RESEARCH COMMUNICATION

Comparison of Lifestyle Risk Factors by Family History for Gastric, Breast, Lung and Colorectal Cancer

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Abstract

To assess the theoretical impact of lifestyle of a cancer family history in first-degree relatives (CFH) and clarify interactions between CFH and lifestyle factors, hospital-based comparison and case-reference studies were conducted in Nagoya, Japan. Totals of 1988 gastric, 2455 breast, 1398 lung and 1352 colorectal cancer patients, as well as 50,706 non-cancer outpatients collected from 1988 to 1998, were checked for lifestyle factors, which included dietary and physical exercise habits, as well as smoking/drinking status. General lifestyle factors with non-cancer outpatients did not differ by the CFH status. Case-reference analyses showed that frequent intake of fruits, raw vegetables, carrots, pumpkin, cabbage and lettuce, as well as frequent physical exercise, were associated with decreased risk for all four sites of cancer, while habitual smoking increasing the risk of gastric, and more particularly, lung cancer. Interestingly, the study revealed the magnitude of odds ratios for the above lifestyle factors obtained from CFH positives to be similar to those from CFH negatives for these four sites of cancer. There were no significant interactions between CFH and any particular lifestyle factor. In conclusion, our results suggest no appreciable influence of CFH on lifestyle related risk factors for gastric, breast, lung, and colorectal cancer. Habitual smoking increased, while frequent physical exercise and raw vegetables intake decreased cancer risk, regardless of the CFH status.

Key Words: Cancer risk factors - cancer family history - interactions - gastric - breast - colorectal - lung

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Introduction

Cancer family history in first-degree relatives (CFH) is considered to be a risk factor for neoplastic development in several organ sites. Our previous study demonstrated an odds ratio (OR) of 1.81 for Japanese with a gastric CFH (GCFH) (Huang et al., 1999). Compared to individuals without breast CFH (BCFH), those with a BCFH have been reported to have a two fold higher risk of the disease (Pharoah et al., 1997); a lung CFH (LCFH) is associated with two to fourfold excess risk for lung cancer (Lynch et al.,1986; Ooi et al., 1986; Sellers et al., 1988; Liu et al., 1991; McDuffie et al., 1991; Bromen et al., 2000; Chan-Yeung et al., 2003; Osann et al., 1991), and a colorectal CFH (CCFH) with an approximately twofold elevated risk of colorectal cancer (Bonelli et al., 1988; Fuchs et al., 1994; Kune et al., 1989; La Vecchia et al., 1992; Ponz de Leon et al., 1989; St John et al., 1993; Slattery et al., 1994). At the same time, lifestyle factors are also widely accepted to correlate with risk of cancers, especially with lung and gastric cancers, and probably with breast, ovary and colorectal cancers (Tajima et al., 2000). It is not clear whether lifestyle differs with CFH, although after a first-degree relative suffers from cancer, it is conceivable that family members might take warning and change their habits. This could be reflected by differences in risk factor exposure and odds ratios (ORs) between persons with and without CFH. Our previous research (Huang et al., 2000), however, revealed that lifestyle did not differ with GCFH, and that lifestyle is a major factor for gastric cancer, regardless of family history. Whether this can be extrapolated to other sites of cancer remains unclear and our working hypothesis is that a CFH may indeed exert an impact on lifestyle factors.

Any risk implied with a CFH is a combination of genetic

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and/or environmental factors shared by family members, so that the interplay needs to be further investigated. To deal with these issues, we here made a comparison of lifestyle factors among non-cancer outpatients by their CFH status, and conducted case-reference studies in CFH negative and positive CFH subjects separately to examine the influence, using a large-scale database from the Hospital-based Epidemiological Research Program at Aichi Cancer Center (HERPACC).

Materials and Methods

Data Collection

The data set of the HERPACC study has been collected from self-administered questionnaires, completed by all first-visit outpatients to Aichi Cancer Center Hospital (ACCH) in Aichi Prefecture, Japan, since 1988. General descriptions of the questionnaire and data collection procedure have been documented elsewhere (Tajima et al., 2000; Huang et al., 2000; Tajima et al., 1985; Hamajima et al., 1994; Inoue et al., 1997). Briefly, a trained interviewer invites all outpatients who are waiting to be examined to complete a questionnaire, which includes items on demography, medical history, family history of disease in parents and siblings, smoking and drinking habits, dietary habits, physical exercise, bowel habits, and reproductive history before symptoms appeared. The following items are addressed in the questionnaire: information on intake of miso soup, bean curd, pickled vegetables, green tea, coffee, fruit and raw fresh vegetables, milk, eggs, fish (dried, salted) and meat (chicken, beef, pork). Habitual smoking and drinking are divided into three categories as current, former and never. At the time of questionnaire collection, all written responses are checked to find if there are any unanswered questions and the information collected is input into a computer system at the Aichi Cancer Center Research Institute. Medical data obtained from ACCH are entered in tandem to allow linkage with questionnaire data and identify cancer cases among the interviewees. An identification index, including name, sex, residence, date of birth, date of visit to the ACCH, and the identification number in the ACCH record, is used for the linkage. In the linkage process, lists of cancer patients diagnosed in a given year, as well as cases confirmed in the years after the diagnosis, are employed to avoid misclassification. Individuals visiting two or more times in one year are also checked to prevent double counting.

