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Egg consumption, serum total cholesterol concentrations and coronary heart disease incidence: Japan Public Health Center-based prospective study

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Limited egg consumption is often recommended to reduce serum cholesterol concentration for the prevention of CHD. We examined the association of egg consumption and total cholesterol concentration with the risk of CHD. A total of 90 735 subjects (19 856 men and 21 408 women, aged 40–59 years in cohort I; 23 463 men and 26 008 women, aged 40–69 years in cohort II) were followed from 1990–4 to the end of 2001 under the Japan Public Health Center-based prospective study. Total cholesterol was obtained in 36 % of the subjects. Men and women were combined for the analyses. The subjects were categorised into four groups according to egg consumption. Subjects with total cholesterol ≥2200 mg/l were less frequent in frequent egg consumption groups in both cohorts (trend $P<0{\cdot}0001$). Subjects with <1 d/week of egg consumption were more likely to avoid a cholesterol-rich diet. Egg consumption was not associated with the risk of CHD, although total cholesterol was significantly related to the risk of CHD. The multivariate hazard ratio of CHD in subjects with total cholesterol ≥2400 *v.* <1800 mg/l was 2·17 (95 % CI 1·22, 3·85; trend $P=0{\cdot}0018$). In conclusion, eating eggs more frequently, up to almost daily, was not associated with an increase in CHD incidence for middle-aged Japanese men and women. Subjects with hypercholesterolaemia were less frequently in frequent egg consumption groups, probably because they avoided eating eggs.

Cholesterol: Coronary disease: Risk factors: Epidemiology

Since eggs are a concentrated source of cholesterol in the diet, limited egg consumption is often recommended to reduce total serum cholesterol concentrations and to help prevent CHD (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001). While several metabolic-ward studies have demonstrated that dietary cholesterol is one of the major determinants of total cholesterol (Mattson *et al.* 1972; Keys, 1984), other studies have failed to show changes in total cholesterol when eggs were added to diets that already contained moderate amounts of cholesterol (Kummerow *et al.* 1977; Porter *et al.* 1977; Flynn *et al.* 1979; Oh & Miller, 1985). There have been few epidemiological studies in free-living populations that explored the relationship between egg consumption and total cholesterol and/or risk of CHD, and none of the studies found an association between egg consumption and CHD incidence (Nichols *et al.* 1976*a*,*b*; Frank *et al.* 1978; Dawber *et al.* 1982; Hu *et al.* 1999). A study by Hu *et al.* (1999) with 117 933 subjects in the USA showed no relationship between egg consumption of up to one per d and the risk of CHD or stroke. However, in geographic areas where egg consumption makes a greater contribution to total dietary cholesterol intake than in the USA, the results may be different (Ueshima *et al.* 1982; Okayama *et al.* 1995; Yoshida *et al.* 1998). In fact, a recent study using the database of NIPPON DATA80, which included more than 10 000 randomly selected subjects in Japan, found a dose–response relationship between egg consumption and total cholesterol in women, but not in men. We also found statistically non-significant tendencies for a higher mortality due to CHD with an increase in egg consumption in women with a 14-year follow-up (Nakamura *et al.* 2004). Thus, at least a study in Japan, where egg consumption makes a greater contribution to total dietary cholesterol intake than in Western populations, showed that egg consumption was related to total cholesterol

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concentration in women, but was not associated with a higher mortality due to CHD.

The purpose of the present study was to examine the association between egg consumption and total cholesterol concentration, and CHD incidence in a larger number of subjects.

Subjects and methods

Study population

The Japan Public Health Center-based prospective study on cancer and CVD commenced in 1990 for the first group (cohort I) and in 1993 for the second group (cohort II). Cohort I covered four areas administered by public health centres in four prefectures (Iwate, Akita, Nagano and Okinawa). Cohort II included five public health centre areas in five prefectures (Ibaraki, Niigata, Kochi, Nagasaki and Okinawa). Cohort I was comprised of all residents aged 40–59 years on 1 January 1990 and cohort II was comprised of all residents aged 40–69 years on 1 January 1993. The study subjects were identified by population registries maintained by local municipalities. We defined a population-based cohort of 54 512 subjects in cohort I (27 439 men and 27 073 women) and 62 415 subjects in cohort II (31 750 men and 30 665 women). A total of 162 subjects in cohort I and 127 subjects in cohort II were excluded because of the following reasons: being non-Japanese, those who had already moved away at baseline, and those who were outside of the age parameters. This left 54 350 eligible subjects in cohort I and 62 288 eligible subjects in cohort II. The present study was approved by the Institutional Review Board of the National Cancer Center (Tokyo, Japan). The study design is described in detail elsewhere (Watanabe *et al.* 2001).

