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Egg Consumption and Cardiovascular Disease and Mortality The Physicians' Health Study

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Abstract

Background—Reduction in dietary cholesterol is recommended to prevent cardiovascular disease (CVD). Although eggs are important sources of cholesterol and other nutrients, limited and inconsistent data are available on the effects of egg consumption on the risk of CVD and mortality.

Objectives—To examine the association between egg consumption and the risk of CVD and mortality.

Design—Prospective cohort study of 21,327 participants from the Physicians' Health Study I. Egg consumption was assessed using a simple abbreviated food questionnaire. We used Cox regression to estimate relative risks.

Results—After an average follow up of 20 years, a total of 1,550 new myocardial infarction (MI), 1,342 incident strokes, and 5,169 deaths occurred in this cohort. Egg consumption was not associated with incident MI or stroke in a multivariable Cox regression. In contrast, adjusted hazard ratios (95% CI) for mortality were 1.0 (reference), 0.94 (0.87-1.02), 1.03 (0.95-1.11), 1.05 (0.93-1.19), and 1.23 (1.11-1.36) for egg consumption of <1, 1, 2-4, 5-6, and 7+ per week, respectively, (p for trend <0.0001). This association was stronger among diabetic subjects with a 2-fold increased risk of death comparing the highest to the lowest category of egg consumption than non-diabetic subjects (HR: 1.22 (1.09-1.35) (p for interaction 0.09).

Conclusions—Our data suggest that infrequent egg consumption does not influence the risk of CVD and only confers a modest increased risk for total mortality in male physicians. In addition, egg consumption was positively related to mortality and such relation was stronger among diabetic subjects in this selective population.

Keywords

Diet; stroke; myocardial infarction; epidemiology; mortality

Introduction

Coronary heart disease (CHD) remains the leading cause of death in the US. Since elevated low-density lipoprotein (LDL)-cholesterol has been identified as a major risk factor for CHD,

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dietary guidelines to prevent CHD emphasize the reduction in dietary cholesterol to less than 300 mg per day(1;2). Egg is a major source of dietary cholesterol with an average egg containing ~200 mg of cholesterol. On the other hand, eggs contain other nutrients(3;4) such as minerals, folate, B vitamins, proteins, and monounsaturated fatty acids that could reduce the risk of CHD. While some studies have demonstrated positive association between dietary and serum cholesterol (5-9), other did not find any effect (7;10;11). There is a large variability in individual response to dietary cholesterol(11-13). In addition, the effect of dietary cholesterol on LDL-cholesterol observed in positive studies is modest compared to the LDL-raising effects of saturated and trans fatty acids(14;15).

Limited and inconsistent data have been reported on the association between egg consumption and CHD. Among 514 Australian Aborigines, consumption of 2+ eggs per week was associated with a 2.6-fold increased risk of CHD in a prospective analysis(16). Mann et al.(17) reported a 2.7-fold increased risk of death with a higher egg consumption (6+/week) among British subjects. In contrast, other large prospective cohorts with longer follow-ups did not observe any association between egg consumption and CHD or mortality(18-21). Since eggs could serve as a good source for vitamins, proteins, and other nutrients in the US, it is important to determine the net benefit/harm of egg consumption as whole food (as opposed to individual component of eggs such as cholesterol). In the current project, we sought to prospectively assess whether egg consumption was associated with an increased risk of myocardial infarction (MI), stroke, and all-cause mortality. In addition, we assessed the influence of type 2 diabetes and history of hypercholesterolemia as possible effect modifiers of these associations.

Materials and Methods

Study population

The current project used data from the Physicians' Health Study (PHS) I, which was a randomized, double-blind, placebo-controlled trial using a 2×2 factorial design to study low-dose aspirin and beta-carotene for the primary prevention of cardiovascular disease and cancer among US male physicians. A detailed description of the PHS I has been published previously (22). Briefly, 261,248 US male physicians aged 40-85 years were invited to participate in the clinical trial in 1981. After exclusion of subjects with a history of stroke, gout, myocardial infarction, transient ischemic attack, cancer (except nonmelanoma skin cancer), peptic ulcer, current liver or kidney disease, current use of trial treatments, 33,223 individuals were enrolled in an 18-week run-in period. At the end of the run-in period, 22, 071 subjects were randomized to low-dose aspirin, beta-carotene, both agents, or placebo (subsequently referred to as treatment arms). For the current project, after the exclusion of 834 subjects with missing data on egg consumption (n=151) or covariates (n=683), the final sample consisted of 21,327 participants. Each participant gave written informed consent and the study protocol was approved by the Institutional review Board at Brigham and Women's Hospital.

