Journal of Okinawa Prefectural College of Nursing No. 3 March 2002.

Joint intakes of milk, meat and fish and mortality from the six-prefecture cohort study (1966-1981) in Japan

Kinjo Yoshihide, D.H.S.[1] Akiba Suminori, M.D.,Ph.D.[2]

BACKGROUND: From prior analyses on dietary data from the six-prefecture cohort in Japan, we found a possible protective effect of milk, meat and fish for cerebrovascular disease mortality from 1966 to 1981. However, this protective effect had not been examined for cancer and other causes of death.

OBJECTIVES: The purpose of the present analysis is to further elucidate the associations between the joint intakes of dairy milk, meat and fish as main sources of animal protein and fat and the main causes of death in the subjects of the six-prefecture cohort study.

METHODS: The subjects for this analysis were 225,019 men and women aged 40 to 69 at the baseline in December 1965, with neither prior disease history of cancer nor other diseases except for chronic stomach disease. There were 23,108 deaths for men and 16,785 deaths for women during the study period. To evaluate the joint intakes of dairy milk, meat and fish (DMF), data were re-categorized into binary data. For example, DMF (D, M, F) means the combination of dairy milk (1-3 times/week or more), meat (1-3 times/week or more) and fish (4 times/week or more). Thus DMF (d, m, f) was the reference group having dairy milk (less than 1 time/week), meat (less than 1 time/week) and fish (less than 4 times/week). Rate ratio (RR) adjusted for attained age, sex, prefecture, occupation, alcohol drinking, cigarette smoking and DMF was used for comparison.

RESULTS: A weak joint effect on all cancer mortality was observed in DMF (D, M, F) (RR : 1.09, 95%CI: 1.00-1.17), although no statistically significant effect was found in cancer of the colon, rectum, breast, prostate, stomach, lung, oesophagus, gall bladder, liver, pancreas, cervix-uteri and urinary bladder. Neither all respiratory disease nor all external causes of death showed significant association between DMF and mortality. On the other hand, possible protective effects in DMF (D, M, F) were observed for the mortalities of all causes of death (RR=0.85, 95%CI: 0.81-0.88), all cerebrovascular diseases (RR=0.68, 95%CI: 0.62-0.73), all cardiovascular disease (RR=0.86, 95%CI: 0.78-0.95) and all other causes of death (RR=0.83, 95%CI: 0.73-0.89).

CONCLUSION: The present analysis indicates that animal protein and fat was not strongly associated with cancer mortality. On the other hand, relatively high animal protein and fat intake, although much lower than that in the western countries, may have helped to reduce mortality from vascular disease in this cohort.

Key word: milk, meat, fish, mortality, dietary habits, cohort study

INTRODUCTION

In Japan, the Ministry of Health and Welfare has conducted an annual nutritional survey, the National Survey, since 1947. The survey is the most important source of information on the nutritional status of the Japanese, including average per capita daily intake of major nutrients and foods. After the second world war, the Japanese experienced dramatic changes in their dietary habits. The most increased, among other things, was milk consumption, followed by meat, oil, fat and fruit, while the intake of rice gradually decreased.[1] Also changed in the post World War II era of Japan was cause-specific mortality. After the second world war, infectious diseases such as tuberculosis markedly decreased. Afterwards, apoplexy began to decrease whereas chronic diseases related to westernized lifestyle rapidly increased. Thus, the leading cause of death in Japan changed from tuberculosis to cerebrovascular attack in the 1960s, and later, in 1981, malignant neoplasms became the leading cause of death.[2] Those changes in causes of death resulted in the longer life expectancy. During the period from 1965 to 1995, the life expectancy increased from 67 to 72 years old, and from 76 to 82 years old in men and women,

1) Okinawa Prefectural College of Nursing,
2) Department of Public Health, Kagoshima University Faculty of Medicine, Kagoshima, Japan

respectively.[3]

The Six-Prefecture Cohort Study conducted by late Dr Hirayama was the largest prospective cohort study in Japan. This study selected six prefectures from northern to southern prefectures in Japan, and collected data on dietary habits and other factors from over two hundred fifty thousand residents. The most important product from this study was the dose-response relationship between passive smoking and lung cancer mortality. [4] Epidemiological findings from the six-prefecture cohort study have also contributed to the cancer prevention on dietary habits including smoking and alcohol drinking.[5] The notion that they were avoidable risks was strongly supported by other studies.[6-8] From further analyses on dietary data of the six-prefecture cohort in Japan, we have found a possible protective effect of milk, meat and fish for cerebrovascular disease mortality from 1966 to 1981.[9] However, that protective effect had not been examined for cancer and other main causes of death. The purpose of the present analysis is to further elucidate the associations between the joint intakes of milk, meat and fish as main sources of animal protein and fat and mortality in the subjects of the six-prefecture cohort study.

MATERIALS AND METHODS

Profile of cohort

A cohort of 265,070 residents, aged 40 or over, from 29 public health districts in six prefectures (Kagoshima, Okayama, Hyogo, Osaka, Aichi and Miyagi) was followed-up from 1966 to 1981 by late Dr. Hirayama and his colleagues.[5] A one-page questionnaire used in the baseline survey included questions about occupation, cigarette smoking, alcohol drinking, tea drinking, and other dietary factors (rice, miso soup, green-yellow vegetables, pickles, meat, fish and dairy milk). At the beginning of each follow-up year, a migration survey was conducted through reference to the local residence registration. During the follow-up period, the deaths were annually ascertained by thorough-checking against death certificates kept at each public health center. The causes of deaths were coded by Dr. Hirayama according to the 7th revision of the International Classification of Disease (ICD-7). The study method, age and sex distribution of the cohort have been reported elsewhere[5,10].