Cases and Referents

Of a total of 80420 first-visit outpatients, who visited ACCH between January 1988 to June 1998, 8057 outpatients were excluded due to interviewer absence, inadmissible age (younger than 18 years old), or a visit for consultation. The questionnaire was finally administered to 72,363 subjects. Among them, 71,277 (98.5%) completed the questionnaire adequately. After linkage between questionnaire data and medical data, we excluded 9032 subjects (12.7%) since the cancer history of at least one of their parents or siblings was unknown. Among the remaining 62,245 subjects, 1,988 cases were confirmed to have gastric, 2455 breast, 1398 lung, 1352 colorectal, 368 esophageal, 366 liver, 88 prostate and 3524 other sites of cancers. To obtain sufficient statistical power, we focused on gastric, breast, lung and colorectal cancers in this study, and recruited the relevant patients as our case group. The 50,706 first-visit non-cancer subjects were regarded as our referent group.

Regarding definitions, GCFH (+) denotes positive GCFH, and GCGH (-) means negative GCGH; likewise for BCFH (+)/BCFH (-), CCFH (+)/CCFH (-) and LCFH (+)/LCFH (-). CFH was defined as positive if study subjects had at least one parent or sibling who had suffered from cancer. Current smokers were those who smoked at least one or more cigarettes per day. Consumption of raw vegetables, fruit, pickled vegetables and other dietary items was divided into two categories according to the intake frequency.

Analytic Methods

For data analysis, statistical significance was assessed by the chi-square test when the proportional frequencies of lifestyle were compared between CFH negative and positive non-cancer outpatients. Proportional frequencies (percent) of each variable were calculated, using the total surveyed non-cancer outpatients as a standard, and compared between CFH negative and positive in each sex and cancer group. Eligible referents used (for the case-reference study) were not matched, because our previous study of HERPACC data showed that a large control produces a steadier estimate than matched analysis (Hamajima et al., 1994). In order to control for confounding effects, multivariate analyses on the risk of the CFH were performed using models including main health-related factors shown to have statistical significance by univariate analyses. Software from the SAS package (SAS Institute Inc., 1990), FREQ and LOGISTIC procedures, was used for these calculations. All tests of statistical significance were two sided. Differences were considered to be significant if $p<0.05$.

Results

Referents and cases were divided into CFH negatives and positives and categorized into six age groups: <40,40-49,50-59,60-69,70-79 and >79 years. Distributions are presented in Table 1.

1) Comparison of lifestyle and risk factors among non-cancer outpatients by CFH status (Table 2).

1-1) Males: frequency of intake of most dietary items did not differ with the CFH status for any specific cancer site. Current smoking rates were 43.9% for GCFH (+) versus 45.2% for GCFH (-), 43.4% for BCFH (+) versus 45.0% for BCFH (-), 44.4% for CCFH (+) versus 45.0% for CCFH (-); and 47.4% for LCFH (+) versus 44.9% for LCFH (-) subjects. Current drinking rates ranged from 64.7% to 67.0% and also did not show significant differences among groups, regardless of the CFH status, for any of the four selected

Table 1. Sex and Age Distributions of Study Subjects by Cancer Family History Status (Aichi Cancer Center: 1988-1998)

	Gastric cancer family history		Breast cancerfamily history		Lung cancer family history		Colorectal cancer family history	
Age (years)	Without	With	Without	With	Without	With	Without	With
Referents:	All referents		All referents		All referents		All referents	
Male								
<40	2889 (23.25)	189 (9.04)	3002 (21.24)	76 (19.74)	2995 (21.74)	83 (11.20)	2948 (21.52)	130 (15.97)
40-49	3015 (24.27)	442 (21.14)	3354 (23.74)	103 (26.75)	3255 (23.63)	202 (27.26)	3269 (23.86)	188 (23.10)
50-59	3113 (25.05)	673 (32.19)	3687 (26.09)	99 (25.71)	3556 (25.81)	230 (31.04)	3545 (25.87)	241 (29.61)
60-69	2472 (19.90)	569 (27.21)	2961 (20.95)	80 (20.78)	2875 (20.87)	166 (22.40)	2864 (20.9)	177 (21.74)
70-79	885 (7.12)	204 (9.76)	1065 (7.54)	24 (6.23)	1033 (7.50)	56 (7.56)	1016 (7.41)	73 (8.97)
>79	51 (0.41)	14 (0.67)	62 (0.44)	3 (0.78)	61 (0.44)	4 (0.54)	60 (0.44)	5 (0.61)
Total	12425 (100)	2091 (100)	14131 (100)	385 (100)	13775 (100)	741 (100)	13702 (100)	814 (100)
Female								
<40	10090 (31.56)	540 (12.80)	10257 (29.43)	373 (27.82)	10439 (30.11)	191 (12.55)	10349 (29.96)	281 (17.11)
40-49	10538 (32.96)	1386 (32.85)	11477 (32.93)	447 (33.33)	11393 (32.86)	531 (34.89)	11373 (32.92)	551 (33.56)
50-59	6743 (21.09)	1214 (28.77)	7622 (21.87)	335 (24.98)	7490 (21.60)	467 (30.68)	7497 (21.70)	460 (28.01)
60-69	3466 (10.84)	814 (19.29)	4140 (11.88)	140 (10.44)	402 (11.60)	259 (17.02)	4013 (11.62)	267 (16.26)
70-79	1086 (3.40)	251 (5.95)	1292 (3.71)	45 (3.36)	1266 (3.65)	71 (4.66)	1256 (3.64)	81 (4.93)
>79	48 (0.15)	14 (0.33)	61 (0.18)	1 (0.07)	59 (0.17)	3 (0.20)	60 (0.17)	2 (0.12)
Total	31971 (100)	4219 (100)	34849 (100)	1341 (100)	34668 (100)	1522 (100)	34548 (100)	1642 (100)
	Gastric cancer family history		Breast cancer family history		Lung cancer family history		Colorectal cancer family history	
Age (years)	Without	With	Without	With	Without	With	Without	With
Cases	Gastric cancer cases		Breast cancer cases		Lung cancer cases		Colorectal cancer cases	
Male								
<40	43 (4.22)	6 (1.87)	NA	NA	22 (2.32)	2(2.67)	21 (2.84)	4 (5.06)
40-49	141 (13.84)	33 (10.28)	NA	NA	92 (9.68)	7(9.33)	88 (11.89)	7 (8.86)
50-59	276 (27.09)	86 (26.79)	NA	NA	244 (25.68)	24(32.00)	229 (30.95)	25 (31.65)
60-69	387 (37.98)	125 (38.94)	NA	NA	356 (37.47)	26(34.67)	282 (38.11)	27 (34.18)
70-79	159 (15.6)	69 (21.50)	NA	NA	226 (23.79)	15(20.00)	114 (15.41)	12 (15.19)
>79	13 (1.28)	2 (0.62)	NA	NA	10 (1.05)	1(1.33)	6 (0.81)	4 (5.06)
Total	1019 (100)	321 (100)	NA	NA	950 (100)	75(100)	740 (100)	79 (100)
Female								
<40	39(7.72)	7(4.90)	315(13.64)	17(11.64)	11(3.18)	0(0.00)	35(7.17)	1(2.22)
40-49	111(21.98)	18(12.59)	896(38.80)	63(43.15)	61(17.63)	6(22.22)	88(18.03)	8(17.78)
50-59	131(25.94)	36(25.17)	577(24.99)	34(23.29)	100(28.9)	6(22.22)	144(29.51)	19(42.22)
60-69	143(28.32)	54(37.76)	391(16.93)	26(17.81)	112(32.37)	11(40.74)	161(32.99)	14(31.11)
70-79	75(14.85)	26(18.18)	120(5.20)	6(4.11)	59(17.05)	4(14.81)	57(11.68)	2(4.44)
>79	6(1.19)	2(1.40)	10(0.43)	0(0.00)	3(0.87)	0(0.00)	3(0.61)	1(2.22)
Total	505(100)	143(100)	2309(100)	146(100)	346(100)	27(100)	488(100)	45(100)