Assessment of egg consumption

Information on egg consumption was self-reported using a simple abbreviated semi-quantitative food frequency questionnaire. Participants were asked to report how often, on average, they have eaten eggs (one) during the past year". Possible response categories included "rarely/never", "1-3/month", "1/week", "2-4/week", "5-6/week", "daily", and "2+/day". This information was obtained at baseline, 24, 48, 72, 96, and 120 months after randomization.

Ascertainment of cardiovascular events and death in the PHS

A questionnaire was mailed to each participant every 6 months during the first year and has been mailed annually thereafter to gather information on compliance with the intervention and the occurrence of new medical diagnoses including MI, stroke, and death. For participants who

do not return the follow-up questionnaire within 5 to 6 weeks of the initial mailing, a second follow-up questionnaire is sent to them. If necessary, a third and a fourth questionnaire are sent to non-respondents followed by a telephone call to obtain follow-up information if the mail is not answered. If the follow-up information is not obtained by questionnaires or telephone call, vital status of the corresponding participants is ascertained. A letter and return postcard are also mailed to the participants at the 6-month interval between annual mailings. Participants are asked to return the postcard if they have experienced any major problem affecting their participation in the study.

All cardiovascular endpoints are adjudicated by the Endpoint Committee of the PHS, which includes cardiologists and neurologists. MI was confirmed based on the World Health Organization Criteria modified to use cardiac enzymes tests. For fatal events, death certificates were obtained for confirmation and review of cause of death. Additional information was obtained from the next of kin and from medical records upon obtaining proper permission from the next of kin. Both cause of death on death certificates and additional information from the next of kin and medical records were used by the Endpoint Committee. Details on endpoint validation in the PHS have been published(23-26).

Other variables

Demographic data were collected at baseline. Information on comorbidity (i.e., atrial fibrillation, hypertension, and diabetes mellitus) has been collected through annual follow-up questionnaires as described above. Data on selected foods such as fruits and vegetables, breakfast cereals; physical activity; smoking; alcohol consumption; parental history of premature MI; and history of hypercholesterolemia were obtained at baseline.

Statistical analyses

Because there was a reasonable correlation between reported egg consumption at baseline and at 24 months (weighted kappa 0.51), we substituted missing values at baseline using reported egg consumption at 24 months in 113 individuals. We grouped adjacent categories to allow sufficient number of person-times per category of egg consumption and to maintain a gradient of exposure. Thus, we classified each subject into one the following categories of egg consumption: less than one per week, one per week, two to four per week, five to six per week, and seven or more eggs per week. For each endpoint (MI, stroke, or death), we calculated person-time of follow up from baseline until the first occurrence of a) endpoint, b) death, or c) censoring date – date of receipt of last follow-up questionnaire. Within each egg consumption group, we calculated the incidence rate of each endpoint by dividing the number of cases by the corresponding person-time. We used Cox proportional hazard models to compute multivariable adjusted hazard ratios with corresponding 95% confidence intervals using subjects in the lowest category of egg consumption as the reference group. We assessed confounding by using 10% change in hazard ratio. Assumptions for the proportional hazard models were tested (by including main effects and product terms of covariates and a logarithmic transformed time factor) and were met (all p values >0.05). We obtained p value for linear trend by assigning the median value of egg consumption in each category to a new variable that was used in the Cox model (we assigned values of 0, 1, 3, 5.5, and 7 from the lowest to the highest egg consumption, respectively). The initial model controlled for age. The parsimonious model also controlled for body mass index (continuous), smoking (never, past, and current smokers), and history of hypertension (yes/no). Lastly, the final multivariable model also controlled for hypercholesterolemia (yes/no), parental history of premature MI (yes/no), diabetes mellitus (yes/no), atrial fibrillation (yes/no), breakfast cereals (0, 1, 2-6, and 7+ servings/week), alcohol consumption (<1, 1-4, 5-6, 7+ drinks/week), vegetable consumption (<3, 3-4, 5-6, 7-13, 14+ servings/week), use of multivitamin (never, past, and current), and physical activity (<1, 1, 2-4, and 5+/ week). Two-way interaction between egg consumption

and treatment assignment was evaluated by including main effect and their product term in the regression model (all p values > 0.05).