In the present analysis, sex, prefecture, attained age, occupation, smoking and alcohol drinking were treated as potential confounding factors. Occupation was classified into the following 5 categories taking into account average years of schooling: (1) farmers, lumbermen, fishermen, and workers in mining and quarrying, (2) workers in transport and communication, craftsmen, production process workers and labourers (3) clerical and related workers, sales workers, and service workers, (4) professional and technical workers, managers and officials, (5) job unknown including in housewives. These categories can be considered as one of surrogates for socioeconomic status.[5]

Cigarette smoking was categorized into the three categories, i.e., non-smokers (never smoked), ex-smokers, and current smokers (a cigarette per day or more). Alcohol drinking was divided to two categories, i.e., not-daily drinkers (1-3 times/-week or less) and daily drinkers (4 times/day or more). To examine the joint effect of animal protein and fat, dairy milk, meat and fish (DMF) were combined. For example, DMF (D, M, F) means the combination of dairy milk (1-3 times/week or more), meat (1-3 times/week or more), and fish (4 times/week or more). Thus DMF (d, m, f) was the reference group, which was for dairy milk (less than 1 time/week), meat (less than 1 time/week), and fish (less than 4 times/week).

Analysis of prior disease history at the baseline showed that the mortality rate of all causes of death among the subjects with cancer or other disease except for chronic stomach disease at recruitment was higher than that among those with no prior disease history at recruitment. However, this mortality among the subjects with prior disease history of stomach disease was not significantly different from that among those with no prior disease. Therefore, the following cohort members were excluded from the present analysis on the

basis of the information at the baseline: (1) those with a history of cancer and other diseases except for chronic stomach diseases (n=7,612), (2) those aged 70 years or older (n=4,490), and (3) those who had missing information on dietary habits and smoking (n=27,949). After this exclusion, a total of 225,019 cohort members remained for analysis.

Statistical procedure

The person-years and the numbers of deaths were aggregated and stratified by attained age (-44, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80+), prefecture, occupation, cigarette smoking, and other dietary factors using DATAB computer program.[11] Thereafter, AMFIT regression program was used for survival analysis with Poisson regression model.[12] The rate ratio (RR) and its 95 % confidence interval (95%CI) were also estimated by the method of maximum likelihood. A more detailed description of the statistical methods is available elsewhere.[10, 12]

RESULTS

Distribution of sex, age, prefecture, occupation, alcohol and tobacco were shown in Table 1 according to the combination of dairy milk, meat and fish consumption (DMF). The proportion of DMF (D, M, F) was slightly higher among men, and decreased with the advancement of age at the baseline. The proportion of DMF (d, m, f) was more prevalent in Kagoshima (20.7%) than in Osaka (3.9%). The proportion of DMF (d, m, F) was the highest in Miyagi prefecture (14.8%). The proportion of DMF (D, M, F) was higher in professionals and managerial workers (34.1%) than in other job groups, suggesting the relationship between dietary habits and socioeconomic status. Frequencies of alcohol and tobacco were associated with the proportion of DMF (D, M, F). Thus, current smokers or daily drinkers (4 times/week or more) tended to consume milk, meat and fish frequently.

Table 2 gives the result for all causes of death. There were 39,893 deaths in the cohort during the period from January 1966 to December 1981.

Table 1. Distribution of sex, age, prefecture, occupation, alcohol and tobacco by combination of dairy milk, meat and fish intake among the subjects from the six-prefecture study in Japan (1966-1981).

			DMF (Dairy milk,*1 Meat,*2 Fish*3) %							
Factor	Category	Number	(d, m, f)	(D, m, f)	(d, M, f)	(d, m, F)	(D, M, f)	(D, m, F)	(d, M, F)	(D, M, F)
Sex	Men	102,919	9.7	3.3	22.9	4.5	24.7	2.2	13.7	18.9
	Women	122,100	14.4	3.3	28.8	5.9	18.2	1.8	15.2	12.6
Age (at the baseline)	40-49	91,723	10.6	2.8	25.8	4.5	23.9	1.8	13.9	16.8
	50-59	80,236	12.0	3.4	25.8	5.4	20.5	2.0	15.2	15.6
	60-69	53,060	15.4	3.9	27.0	6.3	17.4	2.4	14.7	13.0
Prefecture	Kagoshima	37,612	20.7	3.6	26.2	5.7	16.1	1.7	13.1	13.0
	Hyogo	38,433	10.6	2.9	28.4	4.0	21.7	1.6	15.2	15.7
	Aichi	37,070	14.5	5.1	32.1	1.7	31.0	0.8	6.0	8.8
	Osaka	37,559	3.9	1.6	33.2	1.1	31.3	0.6	13.1	15.3
	Okayama	39,458	11.2	2.6	25.0	4.8	16.1	1.8	20.0	18.5
	Miyagi	34,887	12.5	4.2	10.7	14.8	10.5	5.6	19.9	21.9
Occupation*4	Farmers, mining	101,595	18.5	4.0	25.7	8.0	13.6	2.5	15.8	11.8
	Transport, craftsmen	29,017	6.9	2.8	28.0	2.7	29.3	1.4	13.0	15.9
	Clerical, sales, service	44,675	5.2	2.5	23.0	2.7	29.2	1.7	13.9	21.8
	Professional, manager	8,400	2.8	2.4	14.3	1.6	32.8	2.0	10.2	34.1
	Job unknown	41,332	10.0	3.0	31.6	3.7	22.9	1.4	13.9	13.6
Alcohol	1-3 times/week or less	188,708	13.3	3.6	26.8	21.0	5.3	2.0	13.8	14.2
	4 times/week or more	36,311	6.6	2.0	22.4	5.0	21.9	2.1	18.4	21.8
Tobacco (cigarette smoking)	Non-smokers	129,290	14.3	3.4	27.6	5.9	18.4	1.9	15.1	13.5
	Ex-smokers	4,655	9.5	4.7	18.5	3.3	27.5	2.8	11.6	22.2
	Current smokers	91,074	9.5	3.1	24.4	24.7	4.4	2	13.9	17.9