NA: not applicable.

cancer sites.

1-2) Females: as shown in Table 2, frequency of intake of most dietary items did not differ with the status of family history for any of the four sites. Current smoking rate was 13.2% for GCFH (+) versus 13.0% for GCFH (-), 12.6% for BCFH (+) versus 13.1% for BCFH (-), 12.1% for CCFH (+) versus 13.1% for CCFH (-); and 13.6% for LCFH (+) versus 13.0% for LCGH (-) subjects. Current drinking rates ranged from 27.9% to 30.5% and did not show significant differences among the groups, regardless of the CFH for a specific cancer site. Lifestyle factors, especially smoking and drinking habits, were remarkably different between the genders.

2) Case-reference study on the association between lifestyle items and the selected four cancers with GCFH, BCFH, LCFH and CCFH (from Table 3 to Table 6).

In both GCFH (-) and (+) subjects, frequent consumption of fruits, raw vegetables, milk, toufu, carrots, pumpkin, cabbage, lettuce and frozen foods as well as frequent physical exercise decreased, while preference of oily foods, frequent intake of salted fishes, habitual smoking and drinking increased the odds ratio (OR) for gastric cancer (Table 3). Judged by the 95% confidence intervals (95%CI), the magnitude of ORs for each lifestyle factors did not significantly differ between GCFH (-) and (+) subjects.

Both BCFH (-) and BCFH (+) case-reference studies revealed that milk, carrot, pumpkin and physical exercise reduced, whereas preference for coffee increased ORs for breast cancer (Table 4). Appreciable differences in ORs for most lifestyle factors between BCFH (-) and BCFH (+) subjects were not found.

Tables 5 and 6 summarize the data for association of lifestyle factors with risks of lung and colorectal cancers, estimated separately for LCFH (-)/(+) and CCFH (-)/(+) groups. Fruits, raw vegetables, carrots, pumpkin and physical exercise decreased lung and colorectal cancer in all groups. Smoking was a prominent risk factor for lung cancer in both

Table 2. Age Standarized Proportions of Selected Lifestyle and Risk Factors among Non-Cancer Outpatients by Cancer Family History Status (AICHI CANCER CNETER: 1988-1998)

