

A Prospective Study of Egg Consumption and Risk of Cardiovascular Disease in Men and Women

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ELEVATED LOW-DENSITY LIPOPROTEIN (LDL) cholesterol is a major risk factor for coronary heart disease (CHD).¹ Dietary cholesterol raises LDL cholesterol levels and causes atherosclerosis in numerous animal models.² In controlled metabolic studies conducted in humans, dietary cholesterol raises levels of total and LDL cholesterol in blood,^{3,4} but the effects are relatively small compared with saturated and *trans*fatty acids.^{5,6} Studies have found that individuals vary widely in their responses to dietary cholesterol based on monitoring their plasma levels.^{7,8} Prospective cohort studies on the relationship of dietary cholesterol with risk of CHD have been inconsistent, with a significant association found in some,^{9,10} but not in most studies.¹¹⁻¹⁷

To avoid elevations in blood cholesterol and reduce CHD risk, the public has been advised to consume no more than

Context Reduction in egg consumption has been widely recommended to lower blood cholesterol levels and prevent coronary heart disease (CHD). Epidemiologic studies on egg consumption and risk of CHD are sparse.

Objective To examine the association between egg consumption and risk of CHD and stroke in men and women.

Design and Setting Two prospective cohort studies, the Health Professionals Follow-up Study (1986-1994) and the Nurses' Health Study (1980-1994).

Participants A total of 37 851 men aged 40 to 75 years at study outset and 80 082 women aged 34 to 59 years at study outset, free of cardiovascular disease, diabetes, hypercholesterolemia, or cancer.

Main Outcome Measures Incident nonfatal myocardial infarction, fatal CHD, and stroke corresponding to daily egg consumption as determined by a food-frequency questionnaire.

Results We documented 866 incident cases of CHD and 258 incident cases of stroke in men during 8 years of follow-up and 939 incident cases of CHD and 563 incident cases of stroke in women during 14 years of follow-up. After adjustment for age, smoking, and other potential CHD risk factors, we found no evidence of an overall significant association between egg consumption and risk of CHD or stroke in either men or women. The relative risks (RRs) of CHD across categories of intake were less than 1 per week (1.0), 1 per week (1.06), 2 to 4 per week (1.12), 5 to 6 per week (0.90), and ≥ 1 per day (1.08) (P for trend = .75) for men; and less than 1 per week (1.0), 1 per week (0.82), 2 to 4 per week (0.99), 5 to 6 per week (0.95), and ≥ 1 per day (0.82) (P for trend = .95) for women. In subgroup analyses, higher egg consumption appeared to be associated with increased risk of CHD only among diabetic subjects (RR of CHD comparing more than 1 egg per day with less than 1 egg per week among diabetic men, 2.02 [95% confidence interval, 1.05-3.87; P for trend = .04], and among diabetic women, 1.49 [0.88-2.52; P for trend = .008]).

Conclusions These findings suggest that consumption of up to 1 egg per day is unlikely to have substantial overall impact on the risk of CHD or stroke among healthy men and women. The apparent increased risk of CHD associated with higher egg consumption among diabetic participants warrants further research.

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300 mg/d of cholesterol and limit consumption of eggs, which contain about 213 mg of cholesterol per egg.^{1,18} However, eggs contain many other nutrients

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besides cholesterol, including unsaturated fats, essential amino acids, folate, and other B vitamins. In addition, consumption of eggs instead of carbohydrate-rich foods may raise high-density lipoprotein (HDL) cholesterol levels^{19,20} and decrease blood glycemic and insulinemic responses.²¹ For these reasons, it is useful to study directly the relationship of egg consumption with risk of CHD, but few epidemiologic studies have addressed this association.²²⁻²⁴ In this article, we examine prospectively the association between egg consumption and risk of CHD and stroke in 2 large cohorts of men and women.

METHODS

The Health Professionals Follow-up Study

The Health Professionals Follow-up Study (HPFS) began in 1986 when 51 529 men who were US health professionals (dentists, optometrists, pharmacists, podiatrists, and veterinarians), aged 40 to 75 years, answered a detailed questionnaire that included a comprehensive diet survey and items on lifestyle practice and medical history. Follow-up questionnaires were sent in 1988, 1990, 1992, and 1994 to update information on potential risk factors and to identify newly diagnosed cases of cardiovascular and other diseases. We excluded from the analysis men who did not satisfy the a priori criteria of reported daily energy intake between 3360 and 17 640 kJ or who left blank more than 70 items of the 131 total food items in the diet questionnaire (n = 1152). We also excluded men with prior diagnoses of cardiovascular disease (n = 5182) or cancer (n = 1644) at baseline. In the primary analyses, we also excluded men who reported diabetes mellitus (n = 1187) or hypercholesterolemia (n = 4458) at baseline because these diagnoses could have led to changes in diet. Incidence of CHD and stroke during the subsequent 8 years was monitored for 37 851 men during follow-up. The follow-up rate for nonfatal events was 97% of the total potential person-years of follow-up.

