Table 1. Relative risk (RR) of death from pancreatic cancer by sex according to smoking status at baseline

	Males				Females			
	Person-years	No. of deaths	RR[a]	95% CI[b]	Person-years	No. of deaths	RR	95% CI
Never	74,213	19	1.00		415,576	92	1.00	
Ex-smokers	94,227	33	1.1	0.61–1.9	7,587	4	1.8	0.67–5.0
Current smokers	190,702	68	1.6	0.95–2.6	25,100	9	1.7	0.85–3.4

[a] RR: relative risk; adjusted for age, body mass index, and history of diabetes mellitus and gallbladder diseases.
[b] CI: confidence interval.

tion in risk (RR = 1.1). The RR of death from pancreatic cancer associated with ever smoking (ex- and current smokers combined) was 1.4 (95% CI: 0.85–2.3) for males, and 1.7 (95% CI: 0.95–3.1) for females. Based on this risk estimate, the proportion of pancreatic cancers attributable to cigarette smoking was estimated to be 22% in males and 7% in females. Because of the small number of current and ex-smokers among females, we provide the results of detailed analyses only for males.

Table 2 presents the RRs of death from pancreatic cancer according to the number of cigarettes smoked per day, age at starting smoking, years of smoking, and cumulative amount. Among current smokers, we failed to observe a significant dose–response relationship between the average number of cigarettes smoked per day and the risk of death from pancreatic cancer. The RRs of pancreatic cancer were 1.6 (95% CI: 0.91–2.9) for subjects who smoked less than 20 cigarettes per day,

Table 2. Relative risk of death from pancreatic cancer for current male smokers

	Person-years	No. of deaths	RR[a]	95%CI[b]
Cigarettes smoked per day				
Never	74,213	19	1.0	
1–19 (cigarettes/day)	61,178	30	1.6	0.91–2.9
20–39	110,169	29	1.3	0.74–2.4
≧40	16,554	7	3.3	1.38–8.1**[c]
				trend p = 0.59[d]
Age started smoking				
Never	74,213	19	1.0	
≧26 (years old)	16,233	8	1.5	0.65–3.4
23–25	24,789	8	1.3	0.57–2.9
20–22	103,295	38	1.7	0.95–2.9
<20	36,307	11	1.7	0.82–3.7
				trend p = 0.63
Years of smoking				
Never	74,213	19	1.0	
<25 (years)	35,083	2	1.3	0.27–6.2
25–34	53,804	9	2.0	0.80–4.9
35–44	62,343	25	1.7	0.91–3.2
≧45	29,393	29	1.5	0.81–2.7
				trend p = 0.92
Cumulative amount of smoking				
Never	74,213	19	1.0	
<20 (pack-years)	3,399	9	2.0	0.89–4.4
20–39	11,026	29	1.7	0.95–3.1
40–59	5,960	20	1.4	0.73–2.6
≧60	1,955	7	1.7	0.70–4.0
				trend p = 0.53

[a] RR: relative risk; adjusted for age, body mass index, and history of diabetes mellitus and gallbladder diseases.
[b] CI: confidence interval.
[c] $^{**}p < 0.01$.
[d] Trend for current smokers.

Table 3. RR of death from pancreatic cancer according to years since smoking cessation among males

	Person-years	No. of deaths	RR[a]	95%CI[b]
Never	74,213	19	1.00	
Current smokers	190,702	68	1.6	0.95–2.7
Ex-smokers				
1–9 (years)	44,244	17	1.4	0.70–2.6
10–19	26,105	7	0.85	0.36–2.0
≧ 20	15,332	7	0.85	0.36–2.0
				trend $p = 0.04$[c]

[a] RR: relative risk; adjusted for age, body mass index, and history of diabetes mellitus and gallbladder diseases.
[b] CI: confidence interval.
[c] Trend for ex- and current smokers.

1.3 (95% CI: 0.74–2.4) for those who smoked 20–39 cigarettes per day, and 3.3 (95% CI: 1.4–8.1) for those who smoked 40 cigarettes or more per day. Starting smoking at a younger or older age did not appear to be associated with the risk of pancreatic cancer. We also failed to observe a clear dose–response relationship between years of smoking, cumulative amount, and the risk of death from pancreatic cancer.

Table 3 shows the RRs of death from pancreatic cancer for male ex-smokers according to years since cessation. A significant decreasing trend in risk with increasing years after cessation was observed (trend $p = 0.04$). It took more than ten years for the risk among ex-smokers to approach the level of non-smokers. The RRs were 0.85 (95% CI: 0.36–2.0) and 0.85 (95% CI: 0.36–2.0) for those who had quit smoking for 10–19 and ≥20 years, respectively.

Discussion

Our large-scale prospective cohort study confirmed that cigarette smoking was associated with an increased risk of pancreatic cancer. Risk of death from pancreatic cancer was increased approximately 1.6-fold for current smokers as compared with non-smokers. To date at least eight cohort studies have consistently reported that cigarette smoking increases the risk of pancreatic cancer [18–25]. Compared with case–control studies [3–17], the strength of the association was relatively weak in cohort studies, with the RRs ranging from 1.1 to 3.9 for current smokers. Our results were quite similar to those of Hirayama's cohort study [25].

Although heavy smokers had a substantially higher risk of pancreatic cancer, a significant dose–response relationship was not consistently observed among previous studies. In the present study, we failed to observe a significant dose–response relationship between the number of cigarettes smoked, years of smoking, cumulative amount, and the risk of death from pancreatic cancer. This suggests that cigarette smoking is probably a weak pancreatic cancer carcinogen. It has been reported that cigarette smoking may play its role in the later stages of the carcinogenic process [10]. Based on this notion, Howe *et al.* found that limiting cigarette smoking to the 15 years prior to diagnosis considerably strengthened the association and led to a much clearer dose–response relationship [8]. A significant, positive trend in risk with the increasing pack-years of smoking was also observed in another prospective cohort study, when the analysis was confined to cigarette smoking within the past 15 years [19].

In the present analysis we observed that the risk of death from pancreatic cancer among ex-smokers was significantly reduced with the increasing years of smoking cessation. After quitting smoking for more than ten years the risk for ex-smokers was almost identical to that for non-smokers. The reduction is risk of pancreatic cancer after smoking cessation has been reported in several previous studies [11, 13, 14, 19, 24]. Fuchs *et al.* and Nilsen *et al.* reported a more rapid reduction in the risk following smoking cessation. They showed that the relative risk among former smokers approached that for never smokers after less than ten years [19, 24]. In another case–control study based on direct interviews, smokers who quitted for more than 20 years still experienced a 30% higher risk of pancreatic cancer than non-smokers [14]. Though the length of time may differ across studies, the risk reduction after smoking cessation suggests a causal relationship and the importance of smoking cessation for those who are at high risk of pancreatic cancer.

Our cohort study indicated that cigarette smoking is an important risk factor for pancreatic cancer in Japan. Current smokers comprised about 55.3% of male adults in 1988 when the JACC study started, and 51.2% in 1997 [2]. The high prevalence of smoking may have contributed to the continuously rising incidence of pancreatic cancer in Japan. We estimated that 22% of cases with pancreatic cancer could be attributable to cigarette smoking among men. Thus, eliminating cigarette smoking would prevent approximately 2000 deaths annually from pancreatic cancer in Japan. In the absence of effective early detection and therapeutic tools, primary prevention (*i.e.* avoiding exposure to known risk factors) is likely to be the only way to reduce the burden of pancreatic cancer.

The strengths of this study include its prospective design and large size. The data on exposure were collected before the diagnosis and death from pancreatic cancer, which could preclude recall bias. A limitation of this study is that information on cigarette smoking was not updated after the baseline questionnaire survey. Ex-smokers, who used to be current smokers, may resume smoking during the follow-up period. This situation could result in an apparently slow reduction in risk for ex-smokers in this cohort. If current smokers quit smoking during the follow-up period, the true association may be attenuated. In general, the strength of the association between cigarette smoking and pancreatic cancer risk might have been weakened in our cohort study.

In conclusion, our prospective study demonstrated that cigarette smoking was associated with an increased risk of death from pancreatic cancer. Smoking cessation could eventually prevent 22% of the 9000 deaths from pancreatic cancer in Japanese males every year.

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Report

National Nutrition Survey in Japan —Its Methodological Transition and Current Findings—

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Summary The National Nutrition Survey in Japan (J-NNS), an annual nationwide survey on nutrition and diet of the Japanese people, is reviewed. J-NNS was started in the Tokyo Metropolitan area in 1945 following the end of World War II. The survey area was gradually expanded and became nationwide in 1948. The current survey obtains data from more than 12,000 persons of approximately 5,000 randomly selected households. The survey consists of three parts: a physical examination, a dietary intake survey and a dietary habit questionnaire. The physical examination includes anthropometric measurements and a blood test, the dietary intake survey examines nutrient/food intake with a semi-weighed recording method, and the dietary habit questionnaire monitors nutrition/diet-consciousness and dietary habits. In this review, the aim and brief history of the survey are outlined in the first section. The following section, explains its administrative framework, target population, sampling method, annual schedule and question items, focusing on their historical transition. Then the findings of the J-NNS are summarized, which highlights annual changes in the intake of energy, macronutrients, micronutrients and food groups. The current findings of the dietary habit questionnaire are also given in brief.
Key Words National Nutrition Survey in Japan (J-NNS), diet, nutrition, nutrient, food

Outline of the National Nutrition Survey in Japan

1. Objectives

The current aim of the National Nutrition Survey, Japan (J-NNS) is to provide information on the food and nutrient intake of the Japanese people for researchers concerned with the relationships between health and nutrition and for the national policy makers for health promotion.