*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)
*4 see text in detail

Person-years at risk were 3,140,966 in total, 1,393,344 for men, and 1,747,622 for women. Respective RRs were mutually adjusted for attained age and six variables listed in this table. This type of calculation was applied for other causes of death presented in the subsequent tables. For all causes of deaths, significant associations were observed in the DMF ((d, M, f), (d, m, F), (D, M, f), (d, M, F), (D, M, F)), sex, and occupation (except for job unknown). The RR for DMF (D, M, F) was 0.85 with 95%CI of 0.81 to 0.88 compared to DMF (d, m, f) as a reference group. The RR for women was 0.65 with 95%CI of 0.63 to 0.67 compared to men. When compared to Kagoshima prefecture, mortalities in Aichi and Osaka prefectures were significantly higher, and Hyogo and Okayama prefectures were significantly lower. The professionals and managerial workers had the lowest RR when compared to farmers (RR=0.80, 95%CI: 0.75-0.85). Mortality risks were statistically significant among the ex-smokers (RR=1.17, 95%CI: 1.09-1.24) and current smokers (RR=1.30, 95%CI: 1.26-1.34). In alcohol, daily drinkers (RR=1.14, 95%CI: 1.10-1.17) were slightly higher risk than the non-daily drinkers.

Table 3 gives the result for all cancer. Statistically significant risks were observed in the DMF combinations of (d, M, f), (d, M, F), and (D, M, F). In tobacco, the RR for current smokers was 1.50 with 95%CI of 1.42 to 1.58 compared to non-smokers. Alcohol was also associated with this mortality (daily drinkers, RR=1.12, 95%CI: 1.06-1.17).

The DMF was strongly associated with all cerebrovascular diseases (Table 4). In comparison with DMF (d, m, f), a statistically significant RR was observed in all combinations except for DMF (D, m, f). Thus, the RR for DMF (D, M, F) was 0.68 with 95% CI of 0.62 to 0.73. On the contrary to that, alcohol (daily drinkers, RR=1.26, 95%CI: 1.19-1.32) and tobacco (current smokers, RR=1.10, 95%CI: 1.04-1.16) were adverse risk factors for this mortality. When compared to farmers, other job groups showed lower mortality rates of cerebrovascular disease. An exception was no-job group, having

Table 2. Mortality rate ratio for all causes of death from six-prefecture cohort (1966-1981).

Factor	Category	Number of death	RR* (95%CI)
DMF	(d, m, f)	5518	1.00 **
(Dairy milk,*1 Meat,*2 Fish*3)	(D, m, f)	1552	1.02 (0.96-1.08)
	(d, M, f)	10546	0.94 (0.90-0.97)
	(d, m, F)	2228	0.93 (0.87-0.97)
	(D, M, f)	7785	0.90 (0.87-0.94)
	(D, m, F)	901	0.95 (0.88-1.02)
	(d, M, F)	5803	0.91 (0.87-0.95)
	(D, M, F)	5560	0.85 (0.81-0.88)
Sex	Men	23108	1.00 **
	Women	16785	0.65 (0.63-0.67)
Prefecture	Kagoshima	6565	1.00 **
	Hyogo	6516	0.95 (0.92-0.99)
	Aichi	6948	1.11 (1.07-1.15)
	Osaka	6735	1.07 (1.02-1.11)
	Okayama	6843	0.92 (0.89-0.96)
	Miyagi	6286	1.03 (0.99-1.07)
Occupation	Farmers, mining	19093	1.00 **
(socioeconomic status)	Transport, craftsmen	4773	0.95 (0.91-0.98)
	Clerical, sales, service	6652	0.96 (0.93-0.99)
	Professional, managers	1167	0.80 (0.75-0.85)
	Job unknown	8208	1.24 (1.20-1.27)
Alcohol	1-3 times/week or less	31142	1.00 **
	4 times/week or more	8751	1.14 (1.10-1.17)
Tobacco	Non-smokers	18877	1.00 **
(cigarette smoking)	Ex-smokers	1071	1.17 (1.09-1.24)
	Current smokers	19945	1.30 (1.26-1.34)

* adjusted for attained age (-44, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80+) and 6 variables listed
** reference group
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

Table 3. Mortality rate ratio for all cancer from six-prefecture study (1966-1981).

Factor	Category	Number of death	RR* (95%CI)
DMF	(d, m, f)	1270	1.00 **
(Dairy milk,*1 Meat,*2 Fish*3)	(D, m, f)	387	1.09 (0.96-1.22)
	(d, M, f)	2885	1.07 (1.00-1.14)
	(d, m, F)	574	1.02 (0.91-1.12)
	(D, M, f)	2247	1.04 (0.97-1.12)
	(D, m, F)	246	1.11 (0.96-1.27)
	(d, M, F)	1651	1.08 (1.00-1.16)
	(D, M, F)	1745	1.09 (1.00-1.17)
Sex	Men	6616	1.00 **
	Women	4389	0.71 (0.67-0.75)
Prefecture	Kagoshima	1660	1.00 **
	Hyogo	1832	1.06 (0.98-1.13)
	Aichi	1944	1.22 (1.14-1.31)
	Osaka	2044	1.26 (1.17-1.35)
	Okayama	1794	0.94 (0.87-1.01)
	Miyagi	1731	1.11 (1.03-1.19)
Occupation	Farmers, mining	5192	1.00 **
(socioeconomic status)	Transport, craftsmen	1495	0.96 (0.90-1.02)
	Clerical, sales, service	2060	0.97 (0.92-1.03)
	Professional, managers	368	0.83 (0.74-0.92)
	Job unknown	1890	1.01 (0.95-1.07)
Alcohol	1-3 times/week or less	8468	1.00 **
	4 times/week or more	2537	1.12 (1.06-1.17)
Tobacco	Non-smokers	4782	1.00 **
(cigarette smoking)	Ex-smokers	273	1.21 (1.06-1.37)
	Current smokers	5950	1.50 (1.42-1.58)

* adjusted for attained age (-44, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80+) and 6 variables listed
** reference group
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

Table 4. Mortality rate ratio for all cerebrovascular disease from six-prefecture study (1966-1981).