The Nurses' Health Study

The Nurses' Health Study (NHS) cohort was established in 1976 when 121 700 women who were registered nurses residing in 11 large states, aged 30 to 55 years, provided detailed information about their medical history and lifestyle characteristics.²⁵ Every 2 years, follow-up questionnaires have been sent to update information on potential risk factors and to identify newly diagnosed cases of CHD, stroke, and other diseases. In 1980, a 61-item food frequency questionnaire was included to assess intake of specific fats and other nutrients. In 1984, the food frequency questionnaire was expanded to include 116 items. Similar questionnaires were used to update diet in 1986 and 1990. The reproducibility and validity of the food frequency questionnaires have been described in detail elsewhere.^{26,27}

After up to 4 mailings, 98 462 women returned the 1980 diet questionnaire. We excluded those who left 10 or more items blank, those with implausibly high or low scores for total food intake or energy intake (ie, <2100 kJ/d or >14 700 kJ/d) (n = 5994), and those with previously diagnosed cancer (n = 3526), cardiovascular disease (n = 1812), high blood cholesterol (n = 1821), or diabetes (n = 4122) at baseline. Incidence of CHD and stroke during the subsequent 14 years was monitored for 80 082 women during follow-up. The follow-up rate for nonfatal events was 98% of the total potential person-years of follow-up.

Assessment of Egg Consumption

Validated dietary questionnaires were sent to the HPFS participants in 1986 and 1990 and the NHS participants in 1980, 1984, 1986, and 1990. In all the questionnaires, we asked the participants how often, on average, during the previous year they had consumed eggs (unit of consumption was 1 egg). Nine responses were possible, ranging from never to 6 or more times per day. We divided the participants into 5 categories (<1 per week, 1 per week, 2-4 per week, 5-6 per week, ≥1 per day) based

on the frequency distribution of egg consumption. In a validation study in a subsample of the participants, the correlation coefficient between intakes of eggs assessed by the diet questionnaire and by multiple week diet records was 0.8 for both men²⁸ and women.²⁹ We also computed intake of eggs included in other foods such as cakes, cookies, pancakes, muffins, sweet rolls, and donuts. The amount of eggs estimated from other foods was relatively small in both cohorts (men, 0.4 egg per week; women, 0.3 egg per week), so we used the reported egg consumption as our primary exposure variable. In a secondary analysis, we examined the effect of computed total egg consumption.

End Points

The end points were incident CHD (including nonfatal myocardial infarction [MI] and fatal CHD) and stroke occurring between return of the baseline questionnaire and January 31, 1994 (men), or June 1, 1994 (women). We inquired about occurrence of cardiovascular end points on each biennial questionnaire. Participants reporting an incident MI or stroke were asked for permission to review medical records. Nonfatal MI was confirmed by symptoms plus either typical electrocardiographic changes or increased activities in cardiac enzymes (World Health Organization criteria).³⁰ Infarctions that required hospital admission and for which confirmatory information was obtained by interview or letter, but for which no medical records were available, were designated as probable. We included all confirmed and probable cases in the analyses because results were the same after excluding probable cases. Strokes were confirmed if characterized by a typical neurological defect of sudden or rapid onset, lasting at least 24 hours, and attributable to a cerebrovascular event. Strokes caused by infection or neoplasia were excluded. Strokes were subclassified according to the criteria of the National Survey of Stroke as due to ischemia (embolism or thrombosis), subarachnoid hemorrhage, intracerebral hemor-

rhage, or unknown cause.³¹ If no records could be obtained, strokes were considered probable if they required hospitalization and were corroborated by additional information provided by letter or interview.

Deaths were reported by next of kin, coworkers, postal authorities, or the National Death Index. Using all sources combined, we estimate that follow-up for the deaths was more than 98% complete.³² Fatal CHD was defined as fatal MI if this was confirmed by hospital records or autopsy, or if CHD was listed as the cause of death on the death certificate and this was the underlying and most plausible cause, and evidence of previous CHD was available. The statement of the cause of death on the death certificate was never relied on by itself as providing sufficient confirmation of death due to CHD. Sudden death within an hour of the onset of symptoms in subjects with no other plausible cause of death (other than coronary disease) was also included. Fatal stroke was also confirmed by medical records or autopsy reports, or considered probable if these were not obtainable but stroke was listed as the underlying cause on the death certificate.