2. Brief history

The J-NNS has been conducted annually in Japan since 1945, when immediately after the end of World War II, food shortage was severe enough to cause malnutrition in many Japanese. The J-NNS was begun to monitor the nutritional quality of the diets of Japanese people in order to provide information necessary for acquiring food supplies from foreign countries. At first, the survey only covered the Tokyo area, and then the area covered was gradually expanded and became nationwide in 1948 (excluding Okinawa until 1972). In 1952, the Nutrition Improvement Law was enacted, which specifies J-NNS objectives and implementations. As the Japanese food conditions gradually improved, the aim of the survey shifted from ensuring food assistance to improving the diet, physique and health of the Japanese population. During the subsequent economic reconstruction period (1950–1960) and high economic growth periods (1960–1975), which had a significant influence on the socio-economic environment and dietary lives of the Japanese people, the food and nutritional conditions in Japan improved dramatically. An increasing number of people began to suffer from ill health such as obesity and anemia, possibly caused by inadequate nutritional intake. In order to cope with such changes in food and health conditions, the J-NNS underwent a major revision in 1972, in which diagnostic tests were abolished and blood tests and surveys on dietary habits were introduced.

Today, national nutrition surveys are expected to collect basic information required for the prevention of disease and health promotion as well as for nutritional improvement. The J-NNS was revised in 1995 to address this recent demand. In this revision, individual-based data collection was introduced, which has enabled analyses stratified by sex and age.

Methods of National Nutrition Survey in Japan

1. Administrative framework

The Office for Life-Style Related Diseases Control (OLSRDC) of The Ministry of Health, Labor and Welfare of Japan (MHLW) is in charge of budgeting, planning and supervising the J-NNS, and delegates management of the survey to the governments of prefectures and several major cities. The survey itself is carried out by local public health centers. The National Institute of Health & Nutrition (NIHN) has been in charge of collecting and checking the data since 1999; this work was performed by the Statistics and Information Department of the MHLW until then. The OLSRDC is responsible for ana-

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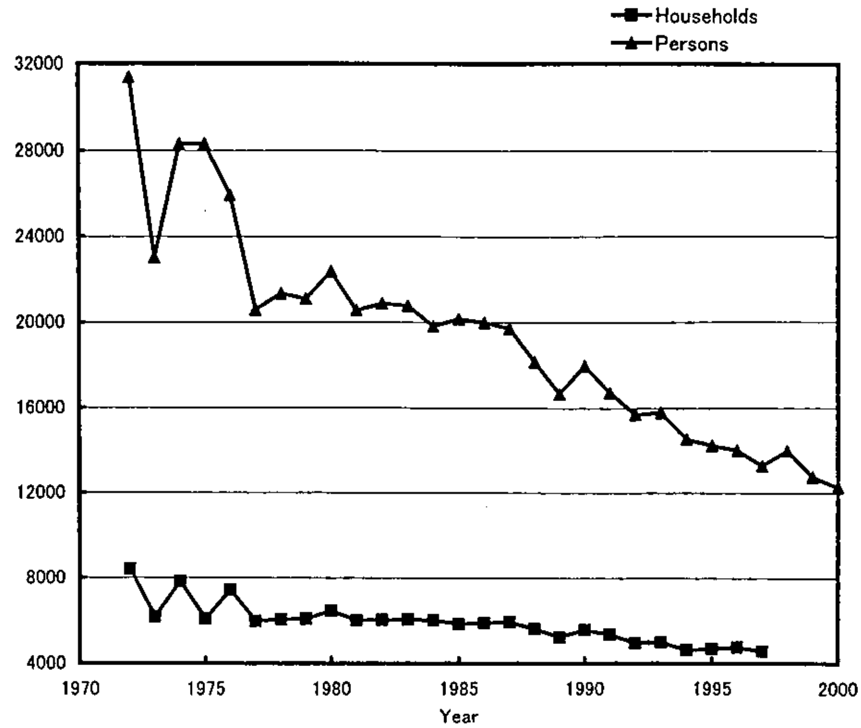

Fig. 1. Annual change in the number of participants of the J-NNS.

lyzing the data and publishing an annual report. The NIHN manages a public database of the J-NNS available on the Internet (http://www.nih.go.jp/eiken/english/index.html).

2. Target population

The population of the J-NNS has been expanded several times. It originally comprised about 3,500 households (about 30,000 persons) living in Tokyo in 1945, was expanded to four cities and 19 prefectures in Feb. 1946, expanded to 29 prefectures in May in the same year and to nationwide, 46 prefectures, in 1948. Finally, Okinawa Prefecture was added in 1972. The resultant population of 47 prefectures throughout the nation has continued unchanged since then, except in 1995, when the survey in Hyogo Prefecture was canceled because of the Great Hanshin Earthquake.

3. Sampling methods

The respondents are selected in a two-stage cluster sampling scheme. In the first stage, 300 regional health center areas are selected randomly from a total of about 1,000 areas so that the selected areas are distributed throughout all 47 prefectures. The 1,000 areas are defined by the annual report of another national survey, "Comprehensive Survey of Living Conditions of the People on Health and Welfare." In the second stage, 20 or fewer households are selected within each regional area. As a result, a total of 6,000 or fewer households comprise the sample on a household basis, and the persons constituting the households comprise the sample on an individual basis. The number of J-NNS participants on a household basis is decreasing year by year (Fig. 1). Since the number of persons included in each household is also decreasing, the number of participants on an individual basis shows a downward trend as well.

4. Schedule

The changes made to the annual schedule of the survey are summarized in Table 1. From 1946 to 1954, the survey was conducted four times per year, each of which was 3 d long. Annual average values for intake were the arithmetic means across the four periods. In 1964, the number of surveys per year was reduced to one, and this has continued unchanged since then. What should be noted is the month(s) in which the survey was conducted. From 1946 to 1963, the survey was conducted in Feb., May, Aug. and Nov. Thereafter, the survey has been conducted in Nov., except in the period from 1965 to 1971, when the survey was in May. The length of the survey period has also changed. It was originally 3 d long, was extended to 5 d between 1964 and 1971, returned to 3 d between 1972 and 1994, and finally shortened to 1 d in 1995. Thus, much attention should be paid to the fact that the annual schedule and length of the survey period(s) have been different throughout the years, especially when the intake of seasonal food is analyzed.

5. Question items

Physical examination. The physical examination is comprised of diagnostic testing of physical symptoms, anthropometric measurements, blood pressure measurement, blood test, an interview on lifestyle and measurement of physical activity. The diagnostic testing of physical symptoms formerly included tests for anemia, angular cheilosis, tendon reflex, edema and so on, which aimed to monitor the prevalence of nutritional deficiency in Japanese people. In light of the improvement of dietary and nutritional conditions in Japan, all the diagnostic tests were removed from the J-NNS in

Table 1. The transition in the annual schedule and sampling methods of the J-NNS.

Year	Month(s)	Duration	Sampling method
1945	Dec.	3 consecutive days	
1946–47	4 times/yr Feb. May Aug. Nov.	〃	Purposive sampling
1948–51	〃	〃	Random cluster sampling
1952–54	4 times/yr May Aug. Nov. Next Feb.	〃	Stratified multistage sampling for survey areas Random sampling of households
1955–63	〃	〃	Multistage random cluster sampling
1964	Nov.	5 consecutive days	〃
1965–71	May	〃	〃
1972–94	Nov.	3 consecutive days	〃
1995–99	〃	1 d	〃

1972. The current anthropometric measurements consist of height and weight for individuals one year of age and older. The anthropometric measurements included chest and sitting height until 1973, and subcutaneous fat thickness between 1972 and 1995 except in 1974. The current blood test is conducted for individuals 20 yr of age and older. Examined are hemoglobin and red blood cell count, total cholesterol, HDL cholesterol, total protein, blood sugar and triglycerides, all of which have been included as test items since 1989 or 1991. The interview on lifestyle started in 1986 for individuals 20 yr of age and older. It monitors the use of antihypertensive medication, smoking, alcohol intake and exercise habit. The physical exercise measurement counts the number of steps in a day using a pedometer for individuals 15 yr of age and older. The blood test and interview on lifestyle were added to the J-NNS to provide information necessary for the prevention of lifestyle-related diseases.