Baseline survey

A self-administered questionnaire was distributed mostly by hand and partly by mail to the study subjects in 1990 for cohort I and in 1993–4 for cohort II. They were asked about their personal and familial medical histories, smoking, alcohol consumption, dietary habits and other lifestyle factors (Tsugane & Sobue, 2001; Tsugane *et al.* 2001; Sobue *et al.* 2001). Among the eligible subjects, 43 160 subjects in cohort I (overall 79 %; 76 % men and 82 % women) and 52 271 subjects in cohort II (overall 84 %; 81 % men and 86 % women) returned the questionnaire. From them, we excluded subjects with a self-reported medical history of myocardial infarction, IHD, stroke or cancer before the survey began (1555 subjects in cohort I and 2032 subjects in cohort II). This additionally reduced the number of eligible subjects to 41 605 subjects in cohort I and 50 239 subjects in cohort II. Finally, we excluded subjects with no egg consumption data (341 subjects in cohort I and 768 subjects in cohort II), leaving 90 735 subjects (19 856 men and 21 408 women in cohort I, and 23 463 men and 26 008 women in cohort II) as study subjects.

The average frequency of egg consumption was reported in four categories in cohort I: 'less than 1 d/week', '1–2 d/week', '3–4 d/week' and 'almost every day'. Subjects in cohort II were asked about the average frequency of egg consumption divided into five categories: 'never', 'less than 1 d/week', '1–2 d/week', '3–4 d/week', and 'almost every day'. Categories: 'never' and 'less than 1 d/week' in cohort II were combined into the one category, resulting in four categories, the same as those of cohort I. The reproducibility of egg consumption, 5 years apart in cohort I, was measured with the Spearman rank correlation in ninety-four men and 107 women (correlation coefficient was 0·29 for men and 0·40 for women) (Tsubono *et al.* 2003), and that of 1 year apart in cohort II in 143 men and 146 women (correlation coefficient was 0·50 for men and 0·53 for women) (Ishihara *et al.* 2003). The validity of egg consumption was estimated with the Spearman rank correlation, with egg consumption based on four 7 d direct diet records among ninety-four men and 107 women in cohort I (correlation coefficient 0·25 for men and 0·28 for women) (Tsubono *et al.* 2003), and that in cohort II in 174 men and 176 women (correlation coefficient 0·47 for men and 0·45 for women) (Ishihara *et al.* 2003).

The frequency of weekly intake of the other twenty-six food items was reported under four categories: 'rarely', '1–2 d/week', '3–4 d/week' and 'almost every day'. The weekly frequency for each food item was calculated according to a score assigned to each frequency category (0, 1·5, 3·5 and 7, respectively).

Also, the subjects were asked whether they were intentionally restricting their intake of certain kinds of foods, for example, in cohort I, 'Do you intend to avoid cholesterol-rich diets?'. In cohort II, the questions were more specific, for example, 'Do you intend to avoid cholesterol-rich diets, such as eggs and fat-rich meat?'.

Smoking status was defined as never smoker, ex-smoker and current smoker, and alcohol consumption was classified into six categories in men: 'non-drinkers' (<1 d/month), 'occasional drinkers' (1–3 d/month), 'weekly alcohol consumption of 1–149 g/week', '150–299 g/week', '300–449 g/week' and '≥ 450 g/week'. The algorithm for calculating the amount of alcohol has been reported previously (Iso *et al.* 2004).