Statistical Analysis

Participants contributed follow-up time from the return of the 1986 (men) or the 1980 (women) questionnaire up to the occurrence of a confirmed end point, death, or the end of follow-up (January 31, 1994, for men and June 1, 1994, for women). The relative risks (RRs) were calculated by dividing the incidence of CHD or stroke among men and women in various categories of egg consumption by the incidence among those in the lowest category of intake (<1 egg per week), adjusting for age (5-year categories). To adjust for other risk factors, we used pooled logistic regression,³³ which is asymptotically equivalent to Cox regression for time-dependent covariates. Multivariate models included as covariates were (1) total energy intake (quintiles); (2) smoking (never, past, current 1-14, 15-24, and ≥ 25 cigarettes/d); (3) alcohol consumption (0-4, 5-9,

10-14, 15-29, and ≥ 30 g/d); (4) history of hypertension; (5) parental history of MI; (6) body mass index (calculated as weight in kilograms divided by the square of height in meters) (quintiles); and (7) current multivitamin use, and (8) vitamin E supplement use. In HPFS, we also adjusted for physical activity in metabolic equivalents per week (quintiles).³⁴ In NHS, we adjusted for regular vigorous exercise (once or more per week) and menopausal status and postmenopausal hormone use. Tests of linear trend across increasing categories of egg consumption were conducted by treating the median values of consumption in categories (servings per day) as a continuous variable.

To reduce intra-individual variation and best represent long-term diet, we used repeated measures of diet in our primary analyses.³⁵ In particular, CHD or stroke incidence was related to the cumulative average of egg consumption from all available questionnaires prior to the beginning of each 2-year follow-up interval. For example, in HPFS, CHD or stroke incidence during the 1986-1990 period was related to egg consumption assessed in 1986, while the incidence during 1990-1994 period was related to the average intake assessed in 1986 and 1990. For those who failed to complete the 1990 diet questionnaire (24%), we used the 1986 values to replace the missing values and a missing data indicator was included in the model to correct for potential bias. Average egg consumption at baseline was the same between the respondents and nonrespondents. In alternative analyses, we analyzed the incidence of CHD in relationship to egg consumption at baseline only. We also related the incidence to the most recent diet by using the baseline diet to predict incidence during 1986-1990, and the 1990 diet to predict incidence during 1990-1994. Because the diagnosis of hypercholesterolemia, diabetes, or hypertension may lead to changes in egg consumption and therefore confound the associations between egg consumption and risk of cardiovascular disease, we did not update

diets for those who developed these conditions.³⁵

RESULTS

In men, the average egg consumption declined from 2.3 eggs per week in 1986 to 1.6 eggs per week in 1990. In women, the average egg consumption declined from 2.8 eggs per week in 1980 to 1.4 eggs per week in 1990. At baseline, egg consumption was positively associated with smoking in men but inversely associated with smoking in women (TABLE 1). Those with higher egg intake consumed more dietary cholesterol and protein but less carbohydrates. Egg consumption was positively associated with bacon intake among both men ($r = 0.35$) and women ($r = 0.21$). Men with higher egg consumption were more likely to consume whole milk, red meat, and bread, and less likely to consume skim milk, chicken, vegetables, and fruits. These relationships were less clear in women.

Association With CHD

We documented 866 incident cases of CHD in men during 8 years of follow-up (1986-1994) and 939 cases of CHD in women during 14 years of follow-up (1980-1994). The age-adjusted RR of CHD comparing more than 1 egg per day with less than 1 egg per week was 1.15 (95% confidence interval [CI], 0.85-1.55; P for trend = .37) for men and 0.85 (95% CI, 0.62-1.16; P for trend = .50) for women (TABLE 2). After adjustment for smoking and other covariates, the corresponding RRs were 1.08 (95% CI, 0.79-1.48; P for trend = .75) for men and 0.82 (95% CI, 0.60-1.13; P for trend = .95) for women. Additional adjustment for dietary fiber intake had little impact on the RRs for women but it further attenuated the association for men (RR for >1 egg per day, 1.01; 95% CI, 0.74-1.38). Because of the relatively strong correlation between consumption of eggs and bacon, we further adjusted for bacon intake. The adjusted RRs across categories of egg consumption are less than 1 per week (1.0), 1 per week (1.00), 2 to 4 per week (1.04), 5 to 6 per week (0.78), and 1 or

more per day (0.93) (*P* for trend = .36) for men; and less than 1 per week (1.0), 1 per week (0.81), 2 to 4 per week (0.96), 5 to 6 per week (0.91), and 1 or more per day (0.78) (*P* for trend = .73) for women. Additional adjustment for other foods including whole milk, fish, beef as main dish, chicken, or cereal had little impact on the results.

