% CI)	
	Mean (95% CI)	Mean (95% CI)		Mean (95% CI)	Mean (95% CI)		P[c]
Total carotene (mg/L)	560 (113, 2779)	573 (115, 2859)	13 (−33, 59)	549 (120, 2504)	519 (105, 2559)	−25 (−57, 6)	0.092
Alpha-carotene	79 (17, 359)	84 (15, 491)	10 (2, 18)	80 (20, 315)	76 (17, 333)	−3 (−9, 2)	0.001
Beta-carotene	475 (91, 2479)	480 (93, 2486)	3 (−38, 43)	462 (95, 2255)	436 (83, 2295)	−22 (−51, 6)	0.196
Vitamin C (mg/L)	14.6 (9.2, 23.1)	14.8 (9.3, 23.4)	0.1 (−0.3, 0.6)	14.8 (9.2, 23.9)	14.4 (9.0, 23.0)	−0.5 (−0.9, −0.1)	0.070

[a] Values at each point were transformed by the natural logarithm before computation because of the skewed distributions. They were back-transformed to show means and 95% CIs.
[b] Difference between baseline and Year 1.
[c] P-values for comparison between intervention group and control group by t-test after adjustment for baseline value.

and one lecture per year may be an efficient model for population-based dietary improvement interventions.

The primary limitation of in this study was that subjects were relatively motivated to reduce salt intake. However, we believe that this finding on salt reduction indicates the effectiveness of this intervention method for motivated persons.

In conclusion, the present dietary intervention method effectively decreased sodium and increased carotene and vitamin C intakes, although the former was more distinct. One year of follow-up is not sufficient from the viewpoint of achieving cancer and cardiovascular disease prevention by lifestyle modification. Further studies are necessary to assess the long term effects of this one-year dietary intervention.

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Original Article

Background Characteristics of Basic Health Examination Participants: the JPHC Study Baseline Survey

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Background: Although epidemiologic studies including the Japan Public Health Center-based Prospective Study on Cancer and Cardiovascular Disease (JPHC study) have frequently used the basic health examination participants as study subjects, their background characteristics have rarely been investigated. The aim of this study is to clarify the background characteristics of participants and to discuss their impact on epidemiologic studies.

Methods: Subjects were 43,140 (Cohort I) and 34,892 (Cohort II) respondents aged 40-59 years who completed a self-administered questionnaire in 1990 or 1993-94 by the JPHC Study. Respondents whose data of the basic health examination were also available were defined as participants. We compared their sociodemographic factors, personal medical history, and lifestyle-related factors with those of non-participants.

Results: Participants tended to be older and less educated. They were more likely to engage in agriculture, forestry and fisheries or to be self-employed persons, or homemakers. Male participants smoked less and were more likely to drink alcohol beverage moderately. Female participants smoked and drank less but tended to participate more in sports and physical exercise in their leisure time. Both male and female participants tended to eat fruits and green vegetables more often than non-participants. In short, participants had a different socioeconomic status from non-participants and a favorable lifestyle profile, especially among women. These findings were principally consistent between the two cohorts.

Conclusion: These differences between participants and non-participants in the basic health examination might cause a selection bias that limits the application of the results to only participants in the basic health examination.

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Key words: basic health examination, participants, selection bias, population-based study

Many epidemiologic studies in Japan have targeted participants in the basic health examination (*Kihon-kenkou-shinsa*) under the Health and Medical Service Law for the Aged (*Roujin-hoken-hou*) because of the ease in obtaining their consent to participation and the possibility of high response rates.[1,2] This could lead to a selection bias and limitation of external validity. Although the selection bias has been assessed in epidemiologic studies based on a questionnaire survey that showed respondents had better health status, higher education and income, and healthier lifestyle than non-respondents,[3-8] few have dealt with the selection bias of participants in the basic health examination.

In a large population-based prospective study in Japan, the

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Japan Public Health Center-based Prospective Study on Cancer and Cardiovascular Disease (JPHC study),[9-12] we collected not only information from a self-administered questionnaire but also health examination data and blood samples that were provided by only participants in the basic health examination. It is necessary to clarify the background characteristics of participants in the basic health examination before we analyze the data obtained only from such participants because this could help us to consider the possible selection bias and external validity of the findings. This issue also arises in connection with other epidemiologic studies that targeted participants in the basic health examination.[1,2] In examining the background characteristics of participants, we divided respondents to the baseline questionnaire into two groups, participants in the basic health examination and non-participants, then compared sociodemographic factors, personal medical history, and lifestyle-related factors between groups.

METHODS

Study cohort

This study was conducted as a part of the JPHC study, which began in 1990 for cohort I, and involved five Public Health Centers (PHC): Ninohe PHC in Iwate Prefecture, Yokote PHC in Akita Prefecture, Saku PHC in Nagano Prefecture, Ishikawa PHC in Okinawa Prefecture, and Katsushika PHC in the Tokyo Metropolitan area. Cohort II of the study, begun in 1993, involved six other PHCs: Kasama PHC in Ibaraki Prefecture, Kashiwazaki PHC in Niigata Prefecture, Tosayamada PHC in Kochi Prefecture, Arikawa PHC in Nagasaki Prefecture, Miyako PHC in Okinawa Prefecture, and Suita PHC in Osaka Prefecture.[9-12] The five PHC areas in Cohort I were selected based on the variation in mortality rate for stomach cancer from our previous ecological study, in which randomly selected subjects were intensively examined.[13-15] The six PHC areas in Cohort II were selected considering geographical distribution and feasibility. The study population was defined to be all residents aged 40-59 years old in Cohort I and 40-69 years old in Cohort II at baseline who registered their address in 27 administrative districts (city, town, or village) supervised by nine PHCs except for Katsushika and Suita PHCs. The present study includes 54,498 residents (27,062 men and 27,436 women) in Cohort I and 62,398 residents (30,651 men and 31,747 women) in Cohort II after excluding subjects in Katushika and Suita PHCs due to different definitions of study population. As a baseline survey, we conducted a self-administered questionnaire among all study subjects, but collected health examination data and blood samples only from participants in the basic health examinations. Therefore, available data of the baseline survey differed for each subject. However, all subjects in the JPHC Study Cohort have been followed for their mortality, migration, and incidence of cancer and cardiovascular disease irrespective of whether or not they responded or provided health examination data or blood samples. A detailed design of the study has been reported elsewhere.[16] This study was approved by the institutional review board of the National Cancer Center, Japan. Cohort subjects have been informed of the study design and results by annual or biannual newsletters, while the general population has had access to relevant information through our website (http://www.epidemiology.jp/).