	Gastric cancer family history				Breast cancer family history BCFH				Lung cancer family history				Colorectal cancer family history			
	Male		Female		Male		Female		Male		Female		Male		Female	
Variables	Without	With	Without	With	Without	With	Without	With	Without	With	Without	With	Without	With	Without	With
Pickled vegetables (>=3 times/week)	13.23	12.97	10.96	11.74	13.25	11.14	11.10	10.29	13.38*	10.32	11.07	10.79	13.29	11.82	11.11	9.88
Fruits (>=3 times/week)	56.25	56.64	72.86	72.92	56.38	57.31	72.81	72.69	56.31	57.75	72.81	73.89	56.39	56.14	72.84	72.52
Raw vegetables(>=3 times/week)	69.77*	66.75	73.07	72.91	69.43	71.58	72.96	72.93	69.52	68.45	72.90	74.61	69.58	67.72	72.98	73.02
Green tea (every day)	77.64*	80.78	78.94	78.01	77.97	76.64	78.70	81.00	77.95	77.40	78.84	79.50	77.81	80.52	78.75	79.94
Preference for coffee (yes)	76.99	77.27	71.21	72.73	77.10	77.66	71.20	73.06	76.96*	80.56	71.17*	73.65	76.94	79.86	71.27*	71.48
Miso soup (>=1/day)	63.84	61.57	57.43	59.32	63.57	64.61	57.68	55.07	63.58	63.69	48.41	48.35	63.71	61.75	57.50	59.96
Milk (>=1/day)	38.41	40.58	47.92	49.32	38.72	38.15	47.99	51.24	38.79	37.21	48.07	48.93	38.46*	42.94	48.10	48.14
Eastern type breakfast (yes)	63.85	62.56	53.77	54.17	63.67	61.67	53.88*	51.06	63.56	65.34	53.91	50.94	63.76	61.29	53.87	51.95
Preference for oily foods (yes)	61.48	59.52	48.45	48.31	61.19	62.46	48.41	47.88	61.36	59.53	48.41	48.35	61.12	62.32	48.45	47.39
Bean curd (>=3 times/week)	37.17	35.88	45.41	45.47	36.93	36.82	45.38	45.36	37.00	35.22	45.34	47.79	36.97	36.34	45.33	46.52
Carrots (>=3 times/week)	25.84	25.33	50.62	52.11	25.74	25.32	50.67	51.99	25.90	22.71	50.68	53.03	25.73	25.93	50.74	50.29
Pumpkin (>=3 times/week)	7.07	7.78	13.57	13.60	7.09	9.50	13.55	13.24	7.16	6.80	13.51	14.10	7.27	5.46	13.59	12.56
Cabbage (>=3 times/week)	36.13	35.04	42.58	42.53	35.97	36.01	42.70	40.75	36.11	33.59	42.61	44.13	36.06	34.241	42.72*	40.02
Lettuce (>=3 times/week)	26.12*	23.12	35.92	36.55	25.69	28.19	36.01	34.72	25.82	24.78	35.91	37.76	25.78	25.29	36.07*	33.61
Potatoes (>=3 times/week)	18.71	18.83	37.07	37.27	18.56	21.69	37.17	35.40	18.65	18.44	37.19	35.28	18.72	17.51	35.69	36.64
Egg (>=3 times/week)	61.37	61.75	67.92	67.94	61.32	64.02	67.91	68.18	61.41	62.70	67.84	69.71	61.37	62.27	67.84	69.05
Chicken (>=3 times/week)	15.37	15.03	20.72	19.79	15.39	14.81	20.82	17.48	15.44	13.66	20.73	20.44	15.48	13.38	20.70	19.86
Beef (>=3 times/week)	10.42	10.67	10.51	10.45	10.40	12.44	10.60	8.52	10.46	9.64	10.52	10.87	10.47	9.86	10.52	10.26
Pork (>=3 times/week)	10.90	11.09	16.67	17.62	10.95	10.78	16.76	16.44	10.91	11.41	16.72	17.48	11.01	9.56	16.80	15.65
Sausage (>=3 times/week)	12.58*	10.20	14.30	14.11	12.37	16.77	14.30	13.86	12.43	13.69	14.35	12.61	12.50	12.01	14.30	14.06
Instant foods (>=3 times/week)	3.53	3.35	1.47	1.38	3.48	3.96	1.46	1.59	3.55*	1.92	1.47	1.23	3.55	2.31	1.47	1.13
Frozen foods(>=3 times/week)	5.08	5.10	4.62*	3.77	5.13	3.50	4.55	4.01	5.10	4.41	4.57*	3.55	5.11	4.55	4.54	4.24
Salted fishes(>=3 times/week)	9.58	9.03	8.40	9.35	9.53	7.52	8.52	6.99	9.43	10.25	8.48	7.93	9.52	9.01	8.47	8.42
Cooked fishes(>=3 times/week)	28.66*	31.47	28.90	28.75	29.07	30.24	28.84	30.10	29.08	29.35	28.85	29.60	29.16	28.39	28.80	30.74
Physical exercise(>=3 times/month)	27.64	28.18	22.08	22.67	27.66*	32.84	22.13	23.42	27.75	28.33	22.16	22.01	27.72	28.69	22.16	22.40
Smoking habit																
Current smoker	45.18	43.88	13.02	13.19	45.03	43.35	13.08	12.64	44.89	47.44	13.02	13.59	45.04	44.40	13.11	12.12
Ceased smoking	30.96	33.63	4.42	4.64	31.22	35.26	4.38	5.70	31.24	32.37	4.43	4.28	31.22	32.85	4.42	4.68
Never smoker	23.86	22.49	82.55	82.17	23.76	21.38	82.54	81.66	23.87*	20.18	82.55	82.14	23.75	22.75	82.47	83.20
Drinking habit																
Current drinker	64.81	66.02	28.96	27.87	64.85	64.12	28.81	30.50	64.80	66.39	28.85	29.35	64.72	66.98	28.87	28.89
Ceased	6.00	6.14	1.66	1.29	6.03	5.64	1.61	1.75	6.00	6.17	1.59	1.78	6.08	4.97	1.62	1.55
Never	29.20	27.83	69.37	70.84	29.12	30.24	69.58	67.75	29.20	27.44	69.56	68.87	29.20	28.05	69.51	69.56

*P value <0.05 (obtained from comparison in the same gender group by the specific cancer family history status).