Factor	Category	Number of death	RR* (95%CI)
DMF	(d, m, f)	1730	1.00 **
(Dairy milk,*1 Meat,*2 Fish*3)	(D, m, f)	429	0.91 (0.81-1.01)
	(d, M, f)	3057	0.92 (0.86-0.98)
	(d, m, F)	717	0.89 (0.81-0.97)
	(D, M, f)	1931	0.79 (0.73-0.84)
	(D, m, F)	260	0.84 (0.73-0.96)
	(d, M, F)	1678	0.85 (0.79-0.92)
	(D, M, F)	1324	0.68 (0.62-0.73)
Sex	Men	6231	1.00 **
	Women	4895	0.63 (0.59-0.67)
Prefecture	Kagoshima	1806	1.00 **
	Hyogo	1704	0.94 (0.87-1.00)
	Aichi	1919	1.16 (1.08-1.24)
	Osaka	1605	0.98 (0.91-1.06)
	Okayama	2026	1.02 (0.95-1.09)
	Miyagi	2066	1.28 (1.20-1.37)
Occupation	Farmers, mining	5679	1.00 **
(socioeconomic status)	Transport, craftsmen	1166	0.88 (0.82-0.95)
	Clerical, sales, service	1610	0.88 (0.82-0.93)
	Professional, managers	273	0.72 (0.64-0.82)
	Job unknown	2398	1.26 (1.19-1.32)
Alcohol	1-3 times/week or less	8685	1.00 **
	4 times/week or more	2441	1.26 (1.19-1.32)
Tobacco	Non-smokers	5714	1.00 **
(cigarette smoking)	Ex-smokers	294	1.06 (0.93-1.20)
	Current smokers	5118	1.10 (1.04-1.16)

* adjusted for attained age (-44, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80+) and 6 variables listed
** reference group
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

the RR of 1.26.

The DMF as a protective factor was also found in all cardiovascular disease, although it was not more evident than all cerebrovascular diseases (Table 5). Tobacco was associated with the mortality of this disease (current smokers, RR=1.58, 95%CI: 1.47-1.69), but alcohol was not significant.

The mortality of all respiratory disease was modified by sex and area (Table 6). Mortality rate of respiratory disease was much higher in men than in women. The high mortality in Kagoshima prefecture might be related to air pollution by volcano activity. Respiratory disease mortality among workers with unknown job was higher than that among the rest of the cohort members (RR=1.86, 95%CI: 1.65-2.09). The RR from ex-smokers was higher than that from current smokers (ex-smokers, RR=1.63, 95%CI: 1.31-2.03). Both alcohol and DMF were not associated with this mortality.

Table 7 shows that the results for mortality of external cause. The DMF did not show any significant associations except for DMF (D, M, f). Area difference was also small. Alcohol, but not tobacco, was adversely associated with mortality from this cause of death. The RR among professionals and managerial workers was 0.50 with 95%CI of 0.37 to 0.67.

Table 8 shows the results for all other causes of death. A statistically significant RR was also observed in several combinations of DMF, i.e., (d, M, f), (d, m, F), (D, M, f), (d, M, F) and (D, M, F). The mortality rate in Miyagi prefecture was lower than that in other prefectures (RR=0.68, 95%CI: 0.61-0.74). On the contrary, alcohol and tobacco were risk factors.

Figures 1 to 3 show the RR by the DMF combinations for the cancer sites of colon, rectum, breast, prostate, stomach and lung. The mortality risks of these cancer sites were not associated with the DMF combinations. No associations were also obtained from the oesophagus, gall bladder, liver, pancreas, cervix-uterus and urinary bladder (data not shown).

Table 5. Mortality rate ratio for all cardiovascular disease from six-prefecture study (1966-1981).

Factor	Category	Number of death	RR* (95%CI)
DMF (Dairy milk,*1 Meat,*2 Fish*3)	(d, m, f)	917	1.00 **
	(D, m, f)	257	1.02 (0.88-1.17)
	(d, M, f)	1727	0.93 (0.85-1.01)
	(d, m, F)	390	0.97 (0.86-1.10)
	(D, M, f)	1266	0.91 (0.82-0.99)
	(D, m, F)	152	0.98 (0.82-1.16)
	(d, M, F)	950	0.93 (0.84-1.02)
	(D, M, F)	899	0.86 (0.78-0.95)
Sex	Men	3552	1.00 **
	Women	3006	0.83 (0.77-0.89)
Prefecture	Kagoshima	1068	1.00 **
	Hyogo	1029	0.91 (0.83-0.99)
	Aichi	1162	1.13 (1.03-1.23)
	Osaka	1178	1.11 (1.01-1.21)
	Okayama	1024	0.83 (0.76-0.91)
	Miyagi	1097	1.08 (0.99-1.18)
Occupation (socioeconomic status)	Farmers, mining	2986	1.00 **
	Transport, craftsmen	740	1.02 (0.93-1.11)
	Clerical, sales, service	1099	1.05 (0.97-1.13)
	Professional, managers	208	0.98 (0.84-1.13)
	Job unknown	1525	1.32 (1.23-1.41)
Alcohol	1-3 times/week or less	5272	1.00 **
	4 times/week or more	1286	1.03 (0.95-1.10)
Tobacco (cigarette smoking)	Non-smokers	3119	1.00 **
	Ex-smokers	168	1.29 (1.09-1.52)
	Current smokers	3271	1.58 (1.47-1.69)

* adjusted for attained age (-44, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80+) and 6 variables listed
** reference group
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

Table 6. Mortality rate ratio for all respiratory disease from six-prefecture study (1966-1981).