In secondary analyses, we examined the association between egg consumption and types of stroke (ischemic vs. hemorrhagic) and possible effect modification by diabetes mellitus and hypercholesterolemia using stratified analyses. In addition, we excluded individuals with a follow-up time of 2 years of less. Lastly, we repeated the main analysis using updated egg consumption at 24, 48, 72, 96, and 120 months in a time-dependent Cox model. All analyses were completed using SAS, version 9.1 (SAS Institute, NC). Significance level was set at 0.05.

Results

Among 21,376 participants in the PHS I, the mean age at randomization was 53.7±9.5 years (range 40 to 86 years). The median egg consumption was 1 /week in this population. Table 1 presents baseline characteristics of the study participants. Frequent consumption of eggs was associated with older age; higher body mass index; higher consumption of vegetables and lower frequency of breakfast cereal consumption; higher proportion of current drinkers and smokers, and users of multivitamins; higher prevalence of diabetes and hypertension; and lower prevalence of exercise, hypercholesterolemia, and parental history of premature CHD. During an average follow up of 20 years, 1550 new MI (7.3%), 1342 incident stroke (6.3%), and 5169 cases of deaths (24.2%) occurred in this cohort. In multivariable Cox regression model, egg consumption was not associated with incident myocardial infarction (Table 2), total stroke (Table 3) or types of stroke. From the lowest to the highest category of egg consumption, multivariable adjusted hazard ratios (95% CI) were 1.0; 1.03 (0.86-1.23); 1.08 (0.91-1.28); 1.11 (0.86-1.43); and 0.99 (0.78-1.26), respectively, for ischemic stroke (p for trend 0.74). Corresponding values for hemorrhagic stroke were 1.0; 0.66 (0.44-1.00); 0.92 (0.63-1.36); 1.29 (0.76-2.20); and 1.07 (0.65-1.78), respectively (p for trend 0.11). While egg consumption of up to 6 eggs per week was not associated with the risk of all-cause mortality, consumption of 7 or more eggs per week was associated with a 23% increased risk of death after controlling for confounders (Table 4). Exclusion of individuals whose follow-up times were 2 years or less had and using time-dependent Cox with updated egg consumption over time did not alter the results (data not shown).

In stratified analyses, history of hypercholesterolemia at baseline did not influence the relation between egg consumption and MI, stroke, or total deaths (data not shown). However, when stratified by prevalent diabetes at baseline, there was a stronger and statistically significant association between egg consumption and all-cause mortality among subjects with prevalent diabetes than those without diabetes (Table 5). Compared with the lowest category of egg consumption, intake of 7+ per week was associated with 22% increased risk of death in the absence of prevalent diabetes whereas a 2-fold increased risk of death was observed in the presence of prevalent diabetes (p for interaction between diabetes and egg consumption was 0.029 in the parsimonious model and 0.09 in the multivariable adjusted model, Table 5). For MI, multivariable adjusted hazard ratios (95% CI) were 1.0; 1.07 (0.92-1.25); 1.16 (0.99-1.34); 1.13 (0.90-1.42); and 0.91 (0.73-1.14) from the lowest to the highest category of egg consumption, respectively (p for trend 0.97) in the absence of prevalent diabetes. Corresponding values among subjects with diabetes were 1.0; 1.39 (0.61-3.21); 1.45 (0.64-3.28); 1.82 (0.66-5.03); and 1.06 (0.43-2.64), respectively (p for trend 0.93 and p for interaction 0.48). Lastly, from the lowest to the highest category of egg consumption, multivariable adjusted hazard ratios (95% CI) for stroke were 1.0; 0.94 (0.80-1.11); 1.07 (0.91-1.25); 1.12 (0.88-1.42); and 0.96 (0.77-1.21), respectively, for subjects without diabetes (p for trend 0.42) and 1.0; 1.95 (0.89-4.30); 1.61 (0.72-3.56); 1.69 (0.58-4.91); and 1.83 (0.71-4.23), respectively (p for trend 0.52), for people with diabetes (p for interaction 0.52).

Discussion

In this prospective cohort, we demonstrated that infrequent egg consumption up to 6 eggs per week was not associated with MI, stroke, or total mortality in healthy US male physicians. In addition, consumption of 7 or more eggs per week was associated with a modest but significant increased risk of total mortality in this population. In contrast, egg consumption was associated with an increased risk of all-cause mortality in a dose-response fashion among physicians with diabetes (2-fold increased risk of death for people consuming 7+ eggs per week compared with less than 1/week). Furthermore, our data provided suggestive evidence for an increased risk of MI and stroke with egg consumption among male physicians with diabetes. In contrast, baseline hypercholesterolemia status did not influence the relation between egg consumption and CVD or mortality.