Dietary intake survey. The dietary intake survey monitors the characteristics of household members (name, sex, birth year and month, age, status of pregnancy or lactation, type of occupation and physical activity level), meal intake conditions (meals cooked at home, meals eaten outside home and meals skipped) and dietary intake status (the description of each menu, the description and quantity of each food item, the quantity of waste, the distribution of food among the household members). A semi-weighed recording method is employed. A representative person is selected from each household and he/she is asked to weigh the amounts of each food before and/or after preparation, and amounts wasted or left, and to record those amounts as well as how the food or dish is shared by the household members. If weighing a food is difficult (e.g. restaurant meals), the representative person is asked to record portion sizes. Staff dietitians from the local public health center visit respondent households, provide guidance on how to fill in the questionnaire, check the records and correct inadequate points if any. The quantity of food intake is calculated from the recorded dietary intake status, and then the quantity of nutrient intake is calculated from the quantity of food intake based on food composition tables. The changes made to the food composition tables used for the J-NNS are shown in Table 2. The directory of food nutrient values (shokuhin eiyoka yoran) was used from 1945 to 1947, Standard Tables of Food Composition in Japan from 1948 to 1954, Standard Tables of Food Composition in Japan (revised) from 1955 to 1963, Standard Tables of Food Composition in Japan (3rd edition), the Additional Food Composition Tables for the J-NNS, the food imputation tables for the J-NNS from 1964 to 1970, the weighted average composition tables of 89 food groups from 1971 to 1985, the weighted average composition tables of 97 food groups from 1986 to 1987, Standard Tables of Food Composition in Japan (4th edition) and the composition tables of restaurant/prepared/processed food for the J-NNS from 1988 to 2000, and Standard Tables of Food Composition in Japan (5th edition) from 2001. Among these food composition tables, only the Standard Tables of Food Composition in Japan (5th edition) takes account of the retention rate of nutrients by cooking. This should be noted when the an-

Table 2. The transition of food composition tables and the classification of tomato in the J-NNS.

	Food composition table(s) employed	Classification of tomato
1945		
1946	The directory of food nutrition values	
1947		
1948		
1949		
1950		
1951	Standard Tables of Food Composition in Japan	
1952		
1953		
1954		
1955		
1956		
1957		
1958		
1959	Standard Tables of Food Composition in Japan (revised)	
1960		
1961		Fruit (citrus)
1962		
1963		
1964		
1965		
1966	Standard Tables of Food Composition in Japan (3rd edition) Additional food composition tables for the J-NNS Food conversion tables for the J-NNS	
1967		
1968		
1969		
1970		
1971		
1972		
1973		Other vegetables
1974		
1975		
1976		
1977		
1978	The weighted average composition tables of 89 food groups	
1979		
1980		
1981		
1982		
1983		
1984		
1985		
1986	The weighted average composition tables of 97 food groups	
1987		
1988		
1989		
1990		
1991		
1992		Green/yellow vegetables
1993	Standard Tables of Food Composition in Japan (4th edition) The composition tables of restaurant/prepared/processed food for the J-NNS	
1994		
1995		
1996		
1997		
1998		
1999		
2000		
2001	Standard Tables of Food Composition in Japan (5th edition)	

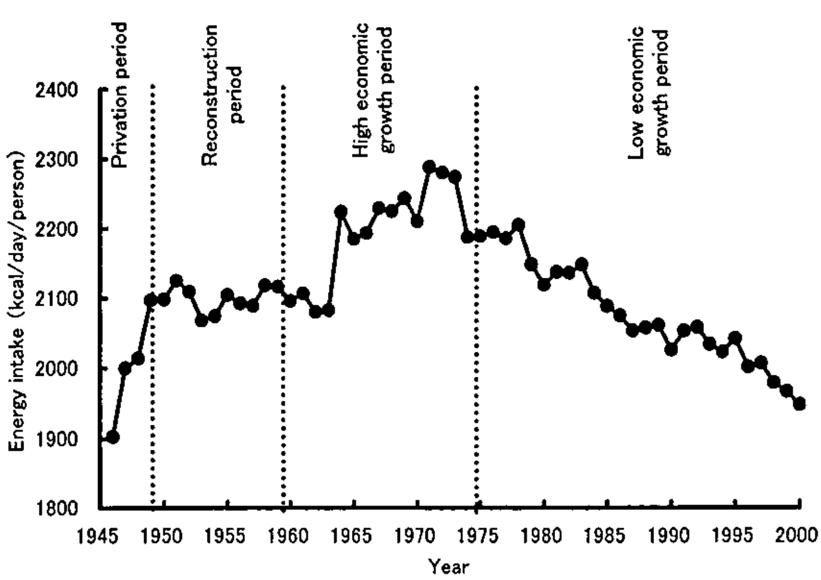

Fig. 2. Annual change in energy intake.

nual change of nutrient intake is analyzed. In addition, the definition of food groups is partly different over the years. A typical example is the classification of tomato (Table 2). Tomato was classified as "fruit (citrus)" until 1963, as "other vegetables" from 1964 to 1983, and as "green and yellow vegetables" from 1984. Another example is mushroom, which was formerly classified as "other vegetables" and was separated as "mushrooms" in 1971 (see Table 4). Another point to notice is the introduction of individual-based data collection in 1995. Since then food and nutrient intake on an individual basis has been calculated using a proportional distribution method and analyzed by sex and age group.

Dietary habit questionnaire. This questionnaire monitors the diet-consciousness and dietary habits of the Japanese people. It includes the questions, "How often are you concerned about your diet or nutrition in terms of improving your health?," "How often in a week do you skip breakfast?," "How often in a week do you eat meals outside of your home?," and so on. While the dietary intake survey provides information on the quantitative aspects of dietary life, the dietary habit questionnaire focuses on the qualitative aspects. Question items included in this questionnaire are revised annually to reflect the social circumstances at the time.

Current Findings of the National Nutrition Survey in Japan

In this section, the results of the J-NNS from 1946 to 2000 are summarized with an emphasis on the annual changes in nutrient/food intake, and the result of the dietary habit questionnaire in 2000 is also summarized. Many other reports of the J-NNS are available in epidemiological and nutritional literature (*1–7*).

1. Nutrient intake

Energy. From a socio-economic standpoint, the 20th century and later history of Japan can be divided into four periods: (i) the privation period (up to 1950), (ii) the reconstruction period (1950–1960), (iii) the high economic growth period (1960–1975), and (iv) the low economic growth period (after 1975). During the privation period, particularly before 1935, the Japanese people relied too much on their staple food (i.e., steamed rice). Steamed rice contributed to more than 80% of their energy intake, though it supplied much vegetable protein (35–40 g/d) as well as carbohydrates. The J-NNS started immediately after the end of the World War II (1945), which corresponds to the final phase of the privation period. As illustrated in Fig. 2, energy intake per capita per day in Japan jumped up from approximately 1,900 to 2,100 kcal during the postwar phase of the privation period. It kept the same level during the subsequent reconstruction period, increased rapidly again during the high economic growth period, started to decrease after the peak of 2,287 kcal in 1971, and continued to decrease during the low economic growth period (see Table 3 for details). The energy intake per capita per day was 1,948 kcal in 2000, which means that Japanese people, on average, consume an adequate intake of energy. However, detailed analyses showed that there was considerable variation in energy intake among households: 23.6% of the households consume at least 20% more than the required level and 10.9% of the households consume at least 20% less than the required level, suggesting the existence of excess and lack of energy intake.

Regarding the nutritional composition of energy intake, the percentage of energy obtained from carbohydrates has been continuously decreasing. It was 80.7% in 1949, but 57.5% in 2000. In contrast, the percentage of energy intake obtained from fat has been increasing. It was 6.9% in 1949, and then after a continuous increase, it went over the upper limit of adequate value (25%) in 1988. Though the increasing trend seems to have slowed down in the past several years, it still remains at a high level (26.5% in 2000). Continuous attention should be paid to this phenomenon since an ex-

Table 3. Annual change in energy and nutrient intake per capita per day in Japan from 1946 to 2000.