In further analyses egg consumption had no significant relationship with either fatal CHD or nonfatal MI (data not shown). After excluding cases with events occurring during the first 2 years of follow-up to reduce the effect of change in diet due to preclinical conditions, the results remained unchanged. In analyses excluding partici-

pants who reported changes in egg consumption in the previous decade from baseline, we observed a significant inverse association for men but a nonsignificant positive association for women. The results from analyses including eggs estimated from other foods were similar to those from the main analyses. We also observed no signifi-

Table 1. Baseline Characteristics According to Egg Consumption Levels in Men and Women*

Characteristics	Men in Health Professionals' Follow-up Study (1986 Baseline) Egg Consumption					Women in Nurses' Health Study (1980 Baseline) Egg Consumption				
	<1 Per Week	1 Per Week	2-4 Per Week	5-6 Per Week	>1 Per Day	<1 Per Week	1 Per Week	2-4 Per Week	5-6 Per Week	>1 Per Day
No. of subjects	11 247	8103	13 845	2280	2376	11 568	16 155	38 109	7160	7090
Current smoker, %	7.2	9.0	10.8	13.9	14.6	34.7	30.6	27.0	26.3	25.4
Current postmenopausal hormone use, %	NA	NA	NA	NA	NA	15.2	15.8	16.9	17.4	16.0
Parental history of myocardial infarction, %	13.1	11.1	11.2	10.5	9.2	15.9	16.1	15.3	14.9	14.5
Multivitamin supplement use, %	41.5	39.9	41.1	41.6	43.3	29.8	30.2	34.1	38.4	40.5
Vitamin E supplement use, %	19.6	17.3	17.6	18.9	20.8	11.4	10.9	12.2	15.1	18.0
History of hypertension, %	17.8	18.4	17.7	15.9	14.3	14.2	13.8	14.1	13.8	14.0
Vigorous exercise ≥1/wk, %	42.8	43.8	45.8	46.2	46.7
Age, y	52.7	52.6	53.8	54.2	54.2	46.4	45.7	45.8	45.5	45.9
Body mass index, kg/m ²	25.2	25.4	25.6	25.8	25.5	23.9	23.9	24.4	24.6	24.4
Alcohol use, g/d	10.1	11.0	12.1	13.1	12.3	6.4	6.5	6.3	6.8	6.7
Physical activity, metabolic equivalent/wk†	22.0	19.6	19.0	18.8	17.5
Energy intake, kJ	7627	8089	8770	9559	9925	5851	6086	6703	7274	7505
Nutrient intakes (energy-adjusted)										
Cholesterol, mg/d	237	266	330	404	536	228	258	342	436	557
Saturated fat, g/d	23.1	24.7	25.5	26.5	27.9	28.0	28.1	27.8	28.3	29.0
Monounsaturated fat, g/d	25.9	27.4	28.1	29.1	30.3	28.4	28.6	28.5	29.1	29.8
Polyunsaturated fat, g/d	13.0	13.2	13.2	13.3	13.4	9.0	9.3	9.4	9.6	9.6
Transfatty acid, g/d	2.7	2.9	2.9	2.9	2.9	4.0	4.1	4.0	4.0	3.8
Dietary folate, µg/d	368	354	348	336	336	240	246	261	264	272
Fiber, g/d	22.6	20.6	19.9	19.0	18.5	13.6	13.4	13.7	13.5	13.3
Protein, g/d	90.7	90.8	92.2	93.4	96.0	72.8	73.0	76.3	77.6	79.9
Carbohydrates, g/d	247	236	229	221	211	160	158	156	150	144
Food intakes, serving per 4200 kJ										
Whole milk	0.05	0.07	0.08	0.10	0.12	0.16	0.17	0.16	0.17	0.18
Skim milk	0.38	0.39	0.36	0.32	0.29	0.36	0.38	0.44	0.39	0.36
Red meat‡	0.27	0.31	0.33	0.34	0.37	0.51	0.51	0.50	0.48	0.48
Bacon	0.03	0.05	0.07	0.11	0.15	0.05	0.06	0.08	0.10	0.12
Chicken	0.19	0.18	0.17	0.16	0.15	0.19	0.17	0.17	0.17	0.17
Breakfast cereal	0.24	0.22	0.19	0.14	0.10	0.19	0.20	0.19	0.15	0.11
Dark bread	0.37	0.34	0.36	0.37	0.44	0.45	0.44	0.50	0.52	0.52
White bread	0.21	0.23	0.26	0.31	0.33	0.49	0.51	0.52	0.51	0.52
Vegetables§	1.75	1.55	1.50	1.42	1.35	1.41	1.35	1.34	1.30	1.30
Fruits	1.09	0.95	0.88	0.82	0.77	1.37	1.34	1.37	1.30	1.31
Legumes¶	0.26	0.23	0.22	0.22	0.23	0.33	0.31	0.31	0.30	0.29