Serum total cholesterol concentration data

The serum total cholesterol concentration data were obtained in subjects who participated in a health check-up programme conducted by each local government. Among the study subjects, health check-up data were obtained in 29 % of men and 46 % of women in cohort I, and 25 % of men and 45 % of women in cohort II. Total cholesterol concentration was analysed enzymically. With regard to the precision and accuracy of the measurement of total cholesterol, all twenty-three laboratories that participated in the present investigation were approved by the Osaka Medical Center for Health Science and Promotion (Japan), a member of the Cholesterol Reference Method Laboratory Network (Myers *et al.* 2000; Nakamura *et al.* 2003).

Hypercholesterolaemia was defined as subjects with total cholesterol concentration ≥ 2200 mg/l.

Follow-up and end-point ascertainment

We followed study subjects until 31 December 2001. The end point for the present study was the incidence of CHD (including CHD death and non-fatal myocardial infarction). Medical

records were reviewed by registered hospital workers or the study physicians, blinded to the lifestyle data. CHD events were registered if they occurred after the date of return of the baseline questionnaire and before 1 January 2002.

The criteria of acute myocardial infarction were based on WHO MONICA Projects (Monitoring of Trends and Determinants in CVD): symptoms plus either diagnostic electrocardiogram changes or elevated cardiac enzymes (Tunstall-Pedoe *et al.* 1994). For complete surveillance of non-fatal myocardial infarction, we asked the possible cases who reported a history of myocardial infarction in a 5-year and 10-year follow-up questionnaire, but had not been registered as a case, by letter or telephone about the onset of myocardial infarction and for permission to review their medical records. Non-fatal myocardial infarction for which confirmatory information was obtained by letter or telephone, but for which no medical records were available, were regarded as probable (8 % of non-fatal myocardial infarctions).

To complete the surveillance for fatal CHD, we also conducted a systematic search for death certificates. The underlying causes of death were coded according to the 9th International Classification of Disease for the National Vital Statistics (known as ICD-9) and until the end of 1994, and according to the 10th International Classification of Disease (known as ICD-10) from the beginning of 1995. For all fatal CHD listed on the death certificate, but which had not been registered, medical records in registered hospitals were reviewed by hospital workers, the study physicians, or research physicians–epidemiologists. When no medical records were available (death certificate information only), we regarded these fatal CHD as probable CHD (36 % of fatal CHD).

Statistical analysis

SAS version 8.02 for Windows (SAS Institute, Cary, NC, USA) was used throughout the analyses. Men and women were analysed together in cohort I and cohort II so that the number of cases was sufficient for the analyses. The χ^2 test was used to compare dichotomous variables, and a one-way ANOVA was used to compare means among the four groups according to egg consumption. The Mantel–Haenszel χ^2 statistical test was used to detect deviation from linearity in the association between nominal variables and the categories of egg consumption, and the ANOVA was used to detect deviation from linearity in the association between continuous variables and the categories of egg consumption. Person-years of follow-up were determined from 1 January 1990 (cohort I) or 1993–4 (cohort II) until the date of a subject's CHD event, the date of moving from a public health centre area, or 31 December 2001, whichever occurred first.

To examine the association between egg consumption and CHD incidence, we calculated the age and sex- and multivariate-adjusted hazard ratios for CHD incidence using a Cox's proportional hazard model, taking the highest egg consumption group, namely almost daily, as the reference (Cox, 1972). For multivariate analyses, age at baseline, sex, BMI (kg/m^2), diabetes defined as subjects with a self-reported diagnosis of diabetes mellitus and/or subjects who were taking diabetes-treating medications, hypertension defined as subjects with a self-reported diagnosis and/or subjects who were taking anti-hypertensive medications, cigarette smoking (never, ex-smoker and current smoker), alcohol intake (six categories), use of cholesterol-lowering drugs, dietary intake categories of meat (beef and pork), fish (fresh and dry), vegetables (green, yellow and others), fruits, whether or not intended to avoid cholesterol-rich diets, and cohort effects were entered as covariates. Tests of linear trends across groups were conducted by assigning an ordinal value from 1 to 4 for each level of consumption and modelling this as a continuous variable in separate Cox proportional hazard models.

The secondary analyses were performed in cohort I and II separately, in self-reported diabetic patients, in subjects excluding those who had an intension to restrict cholesterol-rich diets, and in subjects excluding those who taking cholesterol-lowering drugs or those with total cholesterol concentration $\geq$2200 mg/l. Furthermore, analysis was performed using quantitative variables (cholesterol and systolic blood pressure) in those who participated in a health check-up programme.