Baseline survey

In this study, we used questionnaire and health examination data from the baseline survey. Figure 1 shows the relationship between a study cohort and each baseline survey by Venn diagram.

A self-administered questionnaire was distributed to all cohort subjects in 1990 (Cohort I) and 1993-94 (Cohort II), mostly by hand and partly by mail. The questionnaire consisted of items covering sociodemographic characteristics, personal medical history, smoking status, habitual intake of foods and alcoholic beverages, physical activity and other lifestyle-related factors. The

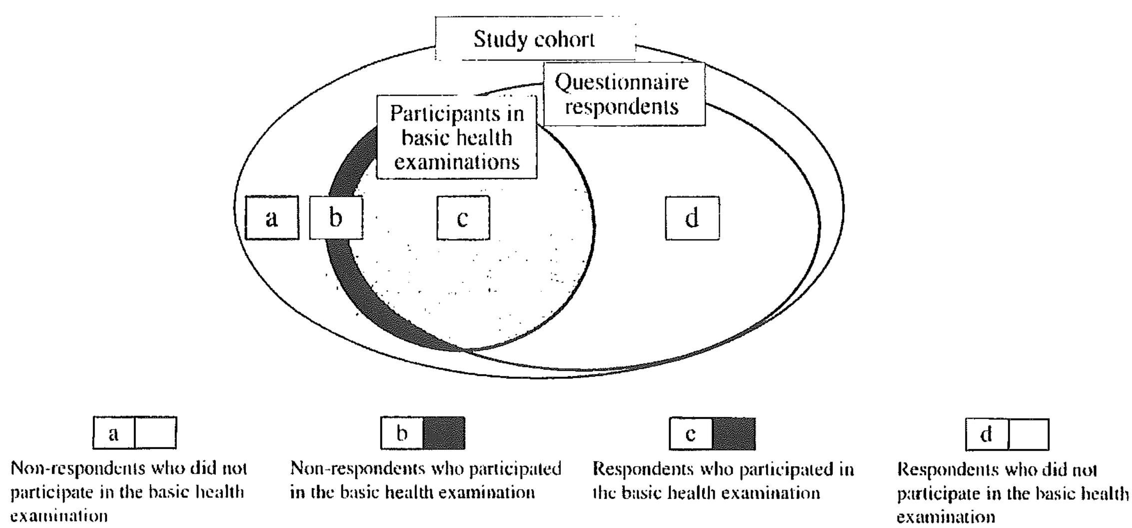

Figure 1. The relationship between study cohort and each baseline survey

questionnaire used for Cohort II was somewhat modified. A total of 43,149 (79%) (20,665 (76%) men and 22,484 (82%) women) in Cohort I and 52,256 (84%) (24,804 (81%) men and 27,452 (86%) women) in Cohort II subjects returned their questionnaire (Figure 1, (c+d)/(a+b+c+d)). Telephone interviews were used to obtain complete answers when information was missing.

We collected the health examination data from the local municipalities involved with their permission. They provided all data obtained from persons aged 40-59 years in the Cohort I area and aged 40-69 years in the Cohort II area who underwent the basic health examination under the Health and Medical Service Law for the Aged within each survey year (Cohort I in 1990, Cohort II in 1993-94). We conducted record linkage between the health examination data and our master files on our cohorts. Basically, data on the subjects in our master files matched the data from the municipal files on the basic health examination in terms of subject sex, name, and birthday. Data were available for 17,923 (33%) (6,532 (24%) men and 11,391 (42%) women) out of 54,498 subjects in Cohort I and 19,561 (31%) (6,598 (22%) men and 12,963 (41%) women) out of 62,398 subjects in Cohort II (Figure 1, (b+c)/(a+b+c+d)).

In this study, respondents (Figure 1, c and d) were divided into two groups by the basic health examination data: those for whom health examination data were available were defined as participants (Figure 1, c); those for whom the data were not available were defined as non-participants (Figure 1, d).

Study variables

To describe characteristics of participants and non-participants in the basic health examination, we compared them on the basis of well-known or commonly used factors related to diseases[12] including their sociodemographic factors (age, PHC area, educational background, and occupation), personal medical history (past history of diabetes mellitus, cerebrovascular disease, hypertension, ischemic heart disease, or cancer, family history of diabetes mellitus, cerebrovascular disease, ischemic heart disease (Cohort I), heart disease (Cohort II), or cancer, medication, and body mass index (BMI)) and lifestyle-related factors (vitamin supplement use, smoking status, alcohol drinking, sports and/or physical exercise in leisure time, and dietary habits).

Educational background was available for only Cohort I, and was grouped into three categories. The Japanese standard occupational classification was used to categorize occupation by open-ended question in Cohort I. In Cohort II, nine self-reported occupations were combined into the following 6 groups: employee and professional; agricultural, forestry, and fishery; self-employed; homemaker; unemployed; and other occupations. The subjects with 2 or more occupations across those groups were classified as a combination group. BMI was calculated from self-reported height and weight.[11] Smoking status was classified as current, past, or never smokers, and pack-year was calculated.[12] We defined non-drinkers (<1 day/month), occasional drinkers (1-3 days/month), and regular drinkers (1-2 days/week or more) based on the frequency of consumption in Cohort I. Non-drinkers were then subdivided into never-drinkers and ex-drinkers in Cohort II. Among regular drinkers, weekly ethanol consumption was calculated by combining the frequency per week and the usual daily amount of alcoholic beverages.[11,18] The weekly intake frequency of 27 (Cohort I) and 33 (Cohort II) food items was reported in four (Cohort I) and five (Cohort II) categories.

Statistical analysis

We excluded 29 subjects (9 in Cohort I and 20 in Cohort II) not of Japanese nationality (7 in Cohort I and 11 in Cohort II), or who had already moved away at the baseline, which we confirmed during the follow-up period (2 in Cohort I and 9 in Cohort II). Subjects aged 60 years and older in Cohort II were excluded because we matched age groups between the two cohorts. Finally, data for analyses included 43,140 subjects (20,658 men and 22,482 women) in Cohort I and 34,892 subjects (16,882 men and 18,010 women) in Cohort II. All analyses were performed separately according to sex and cohort.