Factor	Category	Number of death	RR* (95%CI)
DMF	(d, m, f)	305	1.00 **
(Dairy milk,*1 Meat,*2 Fish*3)	(D, m, f)	101	1.19 (0.95-1.49)
	(d, M, f)	493	0.82 (0.70-0.95)
	(d, m, F)	111	0.87 (0.69-1.09)
	(D, M, f)	504	1.09 (0.93-1.26)
	(D, m, F)	52	1.01 (0.74-1.36)
	(d, M, F)	281	0.84 (0.71-1.00)
	(D, M, F)	323	0.92 (0.77-1.08)
Sex	Men	1413	1.00 **
	Women	757	0.39 (0.34-0.44)
Prefecture	Kagoshima	441	1.00 **
	Hyogo	326	0.67 (0.57-0.77)
	Aichi	356	0.78 (0.67-0.90)
	Osaka	359	0.77 (0.66-0.89)
	Okayama	365	0.72 (0.62-0.83)
	Miyagi	323	0.73 (0.63-0.85)
Occupation	Farmers, mining	1006	1.00 **
(socioeconomic status)	Transport, craftsmen	236	0.89 (0.76-1.03)
	Clerical, sales, service	315	0.91 (0.79-1.04)
	Professional, managers	67	0.78 (0.60-1.01)
	Job unknown	546	1.86 (1.65-2.09)
Alcohol	1-3 times/week or less	1709	1.00 **
	4 times/week or more	461	0.93 (0.83-1.04)
Tobacco	Non-smokers	955	1.00 **
(cigarette smoking)	Ex-smokers	100	1.63 (1.31-2.03)
	Current smokers	1115	1.20 (1.07-1.34)

* adjusted for attained age (-44, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80+) and 6 variables listed
** reference group
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

Table 7. Mortality rate ratio for all external causes of death from six-prefecture study (1966-1981).

Factor	Category	Number of death	RR* (95%CI)
DMF	(d, m, f)	277	1.00 **
(Dairy milk,*1 Meat,*2 Fish*3)	(D, m, f)	78	1.03 (0.79-1.32)
	(d, M, f)	547	0.93 (0.80-1.08)
	(d, m, F)	102	0.86 (0.68-1.08)
	(D, M, f)	378	0.80 (0.68-0.94)
	(D, m, F)	50	1.07 (0.78-1.45)
	(d, M, F)	299	0.88 (0.74-1.04)
	(D, M, F)	305	0.85 (0.72-1.01)
Sex	Men	1312	1.00 **
	Women	724	0.45 (0.39-0.51)
Prefecture	Kagoshima	333	1.00 **
	Hyogo	400	1.22 (1.04-1.41)
	Aichi	350	1.15 (0.98-1.34)
	Osaka	300	1.03 (0.87-1.22)
	Okayama	385	1.08 (0.93-1.25)
	Miyagi	268	0.87 (0.73-1.03)
Occupation	Farmers, mining	1058	1.00 **
(socioeconomic status)	Transport, craftsmen	290	0.85 (0.73-0.97)
	Clerical, sales, service	351	0.81 (0.71-0.92)
	Professional, managers	47	0.50 (0.37-0.67)
	Job unknown	290	0.95 (0.82-1.09)
Alcohol	1-3 times/week or less	1487	1.00 **
	4 times/week or more	549	1.40 (1.25-1.57)
Tobacco	Non-smokers	940	1.00 **
(cigarette smoking)	Ex-smokers	45	0.76 (0.55-1.04)
	Current smokers	1051	0.94 (0.83-1.06)

* adjusted for attained age (-44, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80+) and 6 variables listed
** reference group
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

Table 8. Mortality rate ratio for all other causes of death from six-prefecture study (1966-1981).

Factor	Category	Number of death	RR* (95%CI)
DMF	(d, m, f)	1019	1.00 **
(Dairy milk,*1 Meat,*2 Fish*3)	(D, m, f)	300	1.09 (0.95-1.24)
	(d, M, f)	1837	0.85 (0.79-0.92)
	(d, m, F)	334	0.82 (0.72-0.93)
	(D, M, f)	1459	0.89 (0.81-0.97)
	(D, m, F)	141	0.89 (0.74-1.06)
	(d, M, F)	944	0.81 (0.74-0.89)
	(D, M, F)	964	0.81 (0.73-0.89)
Sex	Men	3984	1.00 **
	Women	3014	0.65 (0.60-0.69)
Prefecture	Kagoshima	1257	1.00 **
	Hyogo	1225	0.92 (0.84-0.99)
	Aichi	1217	0.97 (0.89-1.06)
	Osaka	1249	0.99 (0.91-1.08)
	Okayama	1249	0.88 (0.81-0.96)
	Miyagi	801	0.68 (0.61-0.74)
Occupation	Farmers, mining	3172	1.00 **
(socioeconomic status)	Transport, craftsmen	846	1.00 (0.92-1.08)
	Clerical, sales, service	1217	1.05 (0.97-1.12)
	Professional, managers	204	0.82 (0.71-0.95)
	Job unknown	1559	1.41 (1.32-1.51)
Alcohol	1-3 times/week or less	5521	1.00 **
	4 times/week or more	1477	1.08 (1.01-1.15)
Tobacco	Non-smokers	3367	1.00 **
(cigarette smoking)	Ex-smokers	191	1.14 (0.97-1.32)
	Current smokers	3440	1.28 (1.20-1.37)

* adjusted for attained age (-44, 45-, 50-, 55-, 60-, 65-, 70-, 75-, 80+) and 6 variables listed
** reference group
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