Table 3. Age and Sex- adjusted Odds Ratios for Gastric Cancer According to Lifestyle and Risk Factors (Aichi Cancer Center: 1988-1998)

Variables	GCFH (-) Odds ratio (95% CI)	GCFH (+) Odds ratio (95% CI)
Pickled vegetables (>=3 times/week vs. <3 times/week)	1.10 (0.95-1.27)	1.28 (0.99-1.65)
Fruits (>=3 times/week vs. <3 times/week)	0.81 (0.72-0.91)**	0.78 (0.63-0.96)*
Raw vegetables (>=3 times/week vs. <3 times/week)	0.81 (0.72-0.91)**	0.67 (0.55-0.82)**
Green tea (every day vs. not every day)	1.04 (0.81-1.35)	1.07 (0.64-1.80)
Preference for coffee (yes vs. no)	1.04 (0.90-1.20)	1.04 (0.79-1.37)
Miso soup (>=1/day vs. <1/day)	0.98 (0.88-1.09)	1.14 (0.92-1.40)
Milk (>=1/day vs. <1/day)	0.98 (0.88-1.09)	0.86 (0.70-1.05)
Eastern type breakfast (yes vs. no)	0.98 (0.87-1.11)	1.07 (0.86-1.34)
Preference for oily foods (yes vs. no)	1.16 (1.04-1.29)**	1.16 (0.95-1.41)
Bean curd (>=3 times/week vs. <3 times/week)	0.81 (0.70-0.95)**	0.90 (0.67-1.21)
Carrots (>=3 times/week vs. <3 times/week)	0.81 (0.70-0.94)**	0.71 (0.54-0.92)*
Pumpkin (>=3 times/week vs. <3 times/week)	0.71 (0.59-0.86)**	0.83 (0.60-1.14)
Cabbage (>=3 times/week vs. <3 times/week)	0.85 (0.74-0.99)*	0.73 (0.56-0.95)*
Lettuce (>=3 times/week vs. <3 times/week)	0.82 (0.72-0.94)**	0.87 (0.67-1.10)
Potatoes (>=3 times/week vs. <3 times/week)	0.86 (0.74-0.99)*	1.08 (0.82-1.43)
Egg (>=3 times/week vs. <3 times/week)	1.23 (1.03-1.48)*	1.29 (0.91-1.82)
Chicken (>=3 times/week vs. <3 times/week)	0.93 (0.80-1.09)	1.02 (0.77-1.35)
Beef (>=3 times/week vs. <3 times/week)	1.00 (0.82-1.21)	1.09 (0.77-1.53)
Pork (>=3 times/week vs. <3 times/week)	1.08 (0.90-1.29)	0.93 (0.65-1.32)
Sausage (>=3 times/week vs. <3 times/week)	1.03 (0.86-1.22)	0.87 (0.61-1.26)
Instant foods (>=3 times/week vs. <3 times/week)	1.36 (0.98-1.88)	1.73 (0.93-3.22)
Frozen foods (>=3 times/week vs. <3 times/week)	0.93 (0.68-1.28)	0.44 (0.18-1.10)
Salted fishes (>=3 times/week vs. <3 times/week)	1.03 (0.87-1.23)	1.16 (0.85-1.58)
Cooked fishes (>=3 times/week vs. <3 times/week)	1.08 (0.93-1.26)	0.85 (0.64-1.13)
Physical exercise (>=3 times/month vs. <3 times/month)	0.79 (0.70-0.89)**	0.71 (0.57-0.89)**
Alcohol (current vs. never smoker)	1.18 (1.02-1.37)*	1.14 (0.86-1.50)**
Smoking (current vs. never drinker)	2.47 (2.01-3.03)**	2.54 (1.72-3.76)**

GCFH(+),(-): with, without a gastric cancer family history.
*P value <0.05; **P value <0.01

Table 4. Age and Sex- adjusted Odds Ratios for Breast Cancer according to Lifestyle and Risk Factors (Aichi Cancer Center: 1988-1998)

Variables	BCFH (-) Odds ratio (95% CI)	BCFH (+) Odds ratio (95% CI)
Pickled vegetables (>=3 times/week vs. <3 times/week)	0.86 (0.71-0.94)**	0.79 (0.44-1.44)
Fruits (>=3 times/week vs. <3 times/week)	0.89 (0.80-0.98)**	1.01 (0.67-1.53)
Raw vegetables (>=3 times/week vs. <3 times/week)	0.94 (0.86-1.03)	0.97 (0.66-1.43)
Green tea (every day vs. not every day)	1.06 (0.87-1.29)	1.03 (0.48-2.20)
Preference for coffee (yes vs. no)	1.33 (1.18-1.50)**	1.25 (0.78-2.01)
Miso soup (>=1/day vs. <1/day)	1.07 (0.98-1.17)	1.26 (0.88-1.79)
Milk (>=1/day vs. <1/day)	0.83 (0.76-0.91)**	0.73 (0.52-1.04)
Eastern type breakfast (yes vs. no)	0.96 (0.87-1.06)	0.98 (0.65-1.46)
Preference for oily foods (yes vs. no)	1.02 (0.94-1.11)	0.86 (0.61-1.23)
Bean curd (>=3 times/week vs. <3 times/week)	0.93 (0.81-1.06)	0.76 (0.46-1.26)
Carrots (>=3 times/week vs. <3 times/week)	0.79 (0.70-0.90)**	0.56 (0.35-0.91)*
Pumpkin (>=3 times/week vs. <3 times/week)	0.78 (0.69-0.90)**	0.80 (0.48-1.35)
Cabbage (>=3 times/week vs. <3 times/week)	1.08 (0.95-1.22)	0.96 (0.57-1.59)
Lettuce (>=3 times/week vs. <3 times/week)	0.98 (0.88-1.09)	0.98 (0.62-1.53)
Potatoes (>=3 times/week vs. <3 times/week)	0.90 (0.79-1.01)	0.72 (0.46-1.14)
Egg (>=3 times/week vs. <3 times/week)	1.02 (0.87-1.19)	1.88 (0.85-4.20)
Chicken (>=3 times/week vs. <3 times/week)	0.86 (0.76-0.98)*	1.19 (0.73-1.93)
Beef (>=3 times/week vs. <3 times/week)	0.96 (0.82-1.11)	1.21 (0.64-2.30)
Pork (>=3 times/week vs. <3 times/week)	0.93 (0.81-1.07)	0.76 (0.43-1.37)
Sausage (>=3 times/week vs. <3 times/week)	1.04 (0.90-1.19)	0.74 (0.41-1.36)
Instant foods (>=3 times/week vs. <3 times/week)	1.17 (0.82-1.67)	0.49 (0.07-3.71)
Frozen foods (>=3 times/week vs. <3 times/week)	1.20 (0.97-1.49)	0.95 (0.37-2.43)
Salted fishes (>=3 times/week vs. <3 times/week)	0.95 (0.81-1.11)	0.70 (0.32-1.50)
Cooked fishes (>=3 times/week vs. <3 times/week)	0.91 (0.80-1.03)	1.25 (0.74-2.09)
Physical exercise (>=3 times/month vs. <3 times/month)	0.78 (0.70-0.87)**	0.61 (0.39-0.96)**
Alcohol (current vs. never smoker)	1.08 (0.98-1.19)	0.89 (0.60-1.32)
Smoking (current vs. never drinker)	1.07 (0.94-1.22)	1.23 (0.73-2.07)