Odds ratios (OR) and their 95% confidence intervals (CI) were calculated by unconditional logistic regression to estimate associations between participation in the basic health examination and sociodemographic factors, personal medical history, and lifestyle-related factors. Logistic regression analysis by SAS LOGISTIC procedure (SAS Institute Inc., Cary, NC) was used to adjust for age (40-44, 45-49, 50-54, and 55-59 years) and area (city vs. town and village) because the proportion of participants in the basic health examination varied between city, town and village.[19] Multivariate ORs adjusted for age, educational background (only for Cohort I), and occupation were calculated. Participation in the basic health examination is influenced by occupation because the basic health examination in Japan does not cover subjects who have the periodical health examination (*Teiki-kenkou-shindan*) at their workplaces under the Industrial Safety and Health Law (*Roudou-anzen-esisei-hou*). To test the linear trend, consecutive integers were given to each category. All p values are reported as two-sided, and the significance level was set at $p<0.05$.

RESULTS

Tables 1 and 2 show age- and area-adjusted ORs for participation in the basic health examination according to sociodemographic factors, personal medical history, and lifestyle-related factors in Cohorts I and II. In Cohort I, 5,883 (28%) men and 10,247 (46%) women underwent the basic health examination, against 2,787 (17%) men and 6,708 (37%) women in Cohort II.

Sociodemographic factors

As commonly observed, participation in the basic health examination was associated with the age class, and the ORs for participation showed a significant increase with aging. In Cohort I, subjects categorized in higher educational background groups demonstrated statistically significant decreased ORs for participation in the basic health examination among both men and women. In Cohort I, subjects classified in Table 1 in the Clerk, Sales work, Service work, Agricultural, forestry, and fishery, or Labor categories had significantly higher ORs for participation in the basic health examination than those classified in the Profession category. In Cohort II, a significant elevation of ORs for participation in the basic health examination was observed for agricultural, forestry and fishery, self-employed, homemakers and unemployed groups compared to the employee and profession group.

Personal medical history

Subjects with a past medical history had significantly lower ORs for participation in the basic health examination than those without such a history in Cohort I. A family history was associated with significantly increased ORs for participation in the basic health examination in Cohort I. However, an inverse association among men and no association among women were observed in Cohort II. The uses of any medication were related to the decreased ORs for participation in the basic health examination. Subjects of both sexes and cohorts in the lowest BMI category characteristically showed a significant decrease in ORs for participation in the basic health examination compared to subjects in the middle BMI categories.

Lifestyle-related factors

The uses of any vitamin supplements were significantly related to the decreased ORs for participation in the basic health examination. Smoking status was related to significantly decreased ORs for participation in the basic health examination. As pack-year increased, ORs for participation gradually decreased regardless of sex or cohort and all p for trends reached significant levels. The combined variable of drinking habit and consumption was not related to participation in the basic health examination for men, especially in Cohort II. Female heavy alcohol drinkers (100+ g/week) demonstrated significantly lower ORs than occasional drinkers. In Cohort II, female never-drinkers had significantly higher ORs than occasional drinkers, whereas ex-drinkers had significantly lower ORs than them. Participation in the basic health examination was related to sports and physical exercise in leisure time, however, a different pattern was seen in both sexes. Statistically significant elevation of ORs for participation in the basic health examination was associated with increased frequency of fruit or apple and citrus fruit consumption with the exception of the men in Cohort II. A higher frequency of green vegetable intake was associated with significantly increased ORs in Cohort II, and a non-significant increase was observed in Cohort I. There were significantly decreased ORs related to increased frequency of beef intake in Cohort I. Statistically significant positive associations were observed between the frequency of fish intake and participation in the basic health examination (p for trend<0.0001), although clear association was not seen among men in Cohort II with respect to ORs in each category.

Findings from multivariate analyses

Most personal medical history and lifestyle-related factors were almost unchanged even after adjustment for age, educational background (only in Cohort I) and occupation (data not shown). However, the statistically significant association disappeared among men for the following variables: past history (Cohort I), physical exercise in leisure time and fish (p for trend) (Cohort II). In addition, male drinkers (1-449 g/week) in Cohort I showed significantly elevated ORs compared to occasional drinkers: 1.22 (95%CI 1.07-1.38) for those drinking 1-149 weekly amount (g); 1.21 (95%CI 1.07-1.37) for those drinking 150-299 weekly amount (g); and 1.32 (95%CI 1.16-1.50) for those drinking 300-449 weekly amount (g). Among men in Cohort II, significantly increased ORs for participation in the basic health examination were observed for 'Apple' as follows: 1.32 (95%CI 1.11-1.56) for sometimes; 1.32 (95%CI 1.10-1.60) for 1-2 days/week; and 1.32 (95%CI 1.07-1.63) for 3-4 days/week. As for physical exercise in leisure time, the opposite finding of age- and area-adjustment was obtained among men in Cohort I (1.25 (95%CI 1.14-1.37) for 1-3 days/month and 0.95 (95%CI 0.87-1.04) for 1+ day/week). Significantly increased ORs were observed among women: in Cohort I, the corresponding ORs were 1.34 (95%CI 1.19-1.49) and 1.11 (95%CI 1.03-1.21); in Cohort II, the corresponding ORs were 1.14 (95%CI 1.01-1.30) and 1.30 (95%CI 1.19-1.41).

DISCUSSION

In this study, the differences observed in some sociodemographic factors, personal medical history, and lifestyle-related factors between participants and non-participants might cause a selection bias. Criqui et al.[3] pointed out that two types of bias can occur with substantial non-response in population-based prospective studies: (1) bias in the prevalence of exposure factors or disease due to the differential participation of individuals with given exposures or diseases, or (2) bias in risk rate ratio estimates determined by comparing the incidence rates of disease in the exposed and unexposed group. Our findings implied selection bias would lead to systematic error in estimating the prevalence of risk factors and diseases, thus limiting application of the results to participants in the basic health examination. In addition, estimation of exposure-disease associations might be affected in some cases. However, the degree of bias considered to be important depends on the intended use of the study results. As Greenland[20] pointed out, "A bias that may have been considered insignificant in one context (such as in research establishing the existence of an association) may be considered more significant in a later context (such as in allocating of health care resources based on the strength of the association)."

Although inconsistent findings that might be due to the multiplicity of the comparison or the use of a different questionnaire between two cohorts were observed for several variables, our study basically showed that especially female participants had a favorable lifestyle profile, and obvious associations were

Table 1. Proportions of participants and age- and area-adjusted odds ratios for participation in the basic health examination according to sociodemographic factors, personal medical history, and lifestyle-related factors in 1990: JPHC Cohort I.