Because eggs are rich in dietary cholesterol, metabolic studies have focused on the effects of dietary cholesterol in eggs on serum cholesterol or other intermediate phenotypes. In particular, limited and inconsistent data are available on the impact of egg consumption (not just cholesterol content of eggs) on incident CVD and mortality in a community setting. To the best of our knowledge, only two studies have reported a positive association between egg consumption and CHD. Data from 514 Western Australian Aborigines showed a 2.6-fold increased risk of CHD comparing egg consumption of 2+ vs. < 2/week after ~14 years of follow up(16). Unfortunately, this study did not evaluate the influence of diabetes on the reported association and data on baseline characteristics of that population suggested a lower prevalence of diabetes (4% for both men and women). Of note is that egg consumption in this population was higher that reported among male physicians. Mann et al.(17) reported a graded association between egg consumption and mortality after 13 years of follow up among 10,802 healthy men and women in the UK. Compared with egg consumption of less than 1/week, the incidence rate ratio for total mortality was 1.23 and 2.68 among subjects consuming 1-5 and 6+ eggs/ week, respectively, after adjustment for age, sex, smoking, and social class. Of note is that subjects in this study were younger that those in our study (median age 34 y and 54 y, respectively).

In contrast, data from the Framingham study showed no association between egg consumption and CHD among 912 men and women after 16 years of follow up(18). The average weekly egg consumption in Framingham was ~6 /week for men and 4/week for women. In a case-control study among 936 Italian women, egg consumption was not associated with MI with age-adjusted odds ratios were 1.0, 1.2, and 0.8 for egg intake of <1, 1-2, and >2/week(27). In a large cohort of 5186 women and 4077 men, Nakamura et al.(20) reported no association between egg consumption and all-cause mortality as well as CVD deaths in Japanese men after 14 years of follow up. There was little effect observed in women in that study. Other large cohorts reported no association between egg consumption and CHD, stroke, and mortality (19;28). However, in these later studies, there was suggestive evidence for an increased risk of CVD among subjects with diabetes. Qureshi et al.(28) reported a 2-fold increased risk of CHD among people reporting an intake of 6+ eggs/wee compared with intakes of < 1/week. In addition, comparing to egg intake of < 1/week, Hu et al.(19) reported a 2-fold increased risk of CHD for egg consumption of >1/week among 37,851 diabetic men from the Health Professionals Follow-up Study after adjustment for potential confounders; In the same paper, the corresponding increase risk of CHD was 49% among diabetic women from the Nurses' Health Study. These findings among diabetics are consistent with our report of a dose-response association between egg consumption and all-cause mortality among PHS participants with prevalent diabetes at baseline. Could a biological mechanism help explain the positive association between egg consumption and CVD or mortality among diabetics?

Overall, epidemiologic studies suggest that among hyperresponders, dietary cholesterol from egg leads to a modest increase serum LDL and HDL cholesterol and no effect on LDL/HDL ratio (8;29-32). It is estimated that each 100 mg of dietary cholesterol results in 1.9 mg/dL increase in LDL and 0.4 mg/dL increase in HDL(32). Of note is that this estimation does not take into account the effects of saturated fat or response type to dietary cholesterol. In addition, in randomized trials, consumption of eggs was associated with an increase in LDL peak diameter and a decrease in smaller LDL subfraction, suggesting that egg consumption may lead to a less atherogenic lipoprotein profile(13;33). In the same study, 5 of the children with LDL phenotype B shifted to pattern A (low-risk pattern)(13). However, other investigators did not report an effect of egg consumption on LDL subfraction(29). Because of the wide variability in individual response to dietary cholesterol (hyper-responders vs. hypo-responders), it is not known whether such differential response to egg consumption could selectively influence glucose metabolism and thus help understand our findings of increased risk of death among people with diabetes in particular. Furthermore, it has been shown that baseline cholesterol influences individual response to dietary cholesterol (with higher baseline serum cholesterol leading to little effects of dietary cholesterol)(34). At present, we can only speculate that perhaps among diabetic subjects, dietary cholesterol might lead to a less favorable lipoprotein profile in terms of serum concentration and particle size, with a shift to smaller and dense LDL particle size, leading to accelerated atherosclerosis and its complications. Testing of such hypothesis in an experimental design among diabetics is warranted.