BCFH(+),(-): with, without a breast cancer family history.
*P value <0.05; **P value <0.01.

Table 5. Age and Sex- adjusted Odds Ratios for Lung Cancer According to Lifestyle and Risk Factors (Aichi Cancer Center: 1988-1998)

Variables	LCFH (-) Odds ratio (95% CI)	LCFH (+) Odds ratio (95% CI)
Pickled vegetables (>=3 times/week vs. <3 times/week)	1.07 (0.91-1.25)	1.16 (0.62-2.19)
Fruits (>=3 times/week vs. <3 times/week)	0.64 (0.57-0.73)**	0.63 (0.41-0.97)*
Raw vegetables (>=3 times/week vs. <3 times/week)	0.70 (0.62-0.79)**	0.89 (0.57-1.37)
Green tea (every day vs. not every day)	1.10 (0.83-1.47)	1.67 (0.51-5.53)
Preference for coffee (yes vs. no)	1.61 (1.37-1.90)**	1.26 (0.68-2.31)
Miso soup (>=1/day vs. <1/day)	1.15 (1.02-1.30)*	1.28 (0.82-2.00)
Milk (>=1/day vs. <1/day)	0.82 (0.73-0.93)**	0.66 (0.43-1.02)
Eastern type breakfast (yes vs. no)	1.05 (0.92-1.20)	1.24 (0.65-2.38)
Preference for oily foods (yes vs. no)	0.92 (0.82-1.04)	1.11 (0.73-1.69)
Bean curd (>=3 times/week vs. <3 times/week)	1.03 (0.86-1.23)	1.24 (0.65-2.38)
Carrots (>=3 times/week vs. <3 times/week)	0.85 (0.73-0.99)*	0.84 (0.49-1.44)
Pumpkin (>=3 times/week vs. <3 times/week)	0.96 (0.80-1.16)	0.59 (0.27-1.31)
Cabbage (>=3 times/week vs. <3 times/week)	0.85 (0.73-0.99)*	0.83 (0.48-1.45)
Lettuce (>=3 times/week vs. <3 times/week)	0.80 (0.69-0.93)**	1.19 (0.69-2.06)
Potatoes (>=3 times/week vs. <3 times/week)	1.00 (0.85-1.17)	1.11 (0.62-1.99)
Egg (>=3 times/week vs. <3 times/week)	1.09 (0.90-1.32)	1.28 (0.59-2.76)
Chicken (>=3 times/week vs. <3 times/week)	0.76 (0.64-0.91)**	1.16 (0.64-2.11)
Beef (>=3 times/week vs. <3 times/week)	1.00 (0.81-1.24)	1.31 (0.65-2.65)
Pork (>=3 times/week vs. <3 times/week)	1.07 (0.87-1.31)	1.17 (0.62-2.22)
Sausage (>=3 times/week vs. <3 times/week)	0.93 (0.76-1.13)	1.07 (0.54-2.13)
Instant foods (>=3 times/week vs. <3 times/week)	1.13 (0.77-1.65)	0.55 (0.07-4.24)
Frozen foods (>=3 times/week vs. <3 times/week)	0.94 (0.66-1.34)	- (-)[1]
Salted fishes (>=3 times/week vs. <3 times/week)	0.99 (0.82-1.20)	1.41 (0.74-2.67)
Cooked fishes (>=3 times/week vs. <3 times/week)	0.80 (0.68-0.94)**	1.07 (0.56-2.05)
Physical exercise (>=3 times/month vs. <3 times/month)	0.58 (0.51-0.67)**	0.60 (0.36-0.98)*
Alcohol (current vs. never smoker)	0.90 (0.78-1.05)	0.91 (0.53-1.57)
Smoking (current vs. never drinker)	5.92 (4.40-7.96)**	6.03 (1.81-20.1)**

LCFH(+),(-): with, without a lung cancer family history.
*P value <0.05; **P value <0.01.
[1]No cases reported intake of frozen foods for >=3 times/week.