	Men					Women				
	Participants		Age- and area-adjusted [a]			Participants		Age- and area-adjusted [a]		
	n	%	Odds ratio	95% CI [a]	p for trend	n	%	Odds ratio	95% CI [a]	p for trend
No.	5883	28.5				10247	45.6			
Age (years)										
40-44	1326	24.9	1.00		<0.0001	2041	37.4	1.00		<0.0001
45-49	1251	26.1	1.06	(0.97, 1.16)		2230	42.2	1.20	(1.11, 1.30)	
50-54	1445	28.4	1.20	(1.09, 1.31)		2831	48.4	1.56	(1.45, 1.69)	
55-59	1861	34.1	1.49	(1.37, 1.63)		3145	53.3	1.86	(1.72, 2.01)	
PHC area										
Ninohe	1484	33.8	1.00			2836	55.4	1.00		
Yokote	1559	28.0	0.80	(0.73, 0.87)		2964	46.1	0.70	(0.65, 0.75)	
Saku	2168	39.6	0.62	(0.56, 0.68)		3056	54.8	0.57	(0.51, 0.62)	
Ishikawa	672	12.9	0.35	(0.31, 0.39)		1391	25.9	0.31	(0.29, 0.34)	
Educational background										
Junior high school or less	3028	31.2	1.00			5774	49.0	1.00		
High school	2123	28.0	0.88	(0.82, 0.95)		3242	44.1	0.87	(0.82, 0.92)	
College or beyond	560	19.7	0.59	(0.53, 0.65)		900	34.4	0.62	(0.57, 0.68)	
Occupation [a]										
Profession	195	16.2	1.00			253	22.4	1.00		
Manager	109	16.5	1.04	(0.80, 1.35)		12	18.2	0.83	(0.43 1.58)	
Clerk	492	20.5	1.25	(1.03, 1.50)		522	30.4	1.52	(1.27, 1.81)	
Sales work	491	29.3	2.18	(1.81, 2.64)		703	43.1	2.55	(2.14, 3.03)	
Service work	222	28.2	1.87	(1.50, 2.34)		1006	38.5	2.08	(1.77, 2.45)	
Protective service	19	6.6	0.40	(0.25, 0.66)		1	10.0	0.42	(0.05, 3.31)	
Agricultural, forestry, and fishery	2158	49.2	3.88	(3.28, 4.59)		3081	64.6	4.99	(4.28, 5.83)	
Transport and communications	284	16.9	1.09	(0.89, 1.34)		17	20.0	0.94	(0.54, 1.63)	
Labour	1699	26.0	1.61	(1.36, 1.90)		1713	44.0	2.35	(2.01, 2.74)	
Unemployed	140	18.5	1.18	(0.92, 1.51)		2787	44.9	2.82	(2.42, 3.28)	
Past history of DM, CVD, HT, IHD, or Cancer [b]										
No	4637	28.6	1.00			8336	45.8	1.00		
Yes	1219	27.8	0.88	(0.81, 0.95)		1841	44.6	0.83	(0.77, 0.89)	
Family history of DM, CVD, HT, IHD, or Cancer [b]										
No	2319	25.1	1.00			4286	41.7	1.00		
Yes	3564	31.2	1.24	(1.17, 1.33)		5961	48.9	1.26	(1.19, 1.33)	
Any medications										
No	4539	28.9	1.00			7615	46.0	1.00		
Yes	1259	26.7	0.83	(0.77, 0.90)		2513	44.4	0.83	(0.78, 0.88)	
Any vitamin supplement use										
No	4904	29.0	1.00			8137	47.1	1.00		
Yes	708	24.7	0.84	(0.77, 0.93)		1607	38.9	0.75	(0.70, 0.81)	
Body mass index (kg/m²)										
-19.9	481	26.5	0.79	(0.70, 0.90)		940	39.6	0.72	(0.65, 0.80)	
20.0-21.9	1264	29.8	0.96	(0.88, 1.05)		2114	44.6	0.90	(0.83, 0.97)	
22.0-23.9	1734	29.5	1.00			2843	47.4	1.00		
24.0-25.9	1407	28.5	0.99	(0.91, 1.08)		2287	48.7	1.02	(0.95, 1.11)	
26.0+	963	26.6	0.94	(0.86, 1.04)		2008	44.4	0.86	(0.80, 0.94)	

Table 1. (continued)