Year	Energy (kcal)	Protein (g)	Animal protein (g)	Fat (g)	Animal fat (g)	Carbohydrates (g)	Calcium (mg)	Iron (g)	Vitamin A (IU)	Vitamin B_1 (mg)	Vitamin B_2 (mg)	Vitamin C (mg)	Salt (g)
1946	1,903	59.2	11.0	14.7			253	47.5	4,641	1.81	0.67	187	
1947	2,000	60.7	11.0	13.4			251	46.5	2,969	1.82	0.62	153	
1948	2,014	63.0	13.0	13.9			261	44.0	3,074	1.53	0.72	138	
1949	2,097	65.0	14.0	16.0		423.0	200	47.0	2,416	1.60	0.70	115	
1950	2,098	68.0	17.0	18.0		418.0	270	46.0	2,459	1.52	0.72	107	
1951	2,125	68.0	19.0	18.0		424.0	270	49.0	2,262	1.58	0.76	99	
1952	2,109	70.0	23.0	20.0		412.0	373	65.0	2,700	1.14	0.67	77	
1953	2,068	69.0	22.0	20.0		403.0	370	61.0	2,721	1.07	0.65	72	
1954	2,074	68.9	22.1	20.9		402.8	362	60.0	2,814	1.12	0.66	75	
1955	2,104	69.7	22.3	20.3		411.2	338	14.0	1,084	1.16	0.67	76	
1956	2,092	69.1	22.6	21.8		405.1	379	16.0	1,190	1.13	0.70	77	
1957	2,089	69.6	23.2	21.9		403.5	384	14.0	1,253	1.09	0.71	77	
1958	2,118	70.1	23.8	23.7		406.2	388	15.0	1,240	1.07	0.73	77	
1959	2,117	69.3	23.5	23.8		406.3	385	14.0	1,225	1.05	0.74	78	
1960	2,096	69.7	24.7	24.7		398.8	389	13.0	1,180	1.05	0.72	75	
1961	2,106	69.7	25.2	26.1		398.5	393	13.0	1,228	1.04	0.73	76	
1962	2,080	70.4	27.3	28.3		386.0	402	13.0	1,327	1.10	0.77	75	
1963	2,083	70.6	27.7	29.2		381.5	409	13.0	1,452	1.03	0.79	79	
1964	2,223	74.4	28.7	34.3		398.0	476		1,496	1.05	0.82	114	
1965	2,184	71.3	28.5	36.0	14.3	384.2	465		1,324	0.97	0.83	78	
1966	2,193	74.8	29.3	39.7	17.8	380.0	499		1,600	1.03	0.90	118	
1967	2,228	76.6	31.7	42.4	18.9	382.0	529		1,407	1.08	0.92	96	
1968	2,224	76.9	32.4	44.6	19.9	375.0	529		1,421	1.10	0.96	96	
1969	2,242	77.8	33.7	45.8	20.6	377.0	537		1,490	1.17	0.99	104	
1970	2,210	77.6	34.2	46.5	20.9	368.3	536		1,536	1.13	1.00	96	
1971	2,287	78.1	34.8	48.7	22.5	379.2	524	13.5	1,457	1.12	0.92	108	
1972	2,279	82.9	40.4	50.1	27.0	359.0	549	13.9	2,067	1.19	0.98	115	
1973	2,273	84.1	41.9	52.2	29.0	351.0	551	14.1	2,043	1.22	0.98	117	14.5
1974	2,187	78.7	37.9	51.6	26.9	339.0	540	13.3	1,673	1.08	0.94	120	14.4
1975	2,188	80.0	38.9	52.0	27.4	337.3	550	13.4	1,899	1.39	1.23	138	13.5
1976	2,194	79.6	38.0	55.2	26.2	329.0	547	10.9	2,060	1.40	1.21	135	13.7
1977	2,185	79.7	38.6	56.5	27.2	323.0	550	10.9	2,095	1.40	1.24	142	13.4
1978	2,204	81.0	39.8	57.9	27.7	324.0	562	11.0	2,128	1.39	1.26	144	13.4
1979	2,148	79.6	39.4	57.7	27.9	312.0	551	10.7	2,045	1.38	1.23	132	13.0
1980	2,119	78.7	39.2	55.6	26.9	309.0	539	10.4	1,986	1.37	1.21	123	12.9
1981	2,137	79.7	40.2	57.7	28.0	307.0	552	10.7	2,113	1.37	1.24	132	12.5
1982	2,136	79.6	40.0	58.0	28.2	306.0	559	10.8	2,120	1.38	1.26	132	12.3
1983	2,147	80.9	40.9	58.6	28.3	307.0	580	10.9	2,190	1.37	1.29	134	12.4
1984	2,107	79.3	40.4	58.0	28.1	299.0	562	10.7	2,177	1.34	1.26	130	12.2
1985	2,088	79.0	40.1	56.9	27.6	298.0	553	10.8	2,188	1.34	1.25	128	12.1
1986	2,075	78.9	40.1	56.6	27.9	295.0	551	10.7	2,169	1.35	1.26	124	12.1
1987	2,053	78.5	40.1	56.6	27.6	291.0	551	10.5	2,119	1.34	1.25	122	11.7
1988	2,057	79.2	41.7	58.3	28.0	289.0	524	11.1	2,596	1.29	1.32	115	12.2
1989	2,061	80.2	42.4	58.9	28.3	290.0	540	11.4	2,687	1.26	1.36	123	12.2
1990	2,026	78.7	41.4	56.9	27.5	287.0	531	11.1	2,567	1.23	1.33	120	12.5
1991	2,053	80.2	42.7	58.0	28.4	288.0	541	11.2	2,685	1.26	1.35	113	12.9
1992	2,058	80.1	42.5	58.4	28.5	289.0	539	11.3	2,649	1.25	1.36	122	12.9
1993	2,034	79.5	42.2	58.1	28.3	285.0	537	11.2	2,603	1.22	1.34	117	12.8
1994	2,023	79.7	42.5	58.0	28.5	282.0	545	11.3	2,602	1.21	1.35	117	12.8
1995	2,042	81.5	44.4	59.9	29.8	280.0	585	11.8	2,840	1.22	1.47	135	13.2
1996	2,002	80.1	43.1	58.9	29.3	274.0	573	11.7	2,836	1.21	1.43	131	13.0
1997	2,007	80.5	43.9	59.3	29.7	273.0	579	11.6	2,832	1.19	1.43	135	12.9
1998	1,979	79.2	42.8	57.9	29.2	271.0	568	11.4	2,701	1.16	1.42	125	12.7
1999	1,967	78.9	42.3	57.9	29.0	269.0	575	11.5	2,803	1.18	1.43	129	12.6
2000	1,948	77.7	41.7	57.4	28.8	266.0	547	11.3	2,654	1.17	1.40	128	12.3

cessive intake of fat is one of the major risks of cardiovascular heart diseases and cancers as well as obesity and hyperlipemia. The percentage of energy obtained from protein showed a slow increase, rising from 12.4% in 1949 to 15.9% in 2000. Regarding the composition of energy intake in terms of food group, the percentage of grains has been decreasing. It was about 75% in the late 1940's, but has fallen to 41.3% in 2000. Rice, in particular, shows a remarkable decrease in its percentage accounting for energy intake.

Macronutrients. Total protein intake per capita per day increased until around 1975, but since then it has been maintaining the level of about 80 g/d/person with small annual change (Table 3). On the other hand, the intake of animal protein increased rapidly until around 1975, maintained a slow increase after that, and has reached a level of approximately four-fold that of the level in 1946. Accordingly, the percentage of protein from animal sources has been increasing: 18.6% in 1946, over 50% in 1981, and 53.6% in 2000.

Total fat intake per capita per day was around 15 g in the late 1940s, but increased rapidly during the high economic growth period (1960–1975), reaching 58.6 g in 1983, and has remained at the same high level to date (Table 3). The ratio of animal, plant and fish sources accounting for fat intake is approximately 4 : 5 : 1. Regarding the composition of fat intake in terms of food group, the percentage of grains decreased until around 1990, while that of animal and milk increased during the same period. Changes in this area seem to have subsided in recent years.

Carbohydrate intake per capita per day shows a clear decreasing trend (Table 3). It was about 400 g in the late 1940s, dropping below 300 g in 1984, and reaching 266 g in 2000, which can be mainly accounted for by the reduced intake of rice.

Micronutrients. Calcium intake per capita per day kept increasing until 1983 (from 253 to 580 mg), showed a temporary decrease, and is now fluctuating at around 570 mg (Table 3). This may be a slightly underestimated value since it does not consider the recent increased intake of calcium-enriched foods. It is certain, however, that the calcium intake of Japanese people still does not meet the required level of 600 mg/d. Regarding the composition of calcium intake in terms of food group, the proportion of milk and dairy products is increasing, while that of fish and shellfish such as small fry is decreasing. Since milk and dairy products are rich in fat as well as calcium, it is desirable to consume more small fry, seaweeds, green and yellow vegetables, and beans instead of relying on milk.

The data on salt intake calculated from sodium intake is available from 1973 (Table 3). It gradually decreased until 1987, reaching its lowest level of less than 12 g per capita per day. After that it increased until 1995 and has been decreasing slowly since then. In spite of the recent decreasing trend, the recommended amount of salt intake, 10 g/d/person has not yet been met. Geographically, salt intake is higher in the eastern part of Japan than in the western part. The result of analyses by prefecture is summarized elsewhere (*6*). Many epidemiological studies have shown that a high salt intake is associated with a high incidence of hypertension, increasing the risk of circulatory diseases such as stroke and cardiovascular heart disease as well as increasing the risk of gastric cancer. Therefore, it is important to keep salt intake at an adequate level for the prevention of such diseases.

2. Food intake

Grains. The intake of rice gradually increased during the reconstruction period (1950–1960), reaching about 364 g/d/person around 1960, but took a downward turn after that, dropping below 200 g in 1989, and reaching 160.4 g in 2000 (Table 4). The intake of wheat was fluctuating below 70 g/d/person until 1971, but since then it has been fluctuating around 90 g/d/person. The intake of total grains increased until about 1950, and has been continuously decreasing since. This decrease in grain intake is one of the main causes of the downward trend of carbohydrate energy intake, and furthermore, is associated with the upward trend of the fat energy intake. In order to realize an effective reduction of energy intake from fat, it is essential to consider a balance between grain and fat intake.

Vegetables and fruit. The intake of green and yellow vegetables is continuously increasing, while the intake of other vegetables is fluctuating after peaking in 1946 (Table 4). An analysis by age group shows that people over 50 yr of age tend to consume more vegetables. Vegetables are rich in carotene, the precursor of vitamin A, and are relatively rich in vitamin C, vitamin B_6 and folic acid. They are also a good supply source of calcium, iron and potassium. The adequate intake requirement of vegetables is considered to be over 350 g/d/person (containing over 120 g green and yellow vegetables), which is higher than the average intake of total vegetables by Japanese in 2000 (276.0 g/d/person). Therefore, further measures should be taken to increase vegetable intake in Japan. The intake of fruit reached its peak in 1975, decreased after that, and is showing signs of leveling off in recent years.