Table 6. Age and Sex- adjusted Odds Ratios for Colorectal Cancer according to Lifestyle and Risk Factors (Aichi Cancer Center: 1988-1998)

Variables	CCFH (-) Odds ratio (95% CI)	CCFH (+) Odds ratio (95% CI)
Pickled vegetables (>=3 times/week vs. <3 times/week)	1.16 (0.99-1.36)	0.88 (0.47-1.62)
Fruits (>=3 times/week vs. <3 times/week)	0.91 (0.80-1.03)	0.88 (0.59-1.33)
Raw vegetables (>=3 times/week vs. <3 times/week)	0.85 (0.75-0.96)*	1.00 (0.67-1.50)
Green tea (every day vs. not every day)	1.00 (0.76-1.31)	0.92 (0.39-2.21)
Preference for coffee (yes vs. no)	0.92 (0.79-1.08)	0.92 (0.58-1.47)
Miso soup (>=1/day vs. <1/day)	0.89 (0.79-1.00)	1.06 (0.72-1.56)
Milk (>=1/day vs. <1/day)	0.88 (0.78-0.99)*	0.73 (0.50-1.06)
Eastern type breakfast (yes vs. no)	0.98 (0.85-1.11)	1.28 (0.83-1.97)
Preference for oily foods (yes vs. no)	1.11 (0.99-1.25)	0.83 (0.57-1.21)
Bean curd (>=3 times/week vs. <3 times/week)	1.11 (0.92-1.33)	1.17 (0.65-2.11)
Carrots (>=3 times/week vs. <3 times/week)	0.92 (0.79-1.08)	1.27 (0.75-2.16)
Pumpkin (>=3 times/week vs. <3 times/week)	0.92 (0.77-1.12)	1.52 (0.87-2.64)
Cabbage (>=3 times/week vs. <3 times/week)	1.05 (0.89-1.24)	1.13 (0.68-1.87)
Lettuce (>=3 times/week vs. <3 times/week)	0.94 (0.81-1.08)	0.94 (0.58-1.53)
Potatoes (>=3 times/week vs. <3 times/week)	0.94 (0.80-1.10)	1.38 (0.82-2.31)
Egg (>=3 times/week vs. <3 times/week)	1.03 (0.85-1.25)	1.13 (0.61-2.09)
Chicken (>=3 times/week vs. <3 times/week)	1.01 (0.85-1.19)	0.98 (0.56-1.69)
Beef (>=3 times/week vs. <3 times/week)	0.94 (0.76-1.17)	0.97 (0.51-1.85)
Pork (>=3 times/week vs. <3 times/week)	1.07 (0.88-1.31)	1.15 (0.61-2.15)
Sausage (>=3 times/week vs. <3 times/week)	1.11 (0.92-1.34)	0.86 (0.43-1.72)
Instant foods (>=3 times/week vs. <3 times/week)	0.97 (0.64-1.47)	0.58 (0.08-4.37)
Frozen foods (>=3 times/week vs. <3 times/week)	0.86 (0.60-1.24)	1.30 (0.50-3.37)
Salted fishes (>=3 times/week vs. <3 times/week)	1.01 (0.84-1.22)	1.37 (0.78-2.41)
Cooked fishes (>=3 times/week vs. <3 times/week)	0.93 (0.79-1.09)	1.25 (0.69-2.26)
Physical exercise (>=3 times/month vs. <3 times/month)	0.76 (0.66-0.87)**	0.96 (0.64-1.44)
Alcohol (current vs. never smoker)	1.32 (1.11-1.57)**	0.89 (0.522-1.52)
Smoking (current vs. never drinker)	1.08 (0.88-1.32)	1.80 (0.836-3.87)

CCFH(+),(-): with, without a colorectal cancer family history.
*P value <0.05; **P value <0.01.

LCFH (-) (OR=5.92, 95%CI=4.40-7.96) and (+)(OR=6.03, 95%CI=1.81-20.1) subjects; however, the two ORs did not significantly differ.

3) Association of family history with the risk of gastric, breast, colorectal and lung cancers (Table 7). In all cases, elevation of the OR was limited to the specific site in the family history. GCFH (+) subjects thus had a slightly increased OR only for gastric cancer (OR=1.47, 95%CI=1.27-1.68). For breast cancer the value among BCFH (+), relative to (-), was elevated to 1.71 (95%CI=1.43-2.05). Risk of colorectal cancer was higher only among CCFH (+) subjects (OR=1.59, 95%CI=1.20-1.95) and there was an increased OR for lung cancer only among LCFH (+) participants (OR=1.44, 95%CI=1.10-1.88).

A previously described method (Huang et al., 2000) was used to test for possible interactions between CFH and the most relevant-variables (raw vegetable intake, smoking and physical exercise) and none proved statistically significant.