Smoking status										
Never-smokers	1563	31.6	1.00			9733	47.0	1.00		
Past smokers	1392	29.7	0.86	(0.79, 0.94)		130	33.0	0.56	(0.45, 0.70)	
Current smokers	2909	26.6	0.74	(0.69, 0.80)		349	27.2	0.43	(0.38, 0.49)	
Pack-years										
0	1563	31.6	1.00		<0.0001	9733	47.0	1.00		<0.0001
1-9 } 10-19	1251	27.2	0.80	(0.73, 0.88)						
1-9						279	32.7	0.57	(0.49, 0.66)	
10-19						100	25.3	0.38	(0.30, 0.48)	
20-29	1092	26.9	0.78	(0.71, 0.86)						
20-29 } 30+						78	23.6	0.35	(0.27, 0.46)	
30+	1840	28.3	0.76	(0.70, 0.83)						
Alcohol consumption										
Non-drinkers	1088	25.4	0.89	(0.78, 1.0002)		7967	46.4	1.01	(0.93, 1.10)	
Occasional drinkers	572	26.0	1.00			1216	45.7	1.00		
weekly amount (g)										
1-99						689	43.6	0.92	(0.81, 1.05)	
100+						246	32.2	0.61	(0.51, 0.72)	
1-149	1001	28.7	1.07	(0.95, 1.22)						
150-299	1178	29.9	1.09	(0.96, 1.23)						
300-449	1008	33.0	1.24	(1.09, 1.41)						
450+	904	28.0	1.03	(0.91, 1.17)						
Sports and/or physical exercise in leisure time										
<1 day/month	3933	29.1	1.00			7808	44.9	1.00		
1-3 days/month	1028	30.6	1.01	(0.93, 1.10)		785	50.9	1.17	(1.05, 1.31)	
1+ day/week	854	23.9	0.78	(0.71, 0.85)		1478	46.3	0.99	(0.91, 1.07)	
Dietary habits										
Fruit										
Rarely	403	19.4	1.00		<0.0001	297	31.3	1.00		<0.0001
1-2 days/week	1831	25.2	1.40	(1.23, 1.58)		1734	37.0	1.28	(1.10, 1.49)	
3-4 days/week	1819	30.1	1.62	(1.43, 1.84)		2871	43.7	1.59	(1.37, 1.84)	
Almost everyday	1751	34.8	1.77	(1.56, 2.01)		5168	52.1	1.97	(1.70, 2.28)	
Green vegetables										
Rarely	119	24.2	1.00		0.135	133	40.4	1.00		0.053
1-2 days/week	1594	27.7	1.14	(0.91, 1.42)		2039	44.0	1.11	(0.88, 1.40)	
3-4 days/week	2507	29.5	1.25	(1.01, 1.56)		4327	46.6	1.23	(0.98, 1.55)	
Almost everyday	1644	28.1	1.19	(0.95, 1.48)		3698	45.6	1.19	(0.95, 1.50)	
Beef										
Rarely	2785	35.8	1.00		<0.0001	5474	51.9	1.00		<0.0001
1-2 days/week	2527	24.8	0.67	(0.63, 0.72)		3814	40.8	0.72	(0.68, 0.76)	
3-4 days/week	469	21.0	0.54	(0.49, 0.61)		729	35.3	0.57	(0.52, 0.63)	
Almost everyday	28	12.3	0.27	(0.18, 0.41)		58	30.2	0.43	(0.31, 0.59)	
Fish										
Rarely	320	20.7	1.00		<0.0001	669	37.8	1.00		<0.0001
1-2 days/week	2318	26.6	1.30	(1.14, 1.49)		3368	41.1	1.12	(1.003, 1.25)	
3-4 days/week	2227	31.4	1.58	(1.38, 1.81)		3843	48.8	1.47	(1.32, 1.64)	
Almost everyday	959	31.0	1.60	(1.38, 1.86)		2233	51.4	1.66	(1.47, 1.86)	

a) The Japanese standard occupational classification was used to categorize occupation: professional and technical workers (Profession), managers and officials (Manager), clerical and related workers (Clerk), sales workers (Sales work), service workers (Service work), protective service workers (Protective service), agricultural, forestry, and fisheries workers (Agriculture, forestry, and fishery), workers in transport and communications occupations (Transport and communications), craftsmen, mining, production process and construction workers and laborers (Labor).

b) DM, diabetes mellitus; CVD, cerebrovascular disease; HT, hypertension; IHD, ischemic heart disease.

c) Adjusted for age in 1990 (40-44, 45-49, 50-54, 55-59) and area (city, town and village).

d) 95% CI: 95% confidence interval

Table 2. Proportions of participants and age- and area-adjusted odds ratios for participation in the basic health examination according to sociodemographic factors, personal medical history, and lifestyle-related factors in 1993-94: JPHC Cohort II.

	Men					Women				
	Participants		Age- and area-adjusted [c]			Participants		Age- and area-adjusted [c]		
	n	%	Odds ratio	95% CI [d]	p for trend	n	%	Odds ratio	95% CI [d]	p for trend
No.	2787	16.5				6708	37.2			
Age (years)										
40-44	558	10.8	1.00		<0.0001	1338	25.7	1.00		<0.0001
45-49	481	12.5	1.20	(1.05, 1.36)		1308	32.2	1.39	(1.27, 1.53)	
50-54	639	17.1	1.70	(1.51, 1.93)		1705	40.9	2.02	(1.85, 2.21)	
55-59	1109	26.9	3.06	(2.73, 3.42)		2357	51.5	3.09	(2.84, 3.36)	
PHC area										
Kasama	807	11.4	1.00			2167	31.5	1.00		
Kashiwazaki	141	14.9	1.21	(0.998, 1.48)		315	30.8	0.86	(0.74, 0.99)	
Tosayamada	417	16.5	1.52	(1.34, 1.73)		923	33.2	1.08	(0.98, 1.19)	
Arikawa	496	15.8	1.36	(1.20, 1.54)		1628	41.9	1.44	(1.33, 1.57)	
Miyako	926	28.8	5.78	(4.89, 6.83)		1675	48.6	3.92	(3.31, 4.63)	
Occupation										
Employee and Profession	541	6.0	1.00			814	15.8	1.00		
Agricultural, Forestry and Fishery	951	35.3	7.61	(6.74, 8.59)		1198	63.1	7.50	(6.63, 8.48)	
Self-employed	759	26.8	5.64	(4.99, 6.37)		726	36.8	2.85	(2.53, 3.22)	
Homemaker	0	0.0	N.A. [e]	N.A. [e]		2195	44.4	3.94	(3.58, 4.33)	
Unemployed	95	20.3	3.12	(2.44, 3.99)		145	32.8	2.07	(1.67, 2.57)	
Other occupations	17	21.0	4.29	(2.47, 7.43)		14	18.9	1.07	(0.59, 1.93)	
Combination [a]	390	23.7	4.52	(3.91, 5.23)		1578	47.4	4.30	(3.87, 4.76)	
Past history of DM, CVD, HT, IHD, or Cancer [b]										
No	2092	16.0	1.00			5403	36.6	1.00		
Yes	663	18.0	0.96	(0.86, 1.05)		1239	40.2	0.93	(0.85, 1.01)	
Family history of DM, CVD, HD, or Cancer [b]										
No	1508	17.6	1.00			3521	37.8	1.00		
Yes	1279	15.3	0.87	(0.80, 0.94)		3187	36.6	0.96	(0.90, 1.02)	
Any medications										
No	2064	16.2	1.00			5008	36.5	1.00		
Yes	709	17.4	0.91	(0.83, 1.003)		1662	39.8	0.92	(0.85, 0.99)	
Any vitamin supplement use										
No	2084	15.4	1.00			4926	36.3	1.00		
Yes	284	14.5	0.83	(0.72, 0.95)		964	34.8	0.83	(0.76, 0.90)	
Body mass index (kg/m^2)										
-19.9	189	13.2	0.79	(0.66, 0.94)		610	29.9	0.78	(0.70, 0.88)	
20.0-21.9	472	14.8	0.91	(0.81, 1.04)		1401	34.8	0.97	(0.89, 1.07)	
22.0-23.9	793	16.8	1.00			1761	36.9	1.00		
24.0-25.9	632	16.2	0.93	(0.83, 1.05)		1466	41.3	1.17	(1.06, 1.28)	
26.0+	677	19.7	1.16	(1.04, 1.31)		1409	41.2	1.08	(0.99, 1.19)	
Smoking status										
Never-smokers	935	21.8	1.00			6387	38.8	1.00		
Past smokers	631	19.1	0.91	(0.81, 1.02)		47	25.3	0.53	(0.38, 0.74)	
Current smokers	1214	13.2	0.63	(0.57, 0.70)		243	19.4	0.41	(0.36, 0.48)	
Pack-year										
0	935	21.8	1.00		<0.0001	6387	38.8	1.00		<0.0001
1-9	429	15.2	0.78	(0.68, 0.89)		110	23.3	0.54	(0.43, 0.67)	
10-19						82	19.5	0.42	(0.33, 0.54)	
20-29	432	13.6	0.74	(0.65, 0.84)		57	13.1	0.24	(0.18, 0.32)	
30+	904	14.8	0.65	(0.58, 0.72)						