To examine the association between total cholesterol concentration and CHD incidence, we divided the subjects into five categories according to total cholesterol concentration: ' $<$ 1800', '1800–1999', '2000–2199', '2200–2399' and ' $\geq$ 2400' mg/l, and we calculated the age- and sex-adjusted and multivariate-adjusted hazard ratios for CHD incidence using a Cox's proportional hazard model, taking the total cholesterol concentration $<$1800 mg/l group as a reference. For multivariate analyses, we adjusted for age, sex, BMI, systolic blood pressure, diabetes, uses of cholesterol-lowering drugs or anti-hypertensive drugs, smoking (never, ex-smoker and current smoker), alcohol drinking (six categories), whether or not intended to avoid cholesterol-rich diets, consumption frequencies of egg, meat, fish, vegetables, fruits, and cohort effects.All P values $<$0·05 were considered significant. Data are presented as the mean values and SD, unless stated otherwise.

Results

Baseline characteristics

Baseline characteristics in each egg consumption category are shown in Table 1. There were more men and thus current smokers in the 1–2 d/week egg consumption groups (trend P=0·0001 and $P<$0·0001), the reason for which is not clear. The mean age in the less than 1 d/week egg consumption group was higher (trend $P<$0·0001). Weekly drinkers were less frequent in the less than 1 d/week egg consumption group and hypertension was more frequent in the less-frequent egg consumption groups (trend $P<$0·0001 for both). Cholesterol-lowering drugs were more frequently taken in the less-frequent egg consumption groups (trend $P<$0·0001).

A significant trend was noted on the information regarding the intention to avoid a cholesterol-rich diet (trend $P<$0·0001). Namely, the fewer eggs consumed, the more frequent the subjects had an intention of avoiding taking a cholesterol-rich diet. Dietary intake of meat (beef and pork), fish (fresh and dry), vegetables (green, yellow and others) and fruits were more frequent among those who in the more-frequent egg consumption groups (all trends $P<$0·0001).

Data for total cholesterol concentration were available in about 36 % of the subjects. Baseline characteristics in each egg consumption category for the subjects with total cholesterol concentration data are shown in Table 2. An inverse

Table 1. Baseline characteristics according to egg consumption categories*
(Mean values and standard deviations)

Egg consumption...	< 1 d/week (*n* 10 491)		1–2 d/week (*n* 20 802)		3–4 d/week (*n* 31 182)		Almost daily (*n* 28 260)		
Baseline characteristics	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Trend *P*
Men (%)	46·5		50·9		46·6		47·1		0·0001
Age (years)	55·1	8·5	51·9	7·8	51·9	7·7	52·8	7·9	<0·0001
BMI (kg/m^2)	23·7	3·2	23·6	3·1	23·5	3·1	23·5	3·2	<0·0001
Current smoker (%)	28·1		30·5		27·0		26·7		<0·0001
Drinker (≥ one per week) (%)	32·4		38·6		37·5		37·8		<0·0001
Hypertension (%)	17·9		16·0		14·5		14·5		<0·0001
Diabetes (%)	3·5		3·5		3·0		3·6		0·67
Use of cholesterol-lowering drugs (%)	2·7		2·0		1·6		1·2		<0·0001
Cholesterol restriction† (%)	70·7		66·7		66·3		66·2		<0·0001
Meat (d/week)	4·9	1·7	5·0	2·4	5·1	2·2	5·3	2·2	<0·0001
Fish (d/week)	4·8	2·2	4·8	2·1	5·2	2·0	5·4	2·0	<0·0001
Vegetables (d/week)	4·4	2·3	5·0	1·9	5·6	1·7	5·9	1·6	<0·0001
Fruits (d/week)	3·2	2·6	3·5	2·5	4·2	2·5	4·5	2·5	<0·0001

* Cohort I (1990–2001) and cohort II (1993–2001) of Japan Public Health Center-based prospective study, combined.
† Subjects who had an intention to restrict cholesterol-rich diets.

correlation between egg consumption and mean total cholesterol concentration as well as the frequency of the subjects with hypercholesterolaemia (those with total cholesterol concentration ≥2200 mg/l), mean systolic blood pressures were noted (all trends $P<0·0001$). The other baseline characteristics were basically similar to those in Table 1.