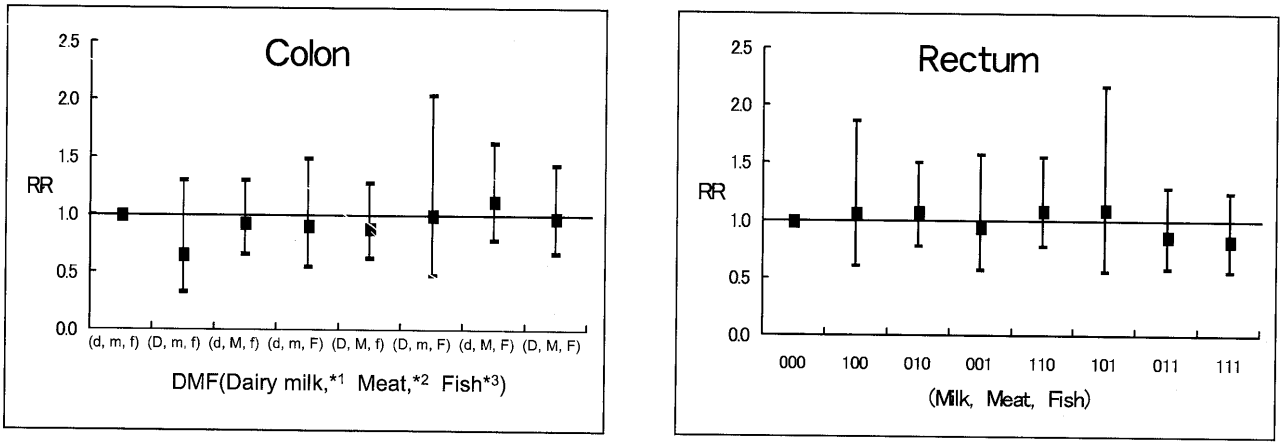

Figure 1. Mortality rate ratio (RR) by the combination of DMF for the cancer sites of colon and rectum. A square and a bar are corresponding to the RR and its 95% confidence interval, where DMF (d, m, f) is reference group.
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

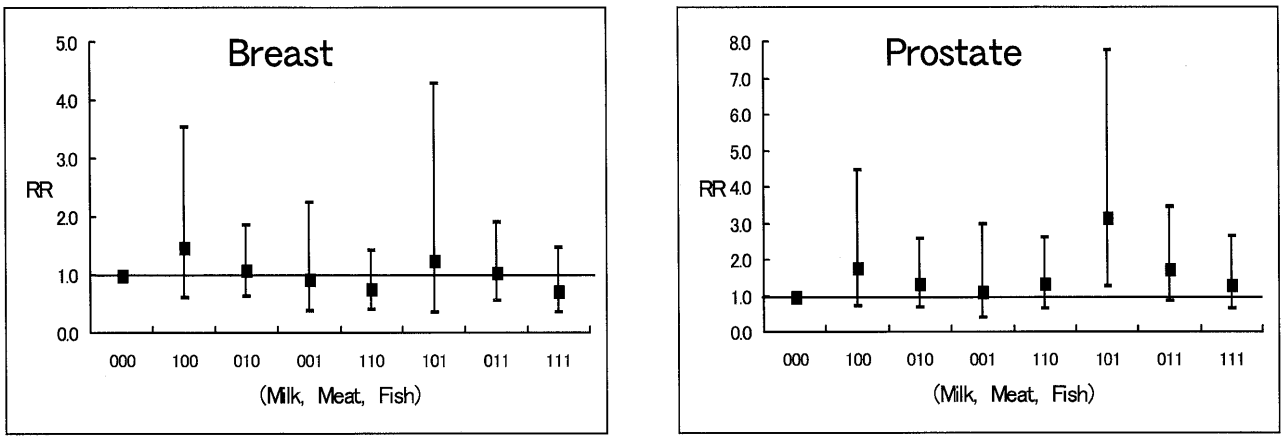

Figure 2. Mortality rate ratio (RR) by the combination of DMF for the cancer sites of breast and prostate. A square and a bar are corresponding to the RR and its 95% confidence interval, where DMF (d, m, f) is reference group.
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

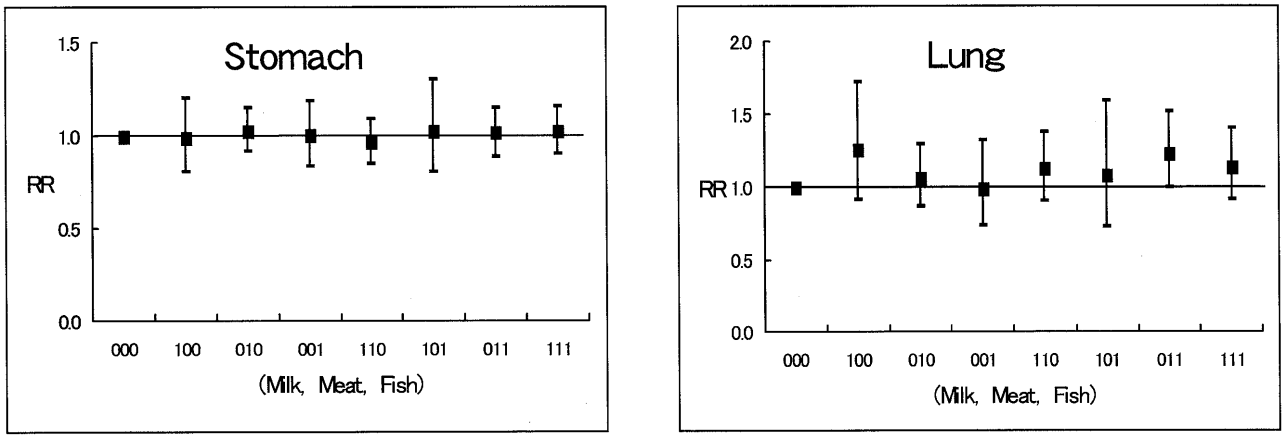

Figure 3. Mortality rate ratio (RR) by the combination of DMF for the cancer sites of stomach and lung. A square and a bar are corresponding to the RR and its 95% confidence interval, where DMF (d, m, f) is reference group.
*1 Dairy milk consumption (d: less than 1 time/week, D: 1-3 times/week or more)
*2 Meat consumption (m: less than 1 time/week, M: 1-3 times/week or more)
*3 Fish consumption (f: less than 4 times/week, F: 4 times/week or more)

DISCUSSION

Life-styles and dietary habits can vary with time. In this cohort study, the second survey was conducted for the randomly selected sub-population of 3 % of the cohort in 1971, six years after the initial survey. Comparison between the results of two surveys showed good correlation and agreement.[13] Those results could be due to the age at the baseline, mainly 40 or over, where individual life-style would be stable. Possibly, the period between the two surveys, which was only 6 years, might be too short to examine the change of life-style over years.