Table 2. (continued)

Alcohol consumption										
Never-drinkers	457	15.9	1.02	(0.85, 1.21)		5436	40.4	1.41	(1.27, 1.58)	
Ex-drinkers	76	16.6	0.95	(0.71, 1.26)		39	23.8	0.64	(0.44, 0.94)	
Occasional drinkers	236	15.4	1.00			536	28.5	1.00		
weekly amount (g)										
1-99						388	29.5	1.04	(0.89, 1.22)	
100+						174	22.0	0.68	(0.56, 0.83)	
1-149	601	15.5	1.07	(0.91, 1.27)						
150-299	552	16.3	1.09	(0.92, 1.29)						
300-449	331	16.2	1.04	(0.86, 1.25)						
450+	292	17.3	1.12	(0.92, 1.35)						
Sports and/or physical exercise in leisure time										
<1 day/month	1978	18.1	1.00			4860	36.4	1.00		
1-3 days/month	372	13.6	0.79	(0.70, 0.89)		487	35.7	1.01	(0.90, 1.14)	
1+ day/week	413	13.5	0.67	(0.60, 0.76)		1291	41.4	1.18	(1.09, 1.28)	
Dietary habits										
Apple										
Never	203	14.4	1.00		0.0501	183	29.4	1.00		<0.0001
Sometimes	1594	17.0	1.23	(1.05, 1.44)		2719	36.3	1.42	(1.18, 1.71)	
1-2 days/week	508	16.0	1.14	(0.96, 1.37)		1461	37.0	1.55	(1.28, 1.87)	
3-4 days/week	275	17.0	1.13	(0.92, 1.38)		1289	38.8	1.57	(1.30, 1.90)	
Almost everyday	141	14.3	0.89	(0.70, 1.13)		914	39.9	1.60	(1.32, 1.95)	
Citrus fruit										
Never	120	16.4	1.00		0.180	83	30.6	1.00		<0.0001
Sometimes	1123	16.4	1.03	(0.83, 1.27)		1385	34.5	1.26	(0.96, 1.66)	
1-2 days/week	526	14.8	0.92	(0.74, 1.14)		958	33.4	1.27	(0.97, 1.68)	
3-4 days/week	475	16.3	1.01	(0.81, 1.26)		1687	37.6	1.52	(1.16, 1.99)	
Almost everyday	484	19.2	1.14	(0.91, 1.43)		2447	40.7	1.63	(1.25, 2.14)	
Green vegetables										
Never	12	9.7	1.00		<0.0001	19	29.7	1.00		<0.0001
Sometimes	556	14.4	1.65	(0.89, 3.03)		885	33.0	1.29	(0.74, 2.24)	
1-2 days/week	740	14.2	1.63	(0.89, 2.99)		1576	33.8	1.40	(0.80, 2.43)	
3-4 days/week	796	17.4	1.88	(1.02, 3.45)		2238	37.4	1.57	(0.90, 2.72)	
Almost everyday	646	22.3	2.33	(1.27, 4.28)		1892	43.4	1.81	(1.04, 3.15)	
Beef										
Never	298	17.6	1.00		0.944	988	36.2	1.00		0.005
Sometimes	1649	16.6	0.99	(0.86, 1.13)		3601	37.6	1.13	(1.03, 1.23)	
1-2 days/week	647	15.3	0.95	(0.82, 1.11)		1648	36.8	1.19	(1.08, 1.32)	
3-4 days/week	118	16.6	0.97	(0.76, 1.23)		290	37.5	1.14	(0.96, 1.35)	
Almost everyday	17	27.9	1.87	(1.04, 3.38)		17	37.0	1.06	(0.57, 1.96)	
Fish										
Never	18	18.8	1.00		<0.0001	37	27.4	1.00		<0.0001
Sometimes	484	15.8	0.90	(0.53, 1.53)		1051	33.1	1.49	(1.01, 2.22)	
1-2 days/week	769	13.8	0.82	(0.48, 1.39)		1988	34.2	1.69	(1.14, 2.50)	
3-4 days/week	877	17.9	1.03	(0.61, 1.75)		2289	39.1	1.95	(1.32, 2.88)	
Almost everyday	608	20.0	1.09	(0.64, 1.85)		1253	44.8	2.25	(1.51, 3.33)	

a) Subjects with multiple occupations

b) DM, diabetes mellitus; CVD, cerebrovascular disease; HT, hypertension; IHD, ischemic heart disease; HD, heart disease.

c) Adjusted for age in 1993 (40-44, 45-49, 50-54, 55-59) and area (city, town and village).

d) 95% CI: 95% confidence interval

e) N.A., not available

observed for smoking and dietary habits. Similar results were reported in studies that targeted not only subjects for cancer screening programs[21-23] but also the general population or some specific groups.[3-8] With respect to studies on the basic health examination, Ozasa[24,25] reported that participants had a healthier behavior, including better dietary habits such as limited salt intake, and eating more fish, vegetables, beans, fruit and seaweed. Some earlier studies[6,7] showed that respondents had higher education and income than non-respondents. Meanwhile, we found that participants in the basic health examination tended to be older and less educated. They were more likely to engage in agriculture, forestry and fisheries or to be self-employed persons or homemakers in our study. This is partly because the basic health examination is provided free or at low cost by local municipalities to all people in Japan duly registered as residents who are 40 years old or more, and are not offered periodical health examinations at their workplace. Therefore, most retired, self-employed, or unemployed (including homemakers) persons underwent the basic health examination. In the present study, non-participants fell into two groups: those eligible to participate in the basic health examination who did not, and those who underwent the periodical health examination at their workplaces and thus had no need to take part in the basic health examination. However, in light of our study aim, we did not need to distinguish between two groups among non-respondents. Although the proportion of non-participants who underwent any health check-ups for the last year were 79% (79% in men and women) in Cohort I and 73% (76% in men and 69% in women) in Cohort II based on the baseline questionnaire, these conditions would lessen the associations between background characteristics and participation in the basic health examination. Nevertheless, relatively great differences were observed for smoking and dietary habits.