Egg consumption and coronary heart disease incidence – age and sex- and multivariate-adjusted Cox analyses

Altogether, there were 462 incidences of CHD during the mean follow-up of 10·2 years. Of them, 120 cases were fatal and 342 cases were non-fatal. Of the 120 cases of fatal CHD, sixty-seven cases died within 1 h after the onset of symptoms.

The number of cases, their male percentage, person-years, age and sex-adjusted as well as multivariate-adjusted hazard ratios and their 95 % CI for CHD incidence according to egg consumption categories are shown in Table 3. The category of almost daily egg consumption was taken as the reference. There was no significant association between egg consumption and CHD incidence.

The secondary analyses in cohort I and II separately ($P=0·23$ and $P=0·98$, respectively), in self-reported diabetic patients (trend $P=0·84$), analyses excluding subjects who had an intention to restrict cholesterol-rich diets (trend

Table 2. Baseline characteristics according to egg consumption categories in subjects with serum total cholesterol concentration data*
(Mean values and standard deviations)

Egg consumption...	< 1 d/week		1–2 d/week		3–4 d/week		Almost daily		
Baseline characteristics	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Trend *P*
Subjects at risk† (*n*)	3633		6962		11 542		10 892		
Men (%)	32·1		36·8		34·3		35·8		0·04
Age (years)	58·0	8·0	54·2	8·0	53·8	7·9	54·7	7·9	<0·0001
BMI (kg/m^2)	23·9	3·3	23·7	3·1	23·6	3·0	23·5	3·3	<0·0001
Current smoker (%)	16·1		19·8		17·6		17·3		0·29
Drinker (≥ one per week) (%)	23·2		29·9		29·5		30·4		<0·0001
Systolic blood pressure (mmHg)	134	19	131	18	130	18	130	18	<0·0001
Diastolic blood pressure (mmHg)	79	11	78	11	78	12	78	11	<0·0001
Hypertension (%)	20·8		17·5		15·2		15·9		<0·0001
Diabetes (%)	2·6		3·0		2·4		3·2		0·16
Total cholesterol (mg/l)	2050	370	2030	360	2000	350	2000	340	<0·0001
Total cholesterol ≥ 2200 mg/l (%)	33·5		29·7		27·5		27·5		<0·0001
Use of cholesterol-lowering drugs (%)	3·0		2·3		1·9		1·2		<0·0001
Cholesterol restriction‡ (%)	76·6		70·0		69·7		69·3		<0·0001
Meat (d/week)	4·8	1·7	4·9	2·5	5·0	2·3	5·2	2·2	<0·0001
Fish (d/week)	5·1	2·1	5·0	2·0	5·5	1·9	5·7	1·8	<0·0001
Vegetables (d/week)	4·8	2·3	5·3	1·8	5·8	1·5	6·1	1·5	<0·0001
Fruits (d/week)	3·6	2·7	4·0	2·5	4·6	2·4	4·9	2·5	<0·0001

* Cohort I (1990–2001) and cohort II (1993–2001) of Japan Public Health Center-based prospective study, combined.
† Total number of subjects was 33 029.
‡ Subjects who had an intention to restrict cholesterol-rich diets.

Table 3. Coronary heart disease incidence according to egg consumption categories in the Japan Public Health Center-based prospective study (Hazard ratios (HR) and 95 % CI)

	< 1 d/week		1–2 d/week		3–4 d/week		Almost daily		
Egg consumption...	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	Trend *P*
Subjects at risk* (*n*)	10 491		20 802		31 182		28 260		
Person-years	96 748		213 907		323 856		292 858		
CHD incidence									
Cases† (*n*)	64		110		147		141		
Men (%)	72		84		76		81		
Incidence (per 1000 person-years)	0·66		0·51		0·45		0·48		
Age and sex-adjusted HR	1·28	0·95, 1·72	1·11	0·86, 1·42	1·01	0·80, 1·27	1	–	0·11
Multivariate-adjusted HR‡	1·19	0·86, 1·64	1·00	0·77, 1·30	1·00	0·79, 1·26	1	–	0·45

* Total number of subjects was 90 735.
† Subtotal of subjects was 462.
‡ Multivariate Cox analysis adjusted for age, sex, BMI, hypertension, diabetes, use of cholesterol-lowering drugs, smoking (never, ex-, and current smoker), alcohol drinking (six categories), whether or not intended to avoid cholesterol-rich diets, consumption frequencies of meat, fish, vegetables, fruits, and cohort effects.