*Values are means unless otherwise indicated. Data, except age, were directly standardized to the age distribution of each study population. Ellipses indicate data not provided; NA, not applicable.
 †The metabolic equivalent value is the energy needed per kilogram of body weight per hour of activity divided by the energy need per kilogram of body weight per hour at rest.
 ‡Composite score of beef, pork, or lamb as the main dish, beef as a sandwich or mixed dish, and hamburger.
 §Composite score of 22 vegetable foods from the men's study and 11 from the women's study.
 ||Composite score of 12 fruits in the men's study and 6 from the women's study.
 ¶Composite score of peas or lima beans and beans or lentils.

cant increase in risk when either only baseline or only recent egg consumption was analyzed. Only 4.8% women reported almost never consuming eggs and 1.6% women reported consuming 2 eggs or more per day. When these 2 extreme groups were compared (using never consumers as the reference group), the multivariate RR was 0.76 (95% CI, 0.43-1.35). The corresponding RR was 1.10 (95% CI, 0.67-1.79) for men.

In all above analyses, participants with diabetes or hypercholesterolemia at baseline were excluded. When these subjects were included in the analyses, the results did not appreciably change. The multivariate RRs as in Table 2 across categories of egg intake were less than 1 per week (1.0), 1 per week (1.05), 2 to 4 per week (1.04), 5 to 6 per week (0.96), and 1 or more per day (1.10) (95% CI, 0.83-1.45; *P* for trend = .78) for men; and less than 1 per week (1.0), 1 per week (0.87), 2 to 4 per week (0.98), 5 to 6 per week (1.03), and 1 or more per day (0.95) (95% CI, 0.74-1.22; *P* for trend = .54) for women.

Associations According to Risk Factor Status

To examine the possibility that a positive association with egg intake is limited to certain subgroups, we conducted additional multivariate analyses stratified by risk factor status including hypercholesterolemia, diabetes, hypertension, smoking, alcohol use, body

mass index, age, vitamin supplement use, parental history of MI, and intakes of saturated fat, polyunsaturated fat, and carbohydrates. We found no evidence of a positive association with higher consumption of eggs in any subgroup except a suggestion that the risk might be elevated among individuals with diabetes. Among diabetic men, the multivariate RRs of CHD across categories of intake were less than 1 per week (1.0), 1 per week (1.0), 2 to 4 per week (1.16), 5 to 6 per week (1.16), and 1 or more eggs per day (2.02); (95% CI, 1.05-3.87; *P* = .04 for trend and *P* = .18 for interaction between egg consumption and diabetes status). The corresponding RRs for diabetic women were 1.0, 0.91, 1.05, 1.87, and 1.49 (95% CI, 0.88-2.52; *P* = .008 for trend and *P* = .07 for interaction). To investigate the possibility that an effect of egg consumption may be more apparent among those with a low-background cholesterol diet,³⁶ we conducted analyses stratified by dietary cholesterol from foods other than eggs. The RRs for more than 1 eggs per day were 1.05 (95% CI, 0.61-1.79) for the men and 0.97 (95% CI, 0.13-7.10) for the women whose non-egg cholesterol intake was low (mean intakes were 88.4 mg/4200 kJ for men and 118.8 mg/4200 kJ for women), compared with 0.97 (95% CI, 0.64-1.46) for the men and 0.79 (95% CI, 0.57-1.11) for the women whose non-egg cholesterol intake was relatively high (mean intakes were 135.9 mg/

4200 kJ for men and 175.9 mg/4200 kJ for women).

The Association With Stroke

We documented 258 incident cases of stroke in men during 8 years of follow-up and 563 cases of stroke in women during 14 years of follow-up. In multivariate analyses (TABLE 3), egg consumption was not significantly associated with risk of total stroke; the RRs for 1 egg or more per day were 1.07 (95% CI, 0.66-1.75; *P* for trend = .50) for men and 0.89 (95% CI, 0.60-1.31; *P* for trend = .77) for women. Adjustment for intake of bacon, vegetables, and fruit further attenuated the association for men (RR for ≥ 1 egg per day, 1.00; 95% CI, 0.57-1.78; *P* for trend = 0.95). In both cohorts, no significant association was observed between egg consumption and risk of ischemic or hemorrhagic stroke.