There seems to have been a sudden change in the intake of vegetables and fruit in 1972 (see Table 4). A similar change was seen in the intake of other food groups such as fats and oils and meats. The cause of this sudden change is unknown. One possibility is that it is related to the new survey schedule started in that year (see Table 1).

Fats and oils. The intake of fats and oils showed so rapid an increase during the high economic growth period (around 1970) and comprised 25% of the total fat intake, though it seems to have leveled off after that. An analysis by age group shows that younger people tend to consume a large amount of fats and oils.

Animal food. The intake of animal food except milk and dairy products (i.e., meats, eggs, fish and shellfish) increased along with the postwar economic growth, but around 1973, the rise began to show signs of slowing down. In contrast, the intake of milk and dairy products maintained a stady rise even after 1973,

Table 4. Annual change in food intake per capita per day in Japan from 1946 to 2000 (g).

Year	Rice	Wheat	Total grains	Nuts	Potatoes	Sugars	Confec-tionary	Fats and oils	Beans	Fruit	Green and yellow vegetables	Other vegetables	Mushrooms	Seaweeds	Condiments and beverages	Fish and shellfish	Meat	Eggs	Milk and dairy products
1946			398.4		277.9	0.5		1.7	30.9	16.9	153.8	152.8				55.0			3.1
1947			410.7		268.6	0.8		1.2	33.2	22.7	96.0	144.1				51.7			2.2
1948			435.8		210.2	6.0		1.2	37.5	31.7	98.2	124.3				60.7			3.0
1949	333.1	65.8	473.1	0.8	169.9	5.2		1.8	49.8	27.5	76.0	168.9		3.4	28.1	55.8	5.4	3.2	4.1
1950	338.7	68.7	476.8	0.9	127.2	7.2		2.6	53.7	41.5	75.6	166.4		3.0	32.0	61.0	8.4	5.6	6.8
1951	354.7	76.3	496.3	0.7	113.6	11.3		3.2	63.0	47.1	66.4	154.3		3.8	39.7	72.5	7.2	7.4	8.3
1952	352.5	68.0	481.2	0.6	84.2	14.5		3.9	68.4	48.9	63.8	158.2		4.1	42.9	82.3	10.6	10.0	10.6
1953	349.8	72.4	478.3	0.5	74.2	14.8		4.2	69.6	37.8	61.0	152.5		4.4	42.2	80.3	10.3	10.3	10.3
1954	342.1	73.2	474.6	0.5	77.0	15.6		4.6	68.2	37.4	59.6	156.3		4.8	40.5	77.7	10.8	11.3	13.1
1955	346.6	68.3	479.6	0.4	80.8	15.8		4.4	67.3	44.3	61.3	184.9		4.3	42.4	77.2	12.0	11.5	14.2
1956	362.7	65.9	474.3	0.5	68.0	15.6		5.1	72.7	65.6	49.6	180.4		5.0	44.5	72.7	15.8	12.9	21.4
1957	351.2	59.7	458.2	0.6	78.0	10.3	17.3	4.8	69.9	64.0	49.7	170.5		5.1	47.6	75.9	15.0	12.8	18.4
1958	354.7	65.5	461.2	0.5	73.0	12.3	18.0	5.7	71.0	77.2	45.8	171.6		5.0	47.9	74.9	17.6	14.8	24.6
1959	364.4	63.7	462.4	0.4	66.7	12.5	18.6	5.8	69.9	67.3	43.1	186.9		4.7	51.8	72.6	18.5	16.5	28.5
1960	358.4	65.1	452.6	0.5	64.4	12.3	20.4	6.1	71.2	68.7	39.0	186.0		4.7	55.2	76.9	18.7	18.9	32.9
1961	363.6	63.4	450.0	0.4	64.4	12.9	21.0	6.6	69.4	75.2	40.0	179.2		4.5	57.1	73.8	21.0	22.6	35.2
1962	352.0	68.4	436.2	0.5	53.8	13.4	23.0	7.6	70.8	67.1	38.6	183.7		4.6	64.0	74.5	27.8	27.3	41.7
1963	350.7	64.6	428.2	0.4	52.8	14.0	23.4	8.1	69.4	82.3	40.7	190.2		4.6	66.1	77.5	28.2	27.6	44.7
1964	354.3	62.9	425.2	0.6	74.0	14.8	30.6	7.9	74.4	127.7	50.7	176.7		4.7	61.4	83.6	30.6	30.2	46.2
1965	349.8	60.4	418.5	0.5	41.9	17.9	31.6	10.2	69.6	58.8	49.0	170.4		6.1	87.8	76.3	29.5	35.2	57.4
1966	334.7	69.4	411.9	1.5	69.1	14.9	24.0	10.8	75.6	120.2	45.7	193.1		3.9	64.2	84.4	34.7	34.0	54.4
1967	318.7	68.0	393.7	1.9	41.1	19.2	32.4	12.9	74.0	82.3	44.0	194.4		6.9	107.7	84.0	34.8	38.9	75.4
1968	308.3	67.0	381.0	1.9	44.9	20.1	36.6	14.0	73.9	79.9	47.7	199.2		6.2	112.4	86.3	37.9	37.9	74.1
1969	305.9	66.5	377.2	1.8	44.1	20.7	36.9	15.2	72.2	99.8	46.2	197.7		6.8	125.0	86.8	40.1	41.3	78.0
1970	306.1	64.8	374.1	1.9	37.8	19.7	36.7	15.6	71.2	81.0	50.2	199.1		6.9	126.7	87.4	42.5	41.2	78.8
1971	308.4	63.3	374.7	1.7	38.8	19.9	37.1	17.3	71.2	110.5	48.8	217.0	2.8	6.8	140.2	84.2	47.0	43.0	86.2
1972	274.7	88.6	365.1	1.5	51.2	13.0	35.9	13.3	64.1	169.2	83.3	193.1	6.1	4.4	116.4	92.7	70.8	38.7	95.2
1973	269.5	90.0	361.3	1.5	50.7	12.4	31.1	14.0	63.6	184.0	81.3	202.5	7.7	4.5	115.7	96.0	73.9	41.3	94.3
1974	252.3	89.8	343.7	1.6	61.7	15.1	28.0	16.2	67.0	183.6	52.3	196.9	7.2	4.7	114.2	91.0	62.8	41.1	96.5
1975	248.3	90.2	340.0	1.5	60.9	14.6	29.0	15.8	70.0	193.5	48.2	189.9	8.6	4.9	119.7	94.0	64.2	41.5	103.6
1976	243.0	91.6	336.3	1.5	63.3	14.8	27.9	17.0	68.5	170.5	56.3	196.5	7.0	5.5	113.4	90.1	64.4	40.3	100.6
1977	234.5	92.4	328.5	1.4	61.9	14.0	27.1	17.7	67.7	180.9	59.3	203.0	7.9	5.0	116.4	88.5	68.4	40.8	106.8
1978	233.7	93.3	328.7	1.6	60.8	14.3	26.4	18.3	67.6	181.3	59.5	198.2	8.2	5.6	122.4	92.8	69.2	41.6	109.9
1979	222.9	96.3	320.7	1.3	63.9	13.6	25.0	18.0	69.4	166.5	51.0	194.7	9.7	5.3	115.6	88.8	71.7	41.1	112.9
1980	225.8	91.8	319.1	1.3	63.4	12.0	25.0	16.9	65.4	155.2	51.0	192.3	8.1	5.1	109.7	92.5	67.9	37.7	115.2
1981	221.8	96.5	319.9	1.5	61.1	12.6	24.7	18.1	66.2	154.6	58.3	195.2	8.3	4.7	108.7	92.0	72.4	39.5	116.4