Our study has additional limitations. We cannot exclude unmeasured confounding or residual confounding as possible explanation of the observed positive association among diabetic subjects. In particular, we were not able to examine the effects of saturated fat, markers of insulin resistance, lipids, and other nutrients or relevant biomarkers on the observed association. While in our study, the lack of detailed dietary questionnaire prevent us from controlling for energy and other major nutrients, this was not the case in the Nurses' Health Study and the Health Professionals' Follow-up Study(19), where total energy intake was accounted for. Changes of dietary patterns may lead to a spurious association between baseline exposure and incident outcome. In our data, we used time-dependent Cox regression model to update reported egg consumption at 24, 48, 72, 96, and 120 months after randomization. Such exposure update over time led to similar conclusion, suggesting that our findings are robust. The fact that our sample consists of male physicians who may have different behaviors than the general population limits the generalizability of our findings. In addition, being knowledgeable about the dietary cholesterol content of eggs might have led to a higher probability to adopt other healthful behaviors, which would attenuate any unfavorable effect of egg consumption. However, this hypothesis is not consistent with the lower frequency of exercise and intake of breakfast cereals and higher proportion of smokers among frequent egg consumers. Similar data were reported in the Health Professional Follow-up Study(19). Because we had limited cases of CHD and stroke, we did not have sufficient power to detect an interaction between prevalent diabetes and egg consumption on the risk of MI or total and subtypes of stroke. Nevertheless, the large sample size, the longer duration of follow up, the robustness of our findings in sensitivity analyses are strengths of the present study.

In conclusion, our data suggest that egg consumption up to 6/week has no major effect on the risk of CVD and mortality and that consumption of 7+/week is associated with a modest increased risk of total mortality in US male physicians. However, among male physicians with diabetes, any egg consumption is associated with an increased risk of all-cause mortality and there was suggestive evidence for an increased risk of MI and stroke. Confirmation of these findings in the general population and among diabetic subjects along with investigation of possible biologic mechanisms is warranted.

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Table 1

Characteristics of 21,327 participants according to categories of egg consumption in the Physicians' Health Study *

Variables	Weekly egg consumption in the Physicians' Health Study					P for trend
	<1 (n=4,564)	1 (n=6,627)	2-4 (n=6,983)	5-6 (n=1,421)	7+ (n=1,732)	
Age (y)	53.0±9.3	53.4±9.3	53.6±9.5	54.1±9.4	56.8±10.1	<0.0001
Body mass index (kg/m^2)	24.5±2.6	24.7±2.7	24.9±2.7	25.2±2.9	25.0±3.2	<0.0001
Vegetable intake (servings / week)	7.9±5.0	8.0±4.6	8.2±4.6	8.2±4.6	8.6±5.1	<0.0001
Breakfast cereal (7+/week) [%]	24.1	24.0	15.9	10.8	11.8	<0.0001
Parental history of premature MI (%)	10.8	9.1	9.5	7.2	7.2	<0.0001
Hypercholesterolemia (%)	13.6	12.2	11.3	10.8	10.5	<0.0001
Current smoking (%)	8.0	9.8	12.0	14.9	16.7	<0.0001
Current alcohol drinking (%)	71.0	75.0	75.5	74.5	73.9	<0.0001
Exercise 1+/ week (%)	71.8	72.6	72.9	72.7	69.9	<0.0001
History of diabetes (%)	1.2	1.8	2.0	2.3	5.2	<0.0001
History of Hypertension (%)	21.9	23.8	23.9	25.4	28.5	<0.0001
History of atrial fibrillation (%)	1.3	1.5	1.3	1.8	1.3	0.67
Current use of multivitamins (%)	20.0	18.6	19.9	20.2	24.0	0.001
Aspirin assignment (%)	49.5	49.5	50.3	51.6	50.1	0.22

* Continuous variables are shown as mean ± SD; P values for trend obtained from analysis of variance or logistic regression model.

Table 2

Hazard ratios (95% CI) for myocardial infarction according to egg consumption

Egg consumption	Cases	Hazards Ratio (95% CI)		
		Age-adjusted	Model 1*	Model 2†
<1 per week	291	1.0	1.0	1.0
1 per week	474	1.10 (0.95-1.27)	1.05 (0.91 – 1.22)	1.12 (0.96 – 1.31)
2-4 per week	546	1.21 (1.05-1.40)	1.14 (0.99 – 1.32)	1.16 (1.00 – 1.36)
5-6 per week	115	1.24 (1.00-1.54)	1.12 (0.91 – 1.40)	1.18 (0.93 – 1.49)
7+ per week	124	1.02 (0.83-1.27)	0.92 (0.74–1.14)	0.90 (0.72 – 1.14)
P for linear trend		0.21	0.94	0.88

*Adjusted for age, body mass index (continuous), smoking (never, past and current smokers), and history of hypertension.