$P=0{\cdot}45$), analyses excluding those who were taking cholesterol-lowering drugs or those with total cholesterol concentration $\geq$ 2200 mg/l (trend $P=0{\cdot}72$), analyses using quantitative variables (cholesterol and systolic blood pressure) in those who participated in a health check-up programme ($P=0{\cdot}09$), all yielded the basically similar results: there was no significant association between egg consumption and CHD incidence.

Total cholesterol concentration and coronary heart disease incidence – age and sex-adjusted and multivariate-adjusted Cox analyses

The number of cases, their male percentage, person-years, age and sex-adjusted as well as multivariate-adjusted hazard ratios and their 95 % CI for CHD incidence according to the total cholesterol concentration categories are shown in Table 4. The percentage of men progressively decreased in the groups with the higher total cholesterol concentration. Total cholesterol concentration was significantly related to CHD incidence (hazard ratio of CHD in those with total cholesterol concentration $\geq$2400 mg/l was 2·17 (95 % CI 1·22, 3·85) as compared with those with total cholesterol concentration $<$1800 mg/l; trend $P=0{\cdot}0018$).

Discussion

In the present study, we found that eating eggs more frequently, up to almost daily, was not associated with any consistent adverse effect on CHD incidence. We confirmed a positive association between total cholesterol concentration and CHD incidence in Japanese as in previous studies (Kodama *et al.* 1990; Kitamura *et al.* 1994; Okamura *et al.* 2003). We also found an inverse correlation between egg consumption and mean total cholesterol concentration as well as the frequency of the subjects with hypercholesterolaemia. The subjects with hypercholesterolaemia were more frequent among the groups of subjects who ate fewer eggs than those in the groups of subjects who ate more eggs. Controversies exist as to the relationship between dietary egg consumption and total cholesterol concentration. Some studies have shown no relationship between egg consumption and total cholesterol concentration (Mattson *et al.* 1972; Nichols *et al.* 1976*a*,*b*; Kummerow *et al.* 1977; Porter *et al.* 1977; Frank *et al.* 1978; Flynn *et al.* 1979; Dawber *et al.* 1982; Keys,

Table 4. Coronary heart disease incidence according to serum total cholesterol concentration categories in men and women (Japan Public Health Center-based prospective study) (Hazard ratios (HR) and 95 % CI)

	< 1800		1800–1999		2000–2199		2200–2399		≥ 2400		
Total cholesterol concentration (mg/l)...	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	Trend *P*
Subjects at risk* (*n*)	9162		7528		6896		4959		4484		
Men (%)	45·0		38·0		31·6		28·1		23·3		< 0·0001
Person-years	96 027		77 847		70 822		50 438		45 423		
CHD incidence											
Cases† (*n*)	28		20		33		22		23		
Men (%)	79		75		70		73		70		
Incidence (per 1000 person-years)	0·29		0·26		0·47		0·44		0·51		
Age and sex-adjusted HR	1	–	0·97	0·54, 1·71	1·93	1·16, 3·20	1·93	1·10, 3·38	2·48	1·42, 4·33	0·0001
Multivariate-adjusted HR‡	1	–	0·94	0·52, 1·68	1·85	1·11, 3·10	1·68	0·95, 3·00	2·17	1·22, 3·85	0·0018

* Total number of subjects was 33 029.
† Subtotal of subjects was 126.
‡ Multivariate Cox analysis adjusted for age, sex, BMI, systolic blood pressure, diabetes, use of cholesterol-lowering drugs or anti-hypertensive drugs, smoking (never, ex-, and current smoker), alcohol drinking (six categories), whether or not intended to avoid cholesterol-rich diets, consumption frequencies of egg, meat, fish, vegetables, fruits, and cohort effects.