Regarding methodological issues, the strengths of the present study include the population-based large sample with high response rate obtained from nine PHCs that covered 27 administrative districts (city, town or village), although study areas were not selected randomly. Our results were principally consistent between the two cohorts. Thus, the external validity of our results might be assured for middle-aged Japanese population except for those living in urban areas. This indicates that attention must be given to interpretation and generalization of results from health examination participants in a rural community. To our knowledge, this is the first study to compare sociodemographic factors, personal medical history, and lifestyle-related factors between participants and non-participants in the basic health examination based on a large population-based sample in Japan.

In spite of these strengths, this study has several limitations. First, the differences in the respective questionnaires made it difficult to confirm consistent findings between Cohort I and Cohort II. This might in part explain the differences in findings between the two cohorts. Second, the subjects surveyed in this study were restricted to respondents to the baseline questionnaire. As mentioned above, non-respondents had an unhealthier lifestyle than respondents,[3,5,6,8] and were less likely to participate in the basic health examination. In the present study, the proportions of non-respondents were 21% (24% in men and 18% in women) in Cohort I and 18% (21% in men and 14% in women) in Cohort II. In addition, participants (Figure 1, b) accounted for 16% (10% in men and 23% in women) of non-respondents in Cohort I and 7% (4% in men and 12% in women) in Cohort II (Figure 1, b/(a+b)). Although it could lead to underestimation of the association between participation to the basic health examination and sociodemographic factors, personal medical history, and lifestyle-related factors, this effect might be relatively small in this study, since nearly 80% or more of our subjects responded to the baseline questionnaire.

Despite these limitations, we found that female participants in particular had a different socioeconomic status from non-participants and showed a healthy lifestyle. These differences between participants and non-participants in the basic health examination might cause a selection bias that limits the application of the results to only participants in the basic health examination.

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APPENDIX

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Original Article

Respiratory Symptoms Correlating to Smoking Prevalence: The National Nutrition Survey and the National Life-style Survey in Japan.

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Background: Although the fact that smoking habits have adverse effects on health, whether the high proportion of smokers elevates the prevalence of symptoms relating to the smoking in a community is still unknown.

Methods: An ecologic study about whole Japan was conducted. Age-adjusted smoking prevalence was calculated using the National Nutrition Survey data from 1986 through 1995 by prefecture and sex. Age-adjusted respiratory symptom prevalence were observed using the National Life-style Survey data in 1995. Correlation among 46 and/or 43 prefectures was examined by sex.

Results: There was a negative correlation between smoking prevalence and wheezing prevalence among males (r=-0.301). Among females, positive correlations were observed on the symptoms of nasal obstruction (r=0.355), nasal discharge (r=0.344), sore throat (r=0.481), cough (r=0.350), sputum (r=0.594), wheezing (r=0.451), palpitation (r=0.363), dyspnea (r=0.587), and frontal chest pain (r=0.472).

Conclusions: Smoking prevalence was deeply related to respiratory symptoms among females in Japan.

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Key words: smoking; signs and symptoms, respiratory; correlation; ecologic studies.

Proportion of smokers among Japanese males has been still high and the reduction of smoking prevalence must be overcome. The proportion was 47.4% among males and 11.5% among females in 2000 according to the National Nutrition Survey.[1] Hazardous effects of smoking to human health are well known.[2-4] Even in indirect smoking exposure, the effects are obvious.[5-7] We have already observed the unique distribution of smoking prevalence by prefecture, and the observation revealed that smoking prevalence related with standardized mortality rates of some causes of deaths.[8,9] In these studies, significant positive correlation with the smoking prevalence was observed for pancreas cancer, decrepitude, unexpected injuries, and traffic injuries in males, and tuberculosis, lung cancer, breast cancer, total heart disease, ischemic heart disease, acute myocardial infarction, pneumonia, chronic obstructive pulmonary disease, asthma, liver disease, and renal failure in females. Thus, prefectures with high proportion of smokers had high standard mortality ratios for some causes of deaths related to smoking. This means excess deaths occurred by smoking. However, health hazardous effects are not only on mortality, but also on morbidity. It is reasonable that incidence rate and prevalence of such diseases as respiratory diseases, cardiovascular diseases, and cancer are high in places where the smoking is prevalent.[10-12] Such observations, however, have not been conducted in Japan yet.

A health promotion plan named "Healthy Japan 21" was kicked off by the national government in 2000. Local governments are

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Demographics, lifestyles, health characteristics, and dietary intake among dietary supplement users in Japan

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Background The associations between supplement use and certain demographics, lifestyles, health characteristics, and dietary intakes have not been studied in a large population in non-Western societies. The objective of our study was to investigate the association between supplement use and demographics, lifestyles, health characteristics, and dietary intake in a population-based cohort study in Japan.

Methods Subjects were the 78 531 participants (45–74 years) who completed a self-administered questionnaire in 1995 or 1998 in a 5-year follow-up survey by the Japan Public Health Center-based prospective Study on cancer and cardiovascular disease. The questionnaire included enquiries about supplement use, occupation, height, weight, smoking, alcohol, physical activity, dietary behaviours, working hours, subjective stress, as well as intakes for 138 foods.

Results The supplement users were likely to have formerly smoked or never smoked. Female supplement users were likely to consume alcohol moderately. The prevalence of users was higher in the elderly, the self-employed, those with lower body mass index, greater physical activity, lower frequency of eating prepared food, higher frequency of eating out, and higher stress level in both sexes after mutual adjustment. Mean intakes of energy and nutrients were lower for users than for non-users.

Conclusion The demographics, lifestyles, health characteristics, and dietary intakes may need to be adjusted when evaluating the effect of dietary supplements on disease because they can become potential confounding factors.