COMMENT

In these 2 large prospective cohort studies of men and women, we found no overall significant association between egg consumption (up to 1 egg per day) and risk of CHD or stroke. We specifically found no evidence for a significant increase in risk with either recent or relatively long-term (over the past decade) egg consumption. Despite somewhat different patterns of egg consumption in men and women, the results from the 2 cohorts were remarkably consistent.

Table 2. Coronary Heart Disease According to Categories of Egg Consumption*

Amount of Eggs Consumed	Men				Women			
	No. of Cases	Person-Years	Age-Adjusted Relative Risk (95% CI)	Multivariate Relative Risk (95% CI)	No. of Cases	Person-Years	Age-Adjusted Relative Risk (95% CI)	Multivariate Relative Risk (95% CI)
Per week								
<1	252	90 118	1.0	1.0	189	175 144	1.0	1.0
1	210	69 091	1.09 (0.90-1.31)	1.06 (0.88-1.27)	346	366 625	0.75 (0.61-0.91)	0.82 (0.67-1.00)
2-4	315	88 077	1.16 (0.98-1.37)	1.12 (0.95-1.33)	331	409 896	0.95 (0.80-1.14)	0.99 (0.82-1.18)
5-6	38	12 216	0.97 (0.68-1.36)	0.90 (0.63-1.27)	43	52 584	0.97 (0.71-1.31)	0.95 (0.70-1.29)
Per day								
≥ 1	51	14 059	1.15 (0.85-1.55)	1.08 (0.79-1.48)	30	52 971	0.85 (0.62-1.16)	0.82 (0.60-1.13)
<i>P</i> for trend			.37	.75			.50	.95

*Adjusted for age (5-year categories), body mass index (quintiles), 2-year time periods, cigarette smoking (never, past, and current [1-14, 15-24, and ≥ 25 cigarettes/d]), parental history of myocardial infarction, multivitamin supplement use, vitamin E supplement use, alcohol consumption (0-4, 5-9, 10-14, 15-29, ≥ 30 g/d), menopausal status and postmenopausal hormone use (women), history of hypertension, physical activity (quintiles of metabolic equivalents in men and vigorous activities at least once a week in women), and total energy intake (quintiles). CI indicates confidence interval.

In subgroup analyses, egg consumption appeared to be associated with increased risk of CHD among individuals with diabetes. This result should be interpreted cautiously due to numerous subgroup analyses, but the consistency of the association in the 2 cohorts argues against a chance finding. The increased risk may be related to abnormal cholesterol transport due to decreased levels of apolipoprotein E³⁷ and increased levels of apolipoprotein C-III³⁸ among patients with diabetes.

We considered the possibility that inaccurate self-reports of egg consumption or confounding by intake of other foods could explain the observed null results. Egg consumption was reported on food frequency questionnaires with relatively high accuracy (correlations were 0.8 between the self-report and multiple week dietary records in our validation studies^{28,29}). Also, egg consumption was assessed several times in both cohorts so that our analyses using updated dietary information could dampen measurement error and take into account changes in eating behavior.

Several metabolic studies have suggested a hypocholesterolemic effect of decholesterolized eggs (ie, Eggbeaters) on blood cholesterol levels compared with whole eggs.^{39,40} We were not able to examine the effect of such products on the risk of CHD because they were not included in the dietary questionnaires on the printed form. However, our questionnaires permit respondents to report other foods that are frequently consumed. In NHS, only 48 women recorded consuming Eggbeaters in the 1984 dietary questionnaire and 105 recorded this in the 1990 questionnaire.

Egg consumption was positively associated with smoking, lower physical activity, and a generally unhealthy eating pattern (ie, more whole milk, red meat, and bacon and less skim milk, vegetables, and fruits) in men. Confounding due to these factors would artifactually produce an elevated risk for egg consumption. As expected, an apparent positive association with higher egg consumption in the age-adjusted analysis in men was attenuated after adjustment for smoking and other covariates. After further adjusting for bacon

intake, which was positively associated with risk of CHD in our cohorts, the RRs became weakly inverse. This speaks to the importance of considering overall eating patterns when examining the effects of egg consumption.