Table 4. Continued

Year	Rice	Wheat	Total grains	Nuts	Potatoes	Sugars	Confec-tionary	Fats and oils	Beans	Fruit	Green and yellow vegetables	Other vegetables	Mushrooms	Seaweeds	Condiments and beverages	Fish and shellfish	Meat	Eggs	Milk and dairy products
1982	218.2	95.9	315.8	1.4	61.0	12.2	25.1	18.3	67.2	159.7	58.7	192.2	8.9	5.0	114.6	90.2	70.8	40.0	124.2
1983	217.9	95.3	314.9	1.6	63.1	12.4	25.2	18.0	69.9	166.4	61.1	189.0	9.0	5.7	113.3	93.4	70.7	40.4	129.4
1984	214.3	93.8	309.8	1.6	60.6	11.6	23.4	18.4	66.2	145.0	73.1	181.7	8.1	5.3	117.4	91.5	71.3	40.3	124.0
1985	216.1	91.3	308.9	1.4	63.2	11.2	22.8	17.7	66.6	140.6	73.9	178.1	9.7	5.6	113.4	90.0	71.7	40.3	116.7
1986	212.1	93.7	307.3	1.7	62.5	11.2	22.9	16.8	65.3	137.0	70.9	189.2	10.0	5.5	113.3	90.5	70.8	41.2	117.9
1987	208.8	91.9	302.1	1.5	61.3	10.7	20.7	17.4	64.4	137.9	71.1	174.0	9.5	5.5	121.2	92.7	69.1	40.1	121.5
1988	200.9	86.1	289.2	1.5	66.6	11.2	20.8	18.1	70.7	124.9	72.8	166.9	9.1	5.9	117.9	96.1	74.1	43.1	122.2
1989	198.0	88.3	288.5	1.6	65.3	10.9	22.0	18.7	68.1	127.9	81.1	172.4	10.2	5.8	120.6	96.2	75.2	43.6	128.4
1990	197.9	84.8	285.2	1.4	65.3	10.6	20.3	17.6	68.5	124.8	77.2	162.8	10.3	6.1	137.4	95.3	71.2	42.3	130.1
1991	198.9	87.2	288.2	1.4	68.8	10.3	21.5	17.4	68.6	112.4	73.2	165.8	10.2	6.1	144.1	96.8	76.4	42.7	128.7
1992	197.3	85.3	284.9	1.5	65.0	11.7	20.9	18.0	67.5	126.1	80.9	177.0	10.7	5.6	146.8	96.8	75.1	43.3	129.0
1993	195.4	86.9	284.4	1.4	62.5	10.2	20.3	17.9	65.9	114.9	81.6	170.2	10.4	5.5	143.3	96.2	73.7	42.7	130.8
1994	192.4	86.4	280.9	1.7	62.2	10.0	19.6	17.6	66.8	117.2	81.8	161.1	10.6	5.8	147.7	97.0	74.5	43.0	132.4
1995	167.9	93.7	264.0	2.1	68.9	9.9	26.8	17.3	70.0	133.0	94.0	184.4	11.8	5.3	190.2	96.9	82.3	42.1	144.4
1996	166.5	93.9	262.9	2.1	67.8	9.7	24.5	16.9	72.3	118.6	98.9	186.8	12.7	5.5	182.4	97.0	77.9	42.1	133.9
1997	165.4	92.2	259.7	2.0	69.4	9.7	24.2	17.0	70.9	130.8	91.6	183.5	13.3	5.2	189.4	98.2	80.3	40.8	134.8
1998	164.8	90.9	257.9	2.1	71.5	9.5	24.3	16.0	72.5	115.5	87.9	172.7	14.0	6.0	193.1	95.9	77.5	40.5	132.9
1999	162.4	89.8	254.4	2.2	67.7	9.5	23.1	16.5	70.4	119.4	94.2	182.3	13.8	5.5	185.9	94.3	78.4	40.4	137.0
2000	160.4	94.3	256.8	1.9	64.7	9.3	22.2	16.4	70.2	117.4	95.9	180.1	14.1	5.5	182.3	92.0	78.2	39.7	127.6

reaching a level nearly 20-fold that recorded in 1950. An analysis by age group shows that people 7–14 yr of age consume more than 300 g/d/person, while people over 20 yr of age consume approximately 100 g/d/person. Regarding the difference between the intake of meat and fish, it is sometimes pointed out that the intake of meat is increasing while that of fish is decreasing. As shown in Table 4, however, the intake of both food groups is gradually increasing, though the rate is slow. The increase in fish intake may attract the attention of Western researchers regarding nutrition. An analysis by age group shows that people under 40 yr of age tend to consume more meat than fish, while people over 40 yr of age tend to consume more fish than meat. Such a difference between age groups suggests that dietary preferences change as one grows older, though it may partly be the reflection of dietary habits unchanged from childhood.

3. Diet-consciousness and dietary habit

Regarding the Japanese people's interest in nutrition and diet, results of the 2000 J-NNS show that 27.9% of the respondents 'often' care about their nutrition or diet, 48.3% 'sometimes,' 18.4% 'not so often' and 5.4% 'never.' An analysis by age group shows that a larger ratio of young people are distributed in the latter two answers, while larger a ratio of older people are distributed in the first two. An analysis by sex shows that females tend to be more nutrition/diet conscious than males. These results suggest the necessity to promote individual attention to nutrition and diet, and to popularize adequate knowledge, especially among young people.

Nearly 30% of the male respondents eat meals outside home at least once a day, according to the J-NNS in 2000. Relying on restaurants or boxed meals from stores generally tends to cause excess fat and salt intake and insufficient intake of vegetables, minerals, vitamins and fiber. Though there are official standards of nutrition labeling for restaurant meals and processed food, nearly 50% of the males surveyed do not have any experience of checking nutrition labels. Based on these results, consumers should be encouraged to take advantage of more nutritional education, and the food/restaurant industry is expected to produce more nutritionally-balanced healthy menus for the improvement of dietary life.

Future of the National Nutrition Survey in Japan

At present, revision of the Nutrition Improvement Law is under consideration so that it will cover not only nutrition and dietary life but also other lifestyles and health promotion. Based on this revision, J-NNS may be revised into a broader survey to monitor various aspects of Japanese peoples' lifestyles.

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Original Article

Soy Product Intake and Serum Isoflavonoid and Estradiol Concentrations in Relation to Bone Mineral Density in Postmenopausal Japanese Women

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Abstract. To evaluate soy intake and serum concentrations of estradiol and isoflavonoids and their relationship to bone mineral density (BMD) and serum bone-specific alkaline phosphatase (bone ALP) activity, we conducted a cross-sectional study of 87 postmenopausal Japanese women. Soy product and isoflavone intake from soy products and intake of nutrients were assessed with a semiquantitative food-frequency questionnaire. BMD (mg/cm^2) was measured by single-energy X-ray absorptiometry at the site of the calcaneus. Serum estradiol (E_2) and the sex hormone-binding globulin (SHBG) were measured by radioimmunoassay. Serum genistein and daidzein concentrations were measured by a high-performance liquid chromatography MS/MS method. A statistically significant correlation was observed between the ratio of E_2 to SHBG and BMD (Spearman $r=0.38$, $p=0.0003$) after controlling for age, body mass index, smoking status, age at menarche, and intake of vegetable fat, vitamin C and salt. Soy product and isoflavone intake and serum isoflavones were not significantly correlated with BMD after controlling for the covariates. Serum ALP was not significantly correlated with soy product and isoflavone intake, the E_2/SHBG ratio or serum isoflavones. The present study supports the association of BMD with serum estradiol; however, it does not support the association of BMD with soy or isoflavone intake or serum isoflavone levels.

Keywords: Bone mineral density; Bone-specific alkaline phosphatase; Estradiol; Isoflavonoids; Postmenopausal Japanese women; Soybeans

Introduction

It is generally recognized that estrogen deficiency following menopause plays a major role in osteoporosis. The isoflavones are structurally similar to estradiol [1]. Hence, the estrogenicity of isoflavones may lead to reduced bone loss. The Japanese consume a diet that is very rich in the isoflavones, genistein and daidzein, which are found in soybeans and soy products. Some researchers assume that the lower incidence of osteoporosis in Japanese women is attributable to a high consumption of soy foods [2].

The synthetic isoflavone derivative, ipriflavone, has been suggested to reduce bone loss [3]. A number of clinical trials to test the efficacy of ipriflavone on bone mass have been conducted but the data are conflicting. There are insufficient data about the effect of naturally occurring isoflavones on bone health. Some well-designed animal studies demonstrated that dietary soy or genistein prevented bone loss [4,5]. In human studies, a relative low average and variation in soy intake may have precluded a cross-sectional assessment of this relationship in non-Asian countries. To our knowledge, five studies have previously addressed the relationship cross-sectionally between dietary soy and bone mineral density (BMD) and all of them were conducted in Japan. The results were inconsistent. Yukawa et al. [6] found no association between soy product intake estimated from 3-

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day diet records and BMD at the lumbar spine L3 in women aged 65–79 years. Kimira et al. [7] also reported no association between isoflavone intake estimated from 3-day diet records and BMD in women aged 28–71 years. Tsuchida et al. [8] observed significantly higher (by 4.5%) BMD of the second metacarpal bone among women aged 40–49 years who had soybeans 2 or more times per week compared with those who had them 0 or 1 times, although the dietary questionnaire for this study was not validated. Horiuchi et al. [9] found a significantly positive correlation (r = 0.23) between soy protein intake estimated from 3-day diet records and Z-scores of BMD at the lumbar spine (L2–L4) in postmenopausal women aged 52–83 years. Somekawa et al. [10] reported a significantly positive correlation (r=0.16) between isoflavone intake and BMD at the lumbar spine (L2–L4) in postmenopausal women aged 44–80 years. None of these studies included measurements of endogenous estrogen status. The endogenous estrogen level may affect the relationship between soy intake and BMD. Similarly, soy intake may affect the relationship between endogenous estrogen level and BMD.

The present study examined the relationships of soy intake and the serum estrogen level with parameters of bone health, BMD, and a bone formation marker, serum bone-specific alkaline phosphatase (bone ALP) activity. We included the measurement of serum isoflavones and isoflavone metabolites (genistein, daidzein and equol). Serum isoflavonoid data should be useful with regard to the bioavailability of isoflavones and to further infer the mechanism for potential biological effects of dietary soy on bone health. We used a validated semiquantitative food-frequency questionnaire to estimate the intake of soy products and other dietary components and took account the potential confounding effects of various dietary and lifestyle factors.

Subjects and Methods

Subjects for this study were participants in a health check-up program provided by a general hospital in Gifu, Japan between September, 1996 and August, 1997. A total of 403 women agreed to participate in the present study and completed a self-administered questionnaire (the response rate was 96.4%). To obtain complete data, a nurse epidemiologist interviewed those who returned the questionnaire with incomplete information.