Keywords Dietary supplements, characteristics, cohort study

Commercially available dietary supplements in Japan have seen tremendous growth over the last decade,[1] and their variety and number continue to increase. The prevalence of dietary supplement users differs depending on the study population as well as the definition of supplements and survey methods used. In the US, where dietary supplements are generally very popular, the prevalence varied from 21% to 55% among a number of different studies.[2] In our previous report for the baseline survey by the Japan Public Health Center-based prospective Study on cancer and cardiovascular disease (JPHC Study) in 1990 and 1993, the users who took vitamin supplements ≥1 week ranged from 4.4% to 22.7% by area.[3]

In epidemiological studies, the use of dietary supplements is an exposure of interest because of its potential effect on disease. When dietary supplement use is associated with both diseases and demographic factors such as sex, age, race, and socio-economic status,[4] and health-related characteristics such as body mass index (BMI), smoking, and alcohol consumption,[5–7] as well as certain psychological factors,[8] it also becomes a confounding factor when determining other risk factors. These

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associations have been investigated extensively in Western countries where supplements have been widely used for decades. However, little is known about the characteristics of dietary supplement users in non-Western countries, including Japan.

In this report, we aimed to determine the characteristics of dietary supplement users among the participants in the JPHC Study cross-sectionally. The objective of our study was to investigate the possible association between supplement use and demographics, lifestyles, health characteristics, and dietary intakes.

Materials and Methods

Subjects

The study population of the JPHC Study were 140 420 adults (29 982 males and 31 613 females in Cohort I, and 38 740 males and 40 085 females in Cohort II) from 11 Public Health Center (PHC) areas in Japan. Cohort I started in 1990 with population-based cohorts of all 40–59 year old residents of four PHC areas (Yokote, Ninohe, Saku, and Ishikawa), together with a health check-up cohort in which all 40 and 50 year old residents of a PHC area (Katsushika) were invited to participate. Cohort II started in 1993 with population-based cohorts of all 40–69 year old residents of five PHC areas (Mito, Kashiwazaki, Chuo-higashi, Kamigoto, and Miyako), together with two health check-up cohorts (Suita 1 and Suita 2). Suita 1 comprised 40 and 50 year old residents of Suita City who participated in a comprehensive municipal health check-up programme. Suita 2 comprised 40–69 year old participants from the Suita Study, in which the participants were randomly selected from all 30–79 year old residents of Suita based on the population registry. The locations of study sites are shown in Figure 1. Study sites of the JPHC Study encompass the prefectures with the lowest and highest mortality rates. They were distributed throughout Japan and consisted of both urban and rural communities.[9] Katsushika and Suita are urban areas located in two major cities in Japan where a large proportion of subjects were engaged with manufacturing, trade, and service sectors. Other areas were rather rural, where farming and fishing were prominent. Baseline surveys were conducted in each cohort at the beginning of the study. Details on the selection of cohort participants and the baseline survey were presented elsewhere.[10]

Data collection

We conducted a 5-year follow-up survey from the baseline in 1995 for Cohort I, and in 1998 for Cohort II. A food frequency questionnaire (FFQ) was collected from 103 769 subjects (45 019 for Cohort I, 58 750 for Cohort II). The response rates ranged from 77% to 90% in all areas except for the metropolitan areas Katsushika (40%), Suita 1 (43%), and Suita 2 (60%), and Ishikawa (63%). This FFQ with 138 food items had been developed to estimate dietary intake,[11] and validated for estimations of various nutrients and food groups.[12–14] It also included questions about dietary supplement use as well as demographics, lifestyles, and health characteristics such as occupation, height, weight, smoking, alcohol consumption, physical activity, dietary behaviours, working hours, and stress.

In the FFQ, general use of any vitamin supplements more than once a week, and use of specific supplements by five categories (Multivitamin, Beta-carotene, Vitamin C, Vitamin E, Others) were probed. For each category, the brand names, frequency, and duration of use were asked. Users of dietary supplements were defined as subjects who used at least one category of dietary supplement ⩾1 week for ⩾1 year. If a subject was a user of at least one category of supplement, he or she was regarded as an overall supplement user. To preclude the incorrect categorization of self-reported dietary supplements, all supplements in the FFQ were re-categorized by the authors using brand names according to the definition of dietary supplements in the Women's Healthy Eating and Living Study.[15] This method of defining the supplement users was validated in our previous study.[16] Recategorizing self-reported categories was shown to improve sensitivity in identifying dietary supplement users. The results from our validation study also indicated that our questionnaire could even identify non-vitamin supplement users to a certain extent (sensitivity of 75%), although we only enquired about vitamin supplement use.

Self-reported occupations were combined into the following six groups: farming, forestry, and fishing; employee and professional; housewife; self-employed; unemployed; and other occupations. The subjects with ⩾2 occupations across those groups were classified as a combination group. Body mass index for each subject was computed based on self-reported height and weight by dividing weight (kg) by the square of height (m). The questionnaire covered smoking status, frequency of alcohol consumption, physical activity, 14 questions on dietary behaviours (frequency of eating miso soup, breakfast, eating out, consumption of prepared foods, fried foods, deep-fried foods, fat on meat, soup from noodle bowls, adding salt or soy sauce to foods at the table, types of vegetable oils used, frequently used cooking methods, well-doneness of cooked meat, eating charred parts of fish), working hours, and self-reported stress.

Individual intakes of energy and 33 nutrients were calculated from 138 food items in the FFQ. The algorithm of the calculation was reported elsewhere.[17] Intake from dietary supplements was not included in that calculation.

Statistical analysis

SAS version 8.02 (SAS Institute Inc., Cary, NC) was used to conduct all the statistical analyses. We excluded subjects who were confirmed to be ineligible during the follow-up because they were not Japanese nationals, had already moved away at the baseline, or were not in the intended age group for this study. Subjects were also excluded for the following reasons: BMI of <10 or >100; failure to supply data in the questionnaire for any of the variables used such as occupation, height, weight, smoking, alcohol consumption, physical activity, dietary behaviours, working hours, and stress; men with a total energy intake of <900 kcal or ⩾4000 kcal; women with a total energy intake of <800 kcal, or ⩾3600 kcal. Of 103 769 subjects who completed the questionnaire, a total of 78 531 subjects (37 298 men and 41 233 women) were finally included in the analysis. The proportion of demographic, lifestyle, health characteristics, and supplement use among those who were excluded was similar to those included in the analysis.

We calculated the prevalence of dietary supplement users for each of the demographic factors, lifestyles, and health