It is possible that participants with high serum cholesterol levels were more likely to reduce their egg intake than others, which might obscure a positive association between egg consumption and risk of CHD. However, in our primary analyses, we excluded subjects with diagnosed hypercholesterolemia at baseline. Also, in our analyses by using updated dietary information, we stopped updating egg consumption at the beginning of the time interval during which individuals reported hypercholesterolemia to avoid confounding due to change in diet during follow-up.⁴¹ Finally, we did not measure blood cholesterol levels in our cohorts. However, blood cholesterol should not be controlled in the analyses as it is an intermediate variable when assessing the relationship between dietary cholesterol and CHD.

In controlled metabolic studies, ingestion of cholesterol by eating egg

Table 3. Stroke According to Categories of Egg Consumption*

Amount of Eggs Consumed	Type of Stroke								
	Total			Ischemic			Hemorrhagic		
	No. of Cases	Age-Adjusted Relative Risk (95% CI)	Multivariate Relative Risk (95% CI)	No. of Cases	Age-Adjusted Relative Risk (95% CI)	Multivariate Relative Risk (95% CI)	No. of Cases	Age-Adjusted Relative Risk (95% CI)	Multivariate Relative Risk (95% CI)
Men									
Per week <1	76	1.0	1.0	51	1.0	1.0	16	1.0	1.0
1	65	1.09 (0.78-1.52)	1.06 (0.76-1.49)	42	1.04 (0.69-1.57)	0.99 (0.66-1.50)	13	1.05 (0.51-2.19)	1.02 (0.49-2.14)
2-4	82	0.99 (0.73-1.36)	0.95 (0.69-1.31)	52	0.94 (0.63-1.38)	0.86 (0.58-1.28)	19	1.12 (0.57-2.18)	1.01 (0.51-2.00)
5-6	18	1.52 (0.91-2.56)	1.43 (0.85-2.43)	11	1.39 (0.72-2.69)	1.25 (0.64-1.87)	4	0.77 (0.26-2.30)	0.67 (0.22-2.07)
Per day ≥1	17	1.25 (0.74-2.12)	1.07 (0.66-1.75)	10	1.09 (0.55-2.15)	0.93 (0.46-1.87)
P for trend		.28	.50		.70	.88		.78	.55
Women									
Per week <1	110	1.0	1.0	63	1.0	1.0	33	1.0	1.0
1	161	0.83 (0.65-1.05)	0.89 (0.70-1.13)	82	0.70 (0.51-0.98)	0.78 (0.56-1.09)	51	0.89 (0.67-1.38)	0.93 (0.60-1.44)
2-4	222	0.81 (0.64-1.01)	0.83 (0.66-1.05)	114	0.75 (0.55-1.03)	0.79 (0.57-1.08)	69	0.80 (0.53-1.21)	0.86 (0.56-1.31)
5-6	34	0.90 (0.61-1.32)	0.89 (0.60-1.32)	21	1.08 (0.66-1.78)	1.11 (0.67-1.84)	9	0.72 (0.34-1.51)	0.75 (0.35-1.58)
Per day ≥1	36	0.92 (0.63-1.35)	0.89 (0.60-1.31)	16	0.80 (0.46-1.39)	0.81 (0.46-1.42)	14	1.09 (0.58-2.03)	1.07 (0.56-2.03)
P for trend		.96	.77		.90	.81		.77	.81

*See footnote to Table 2 for multivariate list. CI indicates confidence interval.

†Ellipses indicate that data in this category are combined with the previous category due to the small number of cases.

yolks or whole eggs raises serum total and LDL cholesterol levels.^{5-7,42} In most egg feeding studies, intakes of other nutrients such as fatty acids, carbohydrates, and protein were balanced between egg and no egg groups so that only dietary cholesterol varied. In our cohorts, participants who consumed more eggs had lower intakes of carbohydrates, suggesting that, in reality, people often substitute eggs for carbohydrate-rich foods such as breakfast cereals. The effects of egg cholesterol on blood cholesterol can be predicted from well-established equations derived from metabolic studies. A 50-g egg contains about 213 mg of cholesterol, 6 g of protein, and 5 g of fat.⁴³ Of the fat, nearly half is monounsaturated fat and 16% is polyunsaturated fat. The equation derived by Keys and Parlin⁴ predicts that adding 1 egg to an average diet (assume 200 mg background cholesterol and 7560 kJ/d) will result in about a 4% increase in total serum cholesterol for a normocholesterolemic person (assume total blood cholesterol of 5.17 mmol/L [200 mg/dL]). If we assume that raising cholesterol levels is the only effect of egg consumption, this would translate into about an 8% increase in CHD risk,⁴⁴ an effect generally too small to be detectable in this and most epidemiologic studies or clinical trials. In NHS, dietary cholesterol (but not eggs) was nonsignificantly associated with CHD,¹⁷ raising the possibility that eggs contain other nutrients that may be beneficial in preventing CHD.