The questionnaire sought information about demographic, smoking and drinking habits, diet, exercise, and menstrual and reproductive histories. Diet was assessed by a semiquantitative food-frequency questionnaire. The women were asked to indicate the average frequency with which they had consumed 169 food items during the year prior to the study and the usual portion size of each item. We included nine food items for soy products (miso soup, tofu, deep-fried tofu, fried bean curd, dried bean curd, fermented soy beans, houba-miso, soymilk and boiled soy beans). The total intake of soy products was calculated as the sum of these nine food items. The intake of foods and nutrients was estimated from the frequency of ingestion and portion size using the Japanese Standard Tables of Food Composition, 4th edition, published by the Science and Technology Agency of Japan. Isoflavone intake from soy products was also estimated using isoflavone concentration data provided by Wakai et al. [11]. Detailed information on the questionnaire including its validity and reproducibility, has been provided elsewhere [12]. For example, the Spearman correlation coefficients comparing estimates of soy product intake from this questionnaire with the estimates from 12 daily diet records kept over a 1-year period were 0.71.

Exercise was assessed by asking the average hours per week spent performing various kinds of activities during the past year. The details, including its validity, are described elsewhere [13].

BMD, expressed in g/cm^2, was measured by single-energy X-ray absorptiometry at the calcaneus. The measurement was obtained with a commercial instrument (OsteoAnalyzer, Siemens-Osteon, HA; precision <1.0%).

A fasting blood sample was collected from each subject in the morning. The samples were stored at 80 °C until assayed. Serum isoflavonoids were measured using the high-pressure liquid chromatography (HPLC)-MS/MS method [14]. This method allows the detection of the isoflavonoids in human serum with improved selectivity, sensitivity and precision. For serum isoflavonoid measurement, β-glucuronidase/sulfatase (2000 units of β-glucuronidase and 1000 units of sulfatase) was added to 0.2–0.5ml of serum. The aglicones of the isoflavones and their metabolites were recovered by diethyl ether extraction. The diethyl ether extracts were evaporated to dryness under nitrogen and redissolved in acetonitrile prior to HPLC-MS/MS analysis. Isoflavonoids in serum extracts were separated using an HPLC method and analyzed by negative-ion multiple-reaction ion- monitoring mass spectrometry using an electorospray interface. The intra-assay coefficients of variations (CVs) were 4.3% for genistein, 4.3% for daidzein and 4.6% for equol. The inter-assay CVs were 4.9% for genistein, 5.6% for daidzein and 6.7% for equol. Serum estradiol (E_2) and sex hormone-binding globulin (SHBG) were measured by radioimmunoassay. Serum E_2 was determined after extraction using a kit purchased from Diagnostic Products Japan, Chiba, Japan. Serum SHBG was determined using a kit purchased from Pharmacia & Upjohn, Tokyo, Japan. Serum bone ALP was determined by enzyme immunoassay method. The intra-assay CVs were 10.9% for E_2. 7.8% for SHBG and 6.8% for bone ALP. The inter-assay CVs were 17.6% for E_2, 7.1% for SHBG and 7.3% for bone ALP. All samples were analyzed at SRL, Tokyo, Japan.

Postmenopausal (defined as cessation of menses for 12 or more months) women were selected for the present analysis. We excluded women who were taking hormone replacement therapy or other hormones (n = 2) and who had a history of breast cancer (n = 3), ovarian cancer (n=1), bone tumor (n = 1) or endogenous diseases such as diabetes mellitus (n = 3) and thyroid disease (n = 3). Of the 90 eligible women, 87 had sufficient sera available for hormone assays.

Spearman correlation coefficients were used to examine the associations of study variables with BMD and serum bone ALP. Intake of soy product and the individual nutrient were log-transformed and adjusted for total energy using the method proposed by Willett [15]. Potentially confounding variables were controlled by first regressing the confounders to the variables of interest and then calculating the partial coefficients between the residuals. We examined a number of potential confounders, including age, weight, height, body mass index, years since menopause, surgical removal of ovaries, hysterectomy, age at menarche, number of births or pregnancies, age at first and last births, lactation, smoking status, age when regular menstrual cycle started, exercise, intake of alcohol and caffeine, intake of macro- and micronutrients, and use of antihypertensive drugs and vitamin supplements. Because serum equol was not detected in 45 women, we used the minimum value (i.e., 2.06 nmol/l) for them in the analysis.

Results

Characteristics of the study subjects are presented in Table 1.

Serum E_2 concentration and the ratio of E_2 to SHBG were significantly correlated with BMD after controlling for age (Table 2). Serum E_2 and the E_2/SHBG ratio were inversely correlated with serum bone ALP, but the correlations were not statistically significant. There were no significant correlations between soy product and isoflavone intake and the bone health parameters after controlling for age. None of the serum isoflavonoids was significantly correlated with BMD and bone ALP after controlling for age.

The other variables which were significantly correlated with BMD after controlling for age were as follows: age at menarche ($r = -0.27$, $p = 0.01$), weight ($r=0.24$, $p=0.03$), body mass index (BMI) ($r = 0.25$, $p=0.02$), intake of vegetable fat ($r = -0.23$, $p = 0.03$), vitamin C ($r=0.23$, $p = 0.04$) and salt ($r = -0.22$, $p=0.04$) and smoking status (age-adjusted BMD values were 314.4, 403.6 and 352.7 g/cm^2 in current, former and never-smokers, respectively; $F = 3.14$, $p = 0.048$). Serum bone ALP was inversely marginally correlated with age at menarche ($r = 0.23$, $p = 0.04$) and carbohydrate intake ($r=0.27$, $p = 0.01$) after controlling for age.

The correlation between serum E_2 and BMD decreased to 0.12 ($p = 0.30$) after additional adjustment for BMI, age at menarche, smoking status, and intake of vitamin C, vegetable fat and salt. The E_2/SHBG ratio was still significantly correlated with BMD after the adjustment ($r = 0.40$, $p = 0.0002$). The correlations of serum bone ALP with serum E_2 and the E_2/SHBG ratio were not altered after additional adjustment for age at menarche and carbohydrate intake. The correlations between soy product and isoflavone intake and BMD or serum bone ALP were close to null. There were no significant correlations between serum isoflavonoid concentrations and the bone health parameters after controlling for the covariates.

The correlation coefficients between the sum of the measured serum isoflavonoid concentrations and the bone health parameters were almost the same whether equol was included or not.

The correlations between E_2/SHBG and BMD were not altered substantially after a further adjustment for isoflavone intake or serum total isoflavonoids ($r = 0.37$). Similarly, the correlations of BMD with soy product and isoflavone intake and serum isoflavonoids were not altered after an additional adjustment for the E_2/SHBG ratio.

Some of women who had had a surgical menopause still had high estrogen levels because their ovaries were

Table 1. Selected characteristics of 87 postmenopausal Japanese women

Variable	Mean±SD	(range)
Age (years)	54.2±6.5	(38–68)
Years since menopause	6.7±5.3	(1.0–23.0)
Height (cm)	154.4±4.7	(144.2–168.0)
Weight (kg)	54.2±7.0	(35.0–79.0)
Body mass index (kg/m^2)	22.9±2.7	(17.5–31.3)
Age at menarche (years)	13.9±1.7	(10–20)
No. of births	2.1±0.8	(0–4)
Exercise (METs · hours/day)	2.1±2.8	(0–12.6)
Alcohol (ml/day)	7.3±13.5	(0-74)
Smoking (%)		
Current	9.2	
Past	5.7	
Nutrient and food intake (per day)		
Energy (kcal)	2198±738	(903–4205)
Soy products (g)	62.4±41.2	(4.9–221)
Isoflavones from soy products (mg)	32.0±17.2	(2.5–79.1)
Protein (g)	92.8±35.1	(35.3–178)
Fat (g)	62.4±25.5	(21.8–30.8)
Crude fiber (g)	6.0±2.9	(1.9–15.5)
Calcium (mg)	859±384	(273–1968)
Vitamin C (mg)	176±115	(29.0–616)
Phosphorus (mg)	1490±552	(542–2855)
Iron (mg)	14.5±6.2	(6.1–33.8)
Sodium (mg)	5618±2230	(2050–11461)
Potassium (mg)	4051±1803	(1697–9996)
Salt (g)	14.0±5.6	(5.1–28.5)
Bone parameters		
Bone mass density (mg/cm^2)	352±70.3	(175–547)
Serum bone ALP activity (IU/l)	24.1±7.7	(10.2–46.3)
Serum hormone concentration		
Estradiol (pmol/l)	76.0±127.9	(19.6–727)
Serum SHB (nmol/l)	79.1±33.0	(28–180)
Ratio of estradiol to SHBG	1.1±1.8	(0.16–10.3)
Serum isoflavonoid concentration		
Genistein (nmol/l)	413.9±643.9	(3.7–4085)
Daidzein (nmol/l)	162.0±203.9	(3.1–906)
Equol[a] (nmol/l)	39.5±96.9	(2.06–716)

METs, metabolic equivalents; ALP, alkaline phosphatase; SHBG, sex hormone-binding globulin.
[a]2.06 nmol/l was allotted to 45 women with an undetectable level of equol (<2.06 nmol/l).