Over 90 percent of the cohort members consumed rice, vegetables including pickles, and miso soup 1-3 times/week or more. Thus, these were popular dietary styles for the Japanese in the 1960s. Associations between respective food items

and cancer mortality risk were intensively examined and reported by Dr Hirayama.[5, 13] In the present multivariate analysis, the joint effect of animal protein and fat from dairy milk, meat and fish were targeted with adjustment for not only cigarette smoking but prefecture and occupation. Other dietary factors in this cohort did not significantly contribute to the risk estimation, which might be due to the fact that mortality risk was largely explained by age and cigarette smoking.

The present results, suggesting the inverse association between mortalities from main causes of death except for all cancer and the joint effect of animal protein and fat, are in line with the changes of leading causes of death in Japan over the years. It changed from cerebrovascular disease to malignant neoplasms in the last 50 years. Time trends of Japanese food consumption reported by the National Nutritional Survey support the present findings to some extent. According to the survey, the increased animal protein and fat intake during the period from the 1960s to the 1980s may have contributed to the extension of life expectancy and the decreasing trend of cerebrovascular disease mortality starting from around 1965. Macroscopic analysis presented in this paper is useful for understanding the changes of mortality and food consumption nationwide.

The present study showed that cancer mortality was relatively lower within the dietary pattern of DMF ((d, m, f) and (d, m, F)). Contrary to that, the adverse joint effect of animal protein and fat on cancer was only marginally significant. On top of that, the present analysis could not confirm such an effect in cancer of the colon, rectum, breast or prostate (Figures 1 and 2) although those cancers are considered to be related to animal fat and their incidence rates in Japan gradually increased since 1960. But the increase in animal fat consumption virtually stopped after 1974. Incidentally, 1973 was the year of the first oil embargo crisis, which might have affected the increasing trend of both breast and prostate cancers.[13] Therefore, it might be an unexpected nationwide dietary intervention against these cancers. Recent trend analysis using WHO mortality database over the past three decades suggests that the colorectal and prostate cancer mortality rates in Japan may never reach rates similar to those of several western countries.[14] Stomach cancer, whose mortality steadily decreased during the last 20 years, has been the primary cause of cancer in both men and women until the lung cancer death rate in men became the leading cause of cancer death in 1993. This decline of stomach cancer risk in Japan may be due to the nationwide campaigns including an active public education, and the use of electric refrigerator, which contributed to the reduction of salty food intake and the increase of fresh fruit and vegetable consumption.[15]

It is well known that several aspects of the traditional Japanese life-style such as heavy work, alcohol drinking and a largely plant-based diet with high salt intake are associated with a high incidence of hypertension and cerebrovascular disease.[16] In the previous analysis of the six-prefecture cohort data, the joint effect of animal protein and fat from dairy milk, meat and fish was strongly associated with a reduction in mortality from haemorrhagic stroke.[9] This result is in line with the Ni-Hon-San study and recent meta-analysis of 13 cohorts.[17, 18] In Japan, the success of a community-based hypertension control program in the early 1970s saw a reduction in salt intake from 13.7 g/day in 1976 to 11.7g/day in 1987.[1, 19] Although fat intake had increased with economic growth, the level of animal fat intake in Japanese is still lower than the levels in the US and European countries. This may explain why no large increase in the ischaemic heart disease mortality has been seen alongside the decrease in stroke mortality in Japan.[20] In the present analysis, the DMF was related to cardiovascular disease in total but not to ischaemic heart disease only (results not shown).

Data obtained from the National Nutritional Survey in Japan showed the increased consumption of green-yellow vegetables, milk and dairy to present, stabilization in animal fat consumption after 1974, and reduction of salt consumption until 1987. However, salt intake increased after 1987, and animal protein intake and fat consumption

increased slightly in the corresponding period. Those trends may be related to increasing mortality rates of heart disease, colon and breast cancers. The possibility can be examined in depth by the recent cohort studies in Japan.[21, 22]

In conclusion, the joint effect of animal protein and fat on the basis of the DMF combination was not strongly associated with the cancers in the present analysis. On the other hand, substantial rises in animal protein and fat intake may have had a protective role for mortality from vascular diseases in this cohort.

ACKNOWLEDGEMENT

The authors wish to express their sincere appreciation to the late Dr. Takeshi Hirayama, who gave us the chance to analyze the six-prefecture cohort data. This study was supported in part by a Grant-in-Aid for Cancer Research (8-1) by Ministry of Health, Labor and Welfare, Japan