The equation developed by Mensink and Katan⁴⁵ predicts that substituting fatty acids from 1 egg for carbohydrates would raise HDL cholesterol by about 2% (assume HDL level of 1.03 mmol/L [40 mg/dL]) and decrease triglycerides also by about 2% (assume triglyceride level of 2.82 mmol/L [250 mg/dL]). The effects of egg consumption on raising HDL levels have been observed in some metabolic studies,^{19,20} but not in others.^{36,40} Also, in egg feeding studies, triglyceride levels were significantly reduced in some,^{19,20} but not other studies.^{36,46} In particular, Schnohr et al¹⁹ observed a reduction of triglyc-

erides by 0.09 mmol/L (7.97 mg/dL) by adding 2 eggs to the usual diet. Packard et al²⁰ observed a reduction of triglycerides by 0.19 mmol/L (16.8 mg/dL) by adding 6 eggs to the diet. In addition, egg intake decreased blood glycemic and insulinemic responses,⁴⁷ especially when egg yolk was ingested (compared with whole egg or egg white).²¹ This might result from further delayed gastric emptying after yolk ingestion. Moreover, adding eggs to pasta produced lower insulin and C-peptide responses.⁴⁸ Holt et al⁴⁹ tested 38 common foods and found that eggs were among the foods that have the lowest glycemic and insulin indexes.

Based on the 116 food items in the 1984 food frequency questionnaire in NHS, we estimated that egg consumption contributed to 32% of total dietary cholesterol. Eggs also made contributions to dietary intakes of many other nutrients, including vitamin D (5%), retinol (4%), folate (4%), α -tocopherol (3%), monounsaturated fat (3%), vitamin B₁₂ (3%), vitamin B₂ (3%), protein (3%), saturated fat (2.5%), linoleic acid (2%), calcium (1.3%), vitamin B₁ (1.2%), and vitamin B₂ (1.2%). It is conceivable that the small adverse effect of cholesterol in an egg on plasma LDL levels is counterbalanced by potential beneficial effects on HDL and triglycerides, and of other nutrients including antioxidants, folate, other B vitamins, and unsaturated fats. Since there is no single biochemical measurement that can represent the effects of various nutrients, it is important to examine the direct relationship between egg consumption and risk of CHD. Only 2 previous prospective cohort studies reported on the association between egg consumption and risk of CHD. In the Framingham Study, egg consumption was not significantly associated with either serum cholesterol or risk of CHD (RR was not provided).²² In the California Adventists Study, the RR for higher intake (≥ 3 per week) vs lowest intake (< 1 per week) was 1.01.²³ In a case-control study conducted in Italy,²⁴ the RR comparing women in the upper third of egg intake with those in the lower third was 0.8.

One potential alternative explanation for the null finding is that background dietary cholesterol may be so high in the usual Western diet that adding somewhat more has little further effect on blood cholesterol. In a randomized trial, Sacks et al³⁶ found that adding 1 egg per day to the usual diet of 17 lacto-vegetarians whose habitual cholesterol intake was very low (97 mg/d) significantly increased LDL cholesterol level by 12%. In our analyses, differences in non-egg cholesterol intake did not appear to be an explanation for the null association between egg consumption and risk of CHD. However, we cannot exclude the possibility that egg consumption may increase the risk among participants with very low background cholesterol intake. Also, we have limited power to examine the effect of high egg consumption (eg, ≥ 2 eggs per day). Nevertheless, the average egg consumption was 0.64 eggs per day in 1995 in the United States,⁵⁰ which is well within the range of consumption in our analyses.

We found no significant association between egg consumption and risk of total stroke or its subtype. Epidemiologic studies⁵¹ have revealed no clear patterns between blood cholesterol and stroke although secondary prevention trials^{52,53} showed significant reductions in stroke incidence among patients with MIs and who were treated with cholesterol-lowering drugs (statins). A recent report from the Framingham Heart Study²⁴ indicated that intakes of total fat, saturated fat, and monounsaturated fat were associated with reduced risk of ischemic stroke, but the study did not examine the effects of dietary cholesterol or egg consumption.

In conclusion, our data suggest that consumption of up to 1 egg per day is unlikely to have substantial overall impact on the risk of cardiovascular disease among healthy men and women. The apparent increased risk of CHD associated with higher egg consumption among diabetics warrants further research.

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