Table 2. Partial correlation coefficients for serum estradiol and soy intake with bone health parameters in 87 postmenopausal Japanese women

	Bone mass density		Serum bone ALP	
	Age-adjusted	Adjusted[a]	Age-Adjusted	Adjusted[b]
Serum estradiol	0.22*	0.12	–0.07	–0.04
Serum SHBG	–0.38**	–0.38**	0.11	–0.09
Estradiol/SHBG	0.43**	0.38**	–0.12	0.04
Soy product intake[c]	–0.04	–0.07	–0.13	–0.03
Isoflavone intake[c]	–0.04	–0.02	–0.12	–0.02
Serum isoflavonoids[d,e]	–0.05	–0.11	0.18	0.16
Serum genistein	–0.05	–0.10	0.16	0.16
Serum daidzein	–0.04	–0.13	0.21	0.20
Serum equol[e]	0.19	0.11	–0.15	–0.11

*$p < 0.05$; **$p < 0.01$.
[a]Adjusted for age, body mass index, age at menarche, smoking status, and intake of vegetable fat, vitamin C and salt.
[b]Adjusted for age, age at menarche and carbohydrate intake.
[c]Energy-adjusted.
[d]Genistein, daidzein plus equol.
[e]2.06 nmol/l was allotted to 45 women with an undetectable level of equol (<2.06 nmol/l).

intact. When we restricted the analysis to 61 women who had a natural menopause, the mean ± SD of serum E_2 concentrations was 44.0 ± 19.1 pmol/l (range 20.0–131 pmol/l). The findings on E_2, the E_2/SHBG ratio, isoflavonoids and soy intake in relation to BMD were not substantially altered; the correlation between E_2/SHBG ratio and BMD remained statistically significant ($r = 0.30, p = 0.03$) after controlling for the covariates.

Three women reported a history of osteoporosis but had never received any pharmacologic treatment, including supplementation of flavonoids. Exclusion of these women did not alter the results of the present study. For example, the correlations of BMD with the E_2/SHBG ratio and serum isoflavonoids were 0.40 and −0.14, respectively, after controlling for the covariates. We could not confirm whether flavonoid supplements had been used by women without a history of osteoporosis.

Discussion

We observed that the E_2/SHBG ratio, which may reflect the bioavailable estrogen level, was significantly associated with BMD. However, none of the serum isoflavone levels, or soy product and isoflavone intake, was associated with BMD, in spite of isoflavone's known estrogenicity.

A recent large randomized, double-masked, placebo-controlled 4-year study failed to show any effect of ipriflavone (600 mg/day) on BMD and fracture rates in postmenopausal women with osteoporosis [16].

Previously, two intervention studies examined the effect of dietary soy on BMD [17,18]. In a study reported by Potter et al. [17], diets with 90 mg, 56 mg, and 0 mg of soy isoflavones per day over 6 months increased BMD of the lumbar spine (L1–L4) in postmenopausal women by 2.2%, –0.2% and –0.6%, respectively. Only the diet with the highest isoflavone level showed a moderate but statistically significant increase in BMD compared with a control diet (with 0 mg isoflavone). In our study, the estimates of soy product and isoflavone intake may be underestimated by our questionnaire because, in the validity test, the soy product and isoflavone intake estimated from the 12 daily diet records over 1 year were about 25% higher than the estimates from the questionnaire. Even considering this bias, most of our women subjects may have had less than 90 mg of isoflavones per day. Their intake of isoflavones and, probably, serum isoflavonoid levels may have been too low to exhibit an estrogenic effect on bone. It is also possible that soy intake when peak bone mass was attained is the determinant of current BMD. Serum isoflavone levels cannot be a long-term markers of soy exposure. No long-term biomarkers are currently available. A dietary history approach to measure the more distant past would be important.

The magnitude of correlation between isoflavone intake and BMD in the present study was similar to that reported by Kimira et al. (r = –0.09) [7]. The association between isoflavone intake and BMD was not very strong even among the studies that reported positive associations [8–10]. Somekawa et al. [10] reported a relatively large association compared with those in the other studies: BMD was greater by 8% in women with a high intake of isoflavones (>65 mg/day; the mean is about 81 mg/day) compared with women with a low intake (<35 mg/day; the mean is about 29 mg/day). Our results were only obtained at the level of the calcaneus. Different compartments of the skeleton may have a different response to soy or isoflavone intake. A discrepancy in the results between the present study and those that reported significant positive associations [8–10] may be due to differences in the bone site used for BMD measurement, BMD measurement method, dietary assessment, range of soy or isoflavone intake among study subjects, and selection of factors used for statistical adjustments.

Serum equol was not detectable in about half the women. The use of the minimum value for them might have affected the real association between serum equol and BMD or serum bone ALP. When we compared BMD and serum bone ALP between women with detectable and undetectable equol levels, there was a marginally significant difference in the mean BMD (356.3 vs 334.4, $p = 0.07$) between the two groups of women after controlling for age and the other covariates. We cannot rule out the possibility that equol, a metabolite of daidzein, may be positively associated with BMD.

It is generally recognized that estrogen deficiency plays a role in the genesis of postmenopausal bone loss. Estrogen therapy has been shown to reduce the rate of bone loss [13,18]. However, the contribution of an endogenous estrogen level after menopause to bone loss has not been studied in depth. The results from the studies evaluating the relationship between serum estrogen concentrations and BMD have been inconsistent. We observed a significant correlation between the E_2/SHBG ratio and BMD. Some previous studies also found a significant positive association between serum E_2 and BMD in postmenopausal women [19,20], but others did not [21,22].

The serum E_2/SHBG ratio and soy product intake or serum isoflavones did not confound each other in relation to BMD. The effect of currently circulating bioavailable estradiol on BMD may be not attenuated by soy intake or serum isoflavone levels.

Serum bone-specific ALP has been considered to be a marker for bone formation and to be associated with future bone loss. Estrogen administration suppresses the rise in the ALP level in postmenopausal women. In the present study, the E_2/SHBG ratio was inversely correlated with the serum ALP level, but the correlation was weak. Soy intake was not associated with serum bone ALP. Dietary soybean did not suppress the total or bone-specific ALP level in the ovariectomized rat model of osteoporosis [4,5].

Although the present study has limitations reflecting the nature of a cross-sectional study and the problems inherent in epidemiologic methods assessing nutritional status, the results support the association of BMD with endogenous estrogen levels; however, they do not support the association with soy or isoflavone intake and serum isoflavonoid levels.

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Weight Change in Relation to Natural Menopause and Other Reproductive and Behavioral Factors in Japanese Women

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PURPOSE: To evaluate the effect of menopause on weight change in Japanese women.
METHODS: Community-based sample of 828 Japanese women who were premenopausal and aged 40 to 54 years completed a self-administered questionnaire asking information on demographic factors, body size, reproductive history and dietary and behavioral factors in 1992. They responded to a follow-up questionnaire asking weight and menopausal status in 1998.
RESULTS: Women gained weight modestly, on average, 0.17 kg during the 6-year study period. Weight gain was significantly higher in women who remained premenopausal at follow-up than those who had natural menopause during the study period. Weight gain was significantly associated with early menarche in women who had natural menopause and with high parity in women remained premenopausal.
CONCLUSION: Reproductive factors rather than sociodemographic and behavioral factors appeared to be associated with weight change during the perimenopausal period. Onset of menopause may diminish weight gain. In contrast, early menarche and high parity showed relationships with weight gain.
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KEY WORDS: Weight gain, Menopause, Menarche, Parity, Diet, Japanese.

INTRODUCTION

Many women report that their weight gain started around the time of menopause (1). Whether menopause has effect on weight gain has been a topic in previous studies. Some, but not all, cross-sectional studies reported no significant difference in body mass index (BMI, kg/m2) between pre- and postmenopausal women (2–4). Longitudinal studies found no distinct increase in the rate of weight gain at the time of menopause (5–8). These results indicated that weight gain appeared to be due to aging, rather than menopausal per se (1). These studies also showed the rate of weight gain during the menopausal period vary in ethnicity. The relation of menopause to weight change may differ by ethnicity.

So far, there were three studies on menopause and body weight in Japanese women. Ijuin et al. (9) cross-sectionally compared BMI between pre- and postmenopausal women and observed significantly higher BMI in postmenopausal women. However, Shibata et al. (10) reported that premenopausal women aged 45 and over were slightly overweight as compared with postmenopausal women with corresponding age. Akahoshi et al. (3) longitudinally studied BMI in women from Adult Health Study of the Radiation Effects Research Foundation for 18 years around the time of natural menopause. BMI increased about 0.5 during the period but did not exhibit a significant increase at the onset of natural menopause. In all of these studies, subjects were not representative of Japanese women. Baseline data from the Takayama Study, a population-based cohort study in Japan, showed somewhat lower BMI in postmenopausal women than premenopausal women in any age group between 35 and 60 years. Japanese women may lose weight around the time of menopause. In the present study, we evaluated the change of weight in relation to menopause during perimenopausal period in a sample from participants in the Takayama Study (11). In addition, we examined whether other reproductive histories and dietary and behavioral factors are related to weight change during the period.

METHODS

All women were participants in the Takayama Study (11) and have been the subjects of reports in the past (12). The rationale, design, and methods of the Takayama Study (11), as well as the characteristics of the participants have been

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