REFERENCES

1. Ministry of Health and Welfare of Japan, Division of Health and Nutrition. Kokumin-Eiyo-no-Genjo (Current Status of National Nutrition) 1955-1993, Dai-ichi Shuppan, Tokyo (1957-1995).
2. Ministry of Health and Welfare of Japan, Health and Welfare Statistics and Information Department. Vital Statistics 1993, Vol. 1, Koseitokei Kyokai, Tokyo 1995.
3. Health and Welfare Statistics Association. Kokumin-Eisei-no-Dokou (Trend of National Health), Koseitokei Kyokai, Tokyo 2000.
4. Hirayama T. Non-smoking wives of heavy smokers have a higher risk of lung cancer: a study from Japan. BMJ, 282: 183-185, 1981.
5. Hirayama T. Life style and mortality: a Large-scale Census-based Cohort Study in Japan. Basel, Switzerland: Karger, 1990.
6. Doll R, Peto R. The cause of cancer: quantitative estimates of avoidable risks of cancer in the United States. J Nat Cancer Inst, 66, 1192-1308, 1981.
7. World Cancer Research Fund and American Institute for Cancer Prevention. Food, nutrition and the prevention of cancer: A global perspective. Washington DC: World Cancer Research Fund and American Institute for Cancer Prevention, 1997.
8. Trichopoulos D, Lagiou P, Trichopoulou A. Evidence-based nutrition. Asia Pacific J Clin Nutr, 9(Suppl.), s4-s9, 2000.
9. Kinjo Y, Beral V, Akiba S, Key T, Mizuno S, Appleby P, Yamaguchi N, Watanabe S, Doll R. Possible protective effect of milk, meat and fish for cerebrovascular disease mortality in Japan. J Epidemiol, 9: 268-274, 1999.
10. Akiba S, Hirayama T. Cigarette smoking and cancer mortality risk in Japanese men and women -Results from reanalysis of Six-prefecture Cohort Study data. Environ Health Perspect, 87, 19-26, 1990.
11. Preston DL, Lubin JH, Pierce DA. In; Epicure User's Guide. Seattle: Hirosoft International, 1991.
12. Preston DL, Kato H, Kopecky KJ, Fujita S. Life span study report 10, Part 1, Cancer mortality among A-bomb survivors in Hiroshima and Nagasaki, 1950-1982. Radiatin Res, 111, 151-178, 1987.
13. Hirayama T. Japanese studies on diet and cancer. IN: Epidemiology of Diet and Cancer, Hill MJ., et al. Eds. Ellis Horwood, London, 17-64, 1994.
14. Boyle P, Kevi R, Lucchuni F, La Vecchia C. Trends in diet-related cancers in Japan: a conundrum ? Lancet, 342, 752, 1993.
15. Hirohata T, Kono S. Diet/nutrition and stomach cancer in Japan. Int. J. Cancer, 10(Suppl.), s34-s36, 1997.
16. Tanaka H, Yokoyama T. Cerebrovascular diseases. In: Oxford textbook of public health. Oxford University Pres, Oxford, p1065-p1079, 1996.
17. Yano K, Reed DM, MacLean CJ. Serum cholesterol and hemorrhagic stroke in the Honolulu Heart Program. Stroke 20, 1460-1465, 1989.
18. Eastern Stroke and Coronary Heart Disease Collaborative Research Group. Blood pressure, cholesterol, and stroke in eastern Asia. Lancet 352, 1801-1807, 1998.
19. Shimamoto T, Isao H, Iida M, Komachi Y. Epidemiology of cerebrovascular disease: Stroke

epidemic in Japan. J Epidemiol 6(Suppl.), s43-s47, 1996.

20. Willett WC. Diet and health: What should we eat? Science, 264, 532-537, 1994.

21. Watanabe S, Sobue T, Kinjo Y. Research activities of cancer epidemiology in Japan. J Epidemiol, 3(Suppl.), s19-s29, 1996.

22. Yoshinaga A, Sasaki S, Tsugane S, and JPHC (Japan Public Health Center) Study Group. Sensitivity of self-reports of cancer in a population-based prospective study: JPHC Study Cohort I. J Clin Epidemiol, 54, 741-746, 2001.

沖縄県立看護大学紀要第３号(2002年３月)

原著

日本の六府県コホート研究(1966-1981)からみた牛乳、肉および魚の同時摂取と死亡

金城芳秀[1)]　秋葉澄伯[2)]

背景：われわれは、六府県コホートデータ(1966-1981)の解析から、牛乳、肉および魚の摂取が脳血管疾患の死亡に防御的な影響を及ぼすことを見つけた。しかし、がんや他の疾患についても同様な影響があるのか未検討であった。

目的：本解析の目的は、六府県コホート研究対象者における動物性蛋白質・脂肪の主たる供給源としての牛乳、肉および魚の同時摂取と主要疾患の死亡率との関係をさらに明らかにすることである。

方法：解析対象は1965年12月のベースライン時に40歳～69歳までの男女225,019人であり、がんやその他疾患（慢性の胃疾患を除く）の既往歴があるものは解析対象から除外した。研究期間中に観察された死亡数は男性23,108人、女性16,785人であった。牛乳（Dairy milk)、肉(Meat)および魚(Fish)の同時摂取（DMFと呼称）の影響をみるために、データは二値データに再カテゴリ化した。例えば、DMF(D, M, F)というのは、牛乳を週１～３回以上、肉を週１～３回以上、および魚を週４回以上摂取することを意味する。すなわちDMF(d, m, f)は参照群であり、牛乳を週１回未満、肉を週１回未満、および魚を週４回未満の摂取とした。死亡リスク（RR）は性、年齢、県、職業、飲酒、喫煙およびDMFを調整して比較に用いた。

結果：全がんに対してDMFは弱い影響がみられ、DMF(D, M, F)におけるRRは1.09、その95%信頼区間(95%CI)は1.0-1.17であった。しかし結腸、直腸、乳房、前立腺、胃、肺、食道、胆嚢、肝、膵、子宮頸および膀胱では統計学的に有意な影響はみつからなかった。またDMFは呼吸器系疾患や外因死とは関連がみられなかった。一方、DMF(D, M, F)においては、全死因(RR=0.85, 95%CI: 0.81-0.95)、脳血管疾患（RR=0.68, 95%CI: 0.62-0.73)、心疾患（RR=0.86, 95%CI: 0.78-0.95)、その他の死因(RR=0.83, 95%CI: 0.73-0.89）となっており、これらの死因に対してDMFは防御的な影響を及ぼしたことが観察された。

結論：　今回の解析結果は、このコホートにおける動物性蛋白質・脂肪の摂取とがん死亡とは強く関連していなかったことを示している。一方、欧米ほど量的に多くはない動物性蛋白質・脂肪の摂取は循環器系疾患の死亡を減らすことに役だっていたのであろう。

キーワード：牛乳、肉、魚、死亡、食習慣、コホート研究

1）沖縄県立看護大学
2）鹿児島大学医学部公衆衛生