Discussion

The ACCH, located in central Japan, is a public hospital accessible to local people without any referrals from physicians or clinics (Inoue et al., 1997). The lifestyles of our referents have been compared with those of general population in the same region (Inoue et al., 1997), and no big difference was detected, suggesting that it is feasible to use ACCH non-cancer outpatients as referents in epidemiological studies. Accordingly, we employes our referents as surrogates for the general population living in central Japan. We hypothesized that subjects with CFH would modify their lifestyle, but we found that dietary habits, physical exercise and smoking/drinking habits in this study, did not differ by GCFH, BCFH, CCFH or LCFH. Regardless of the CFH status, frequent intake of raw vegetable, carrots, and lettuce, as well as frequent physical exercise were protective factors for gastric, breast, lung and colorectal cancers, while smoking/drinking, especially smoking, were common risk factors. The magnitude of ORs with specific lifestyle items was quite similar between CFH (-) and CFH (+) for all four cancers. These observations thus refuted our hypothesis. We can speculate two tendencies in CFH (+) groups: an unhealthy lifestyle due to shared family habits, and a healthy lifestyle due to fear of cancer. However, we doubt if subjects with CFH are aware of their elevated risk. Indeed, several studies have indicated that a substantial proportion of women with a BCFH were unaware of their heightened risk (Costanza et al., 1992; Vogel et al., 1990; Kash et al., 1992; Murabito et al., 2001; Audrain et al., 1995). Even after these subjects are made aware of their elevated risk, this may not result in lifestyle modification, similar to the situation with smoking cessation. Although physicians strongly recommend stopping smoking, only 8.6% of ACCH non-disease outpatients adhere to such advice (Hamajima et al., 1999).Therefore, it may indicate that only information on CFH would be of low effectiveness for promoting lifestyle modification.

We here found that a CFH for a cancer site only slightly elevated the risk for that specific site of cancer with statistical significance. The ORs ranged from 1.4 to 1.7, and were not larger than those of lifestyle factors. No interactions were found between lifestyle factors and family history of current four sites of cancer. Thus, our study indicates that CFH could somewhat increase cancer risk, but the impact could be small compared with lifestyle factors. These results are generally compatible with earlier published findings. A statistically significant increased in gastric cancer was, for example, observed for those with a family history of gastric (OR 1.6) and breast cancer (OR 2.0), but not a family history of lung or gastrointestinal tract neoplasia (with gastric cancer being excluded) in a Swedish study (Lagergren et al., 2000). An Italian study (Negri et al., 1997) showed a statistically

Table 7. Odds Ratios (OR) with Cancer Family History for the Four Selected Cancer Sites (Aichi Cancer Center: 1988-1998)

	Reference		Gastric cancer		Breast cancer		Colorectal cancer		Lung cancer	
	Whole reference n(%)	Female reference n(%)	Cases n(%)	OR[1] (95%CI)	Cases n(%)	OR[2] (95%CI)	Cases n(%)	OR[1] (95%CI)	Cases n(%)	OR[1](95%CI)
Gastric cancer family history										
Without	44396(87.6)	31971(88.3)	1524(76.7)	1.00	2128(86.7)	1.00	1125(83.2)	1.00	1180(84.4)	1.00
With	6310(12.4)	4219(11.7)	464(23.3)	1.47(1.3-1.7)**	327(13.3)	1.02(0.9-1.2)	227(16.8)	1.06(0.9-1.3)	218(15.6)	0.85(0.7-1.0)
Breast cancer family history										
Without	48980(96.3)	34849(96.3)	1928(97.0)	1.00	2309(94.1)	1.00	1320(97.6)	1.00	1365(97.6)	1.00
With	1726(3.7)	1341(3.7)	60(3.0)	1.04(0.8-1.5)	146(5.9)	1.71(1.4-2.1)**	32(2.4)	0.81(0.6-1.3)	33(2.4)	0.83(0.5-1.3)
Colorectal cancer family history										
Without	48250(95.2)	34548(95.5)	1893(95.2)	1.00	2337(95.2)	1.00	1228(90.8)	1.00	1341(95.9)	1.00
With	2456(4.8)	1642(4.5)	95(4.8)	0.75(0.6-1.0)	118(4.8)	0.96(0.8-1.2)	124(9.2)	1.59(1.2-2.0)**	57(4.1)	0.67(0.5-1.0)*
Lung cancer family history										
Without	48443(95.5)	34668(95.8)	1887(94.9)	1.00	2346(95.6)	1.00	1286(95.1)	1.00	1296(92.7)	1.00
With	2263(4.5)	1522(4.2)	101(5.1)	0.96(0.7-1.2)	109(4.4)	0.95(0.8-1.2)	66(4.9)	1.00(0.7-1.3)	102(7.3)	1.44(1.1-1.9)**

[1]comparison between case and whole reference and adjusted by age, gender, smoking and drinking habits, body mass index, physical exercise and consumption of raw vegetables. [2]comparison between case and female reference and adjusted by age, gender, smoking and drinking habits, body mass index, physical exercise and consumption of raw vegetables.
*P value <0.05; **P value <0.01.

significant increase in breast cancer associated with a family history of intestinal (OR 1.32) and breast cancer (OR 2.38), without any link with a family history of lung, gastric or other sites of cancers; furthermore, both women and men were at an increased risk of colon cancer if they had a first-degree relative with colon (for women OR = 2.43; 95% CI = 1.94-3.04; for men OR = 2.15; 95% CI = 1.73-2.66) or breast (for women OR = 1.59; 95% CI = 1.25-2.03; for men OR = 1.30; 95% CI = 1.02-1.66) cancers (Slattery et al., 1994). In the US, Brownson et al reported (Brownson et al., 1997) a statistically significant increased risk of lung cancer among those with a family history of lung cancer (OR 1.3), but not among those with a family history of breast, gastric, colon or rectal cancers.

In conclusion, our study indicated that a CFH for any of the four most common sites has no appreciable influence on whether an individual will alter their lifestyle to reduce risk factors for these cancers. There were no significant interactions between CFH and any particular lifestyle factors. Habitual smoking increased, while frequent physical exercise and raw vegetables intake decreased cancer risk, regardless of the CFH status.

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