1984; Oh & Miller, 1985), two studies have shown an inverse relationship (Tillotson *et al.* 1997; Song & Kerver, 2000), and one found a positive relationship (Nakamura *et al.* 2004). As pointed out by Tillotson *et al.* (1997), the findings of the present study may be explained by the assumption that subjects with high total cholesterol concentration reduced their egg intake more than the others, and therefore we observed an inverse relationship between egg consumption and the frequency of hypercholesterolaemia. This assumption is supported by the trend among categories of egg consumption in the frequencies of intention to avoid taking a cholesterol-rich diet. Therefore, a cause–effect reversal might have occurred between egg consumption and total cholesterol concentration.

Why are the results of the present study and those of the NIPPON DATA80 (Nakamura *et al.* 2004), with regard to the association between egg consumption and total cholesterol concentration, different? It is probably related to the difference in the year the two studies started. The NIPPON DATA80 study started in 1980, and the Japan Public Health Center-based study started in 1990 for cohort I and in 1993 for cohort II. In Japan, public awareness of total cholesterol concentration as one of the risk factors for atherosclerotic diseases was not remarkable until the mid 1980s. According to the National Nutritional Surveys, age-adjusted total cholesterol concentration increased from 1870 to 2020 mg/l for men and from 1900 to 2030 mg/l for women between 1980 and 1989 in Japan (Okayama *et al.* 1993). After the Health and Medical Service Law for the Elderly was enacted in 1983, all Japanese citizens aged 40 years and over had the opportunity to undergo screening for total cholesterol concentration, and those with hypercholesterolaemia were provided with health services such as health education or guidance to prevent coronary disease (Ministry of Health & Welfare, 1987). Furthermore, cholestyramine appeared in the market in July 1985 and pravastatin in October 1989. The campaigns made by pharmaceutical companies to promote cholesterol-lowering drugs started to escalate, especially after the appearance of pravastatin in the market. Along with these movements, eggs became a popular media icon for the many of the dietary excesses of the population and the image for cholesterol, both dietary and serum (McNamara, 2000).

Eggs contain many other nutrients besides cholesterol, including unsaturated fats that may be beneficial in preventing CHD. Also, dietary cholesterol is not the principal factor affecting blood cholesterol concentration. The main dietary determinants of serum cholesterol are saturated fat and *trans*-fat intake. Therefore, restriction of egg consumption alone may not be sufficient for preventing CHD. However, in Japan, the reported *per capita* annual egg consumption in 1999 was 320, which was more than any other countries on the list (Bell, 2001), and previous reports showed that egg consumption made a greater contribution to total dietary cholesterol intake than in the USA (Ueshima *et al.* 1982; Okayama *et al.* 1995; Yoshida *et al.* 1998). Therefore, care for restricting egg consumption may be more important in Japan than in the other countries.

The major strengths of the present study include its prospective design, a general population with a high response rate (80 %), and the relatively low proportion of subjects lost to follow-up (0·04 %). The findings of the present study can be generalised to middle-aged and elderly Japanese men and women, because the study subjects were selected from the general population, and there was a high response rate. Moreover, two cohorts starting at different times produced the same results.

One of the limitations of the study was that we did not specify portion sizes on the food-frequency questionnaires, and thus we do not have reliable nutrient intake values. Therefore, we cannot use total energy intake as a covariate in the analyses. As we included dietary intake categories of meat, fish, vegetables, and fruits as covariates in the analyses, this limitation might have become less problematic. Second, total cholesterol concentration was available only in part of the subjects. However, the trend in the frequencies of intention to restrict taking cholesterol-rich diets was not different between subjects with or without the total cholesterol concentration data. This may imply that subjects with or without the total cholesterol concentration data were not different with regard to their health-conscious attitudes.

Conclusion

We found that eating eggs more frequently, up to almost daily, was not associated with any increase in CHD incidence. We found an inverse correlation between egg consumption and the frequency of hypercholesterolaemia in both sexes in both cohorts, probably because hypercholesterolaemic individuals avoided eating eggs.

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