†Adjusted as in model 1 plus vitamin intake, alcohol consumption (<1, 1-4, 5-6, 7+ drinks/week), vegetable consumption (<3, 3-4, 5-6, 7-13, 14+ servings/week), breakfast cereal (0, 1, 2-6, 7+ servings/week), physical activity (<1, 1, 2-4, 5+/week), treatment arm (4 groups) atrial fibrillation (yes/no), diabetes mellitus, hypercholesterolemia (yes/no), and parental history of premature myocardial infarction (yes/no).

Table 3

Hazard ratios (95% CI) for stroke according to egg consumption

Egg consumption	Cases	Hazards Ratio (95% CI)		
		Age-adjusted	Model 1*	Model 2†
<1/week	257	1.0	1.0	1.0
1/week	386	1.01 (0.86-1.18)	0.96 (0.82 – 1.12)	0.96 (0.82 – 1.13)
2-4/week	459	1.13 (0.97-1.32)	1.07 (0.92 – 1.25)	1.06 (0.91 – 1.24)
5-6/week	103	1.22 (0.97-1.54)	1.13 (0.90 – 1.42)	1.13 (0.89 – 1.42)
7+/week	137	1.17 (0.95-1.44)	1.06 (0.86 –1.30)	0.99 (0.80 – 1.23)
P for linear trend		0.02	0.14	0.40

*Adjusted for age, body mass index (continuous), smoking (never, past and current smokers), and history of hypertension.

†Adjusted as in model 1 plus vitamin intake, alcohol consumption (<1, 1-4, 5-6, 7+ drinks/week), vegetable consumption (<3, 3-4, 5-6, 7-13, 14+ servings/week), breakfast cereal (0, 1, 2-6, 7+ servings/week), physical activity (<1, 1, 2-4, 5+/week), treatment arm (4 groups) atrial fibrillation (yes/no), diabetes mellitus, hypercholesterolemia (yes/no), and parental history of premature myocardial infarction (yes/no).

Table 4

Hazard ratios (95% CI) for all-cause mortality according to egg consumption

Egg consumption	Cases	Hazards Ratio (95% CI)		
		Age-adjusted	Model 1*	Model 2†
<1/week	1000	1.0	1.0	1.0
1/week	1469	0.98 (0.90-1.06)	0.93 (0.85 – 1.00)	0.94 (0.87 – 1.02)
2-4/week	1685	1.06 (0.98-1.15)	1.01 (0.93 – 1.09)	1.03 (0.95 – 1.11)
5-6/week	366	1.11 (0.98-1.25)	1.03 (0.91 – 1.16)	1.05 (0.93 – 1.19)
7+/week	649	1.41 (1.28-1.55)	1.27 (1.15 –1.40)	1.23 (1.11 – 1.36)
P for linear trend		<0.0001	<0.0001	<0.0001

*Adjusted for age, body mass index (continuous), smoking (never, past and current smokers), and history of hypertension.

†Adjusted as in model 1 plus vitamin intake, alcohol consumption (<1, 1-4, 5-6, 7+ drinks/week), vegetable consumption (<3, 3-4, 5-6, 7-13, 14+ servings/week), breakfast cereal (0, 1, 2-6, 7+ servings/week), physical activity (<1, 1, 2-4, 5+/week), treatment arm (4 groups) atrial fibrillation (yes/no), diabetes mellitus, hypercholesterolemia (yes/no), and parental history of premature myocardial infarction (yes/no).

Table 5

Hazard ratios (95% CI) for all-cause mortality according to baseline prevalent diabetes and egg consumption

Egg consumption	Subject without prevalent diabetes				Subjects with prevalent diabetes		
	Cases	Model 1*	Model 2†		Cases	Model 1*	Model 2†
<1/week	971	1.0	1.0		29	1.0	1.0
1/week	1408	0.92 (0.85-1.00)	0.93 (0.85 – 1.01)		61	1.20 (0.77-1.87)	1.30 (0.82-2.07)
2-4/week	1605	0.99 (0.92-1.08)	1.01 (0.93 – 1.10)		80	1.30 (0.85-1.99)	1.49 (0.95-2.33)
5-6/week	341	0.99 (0.88-1.12)	1.00 (0.88 – 1.13)		25	2.48 (1.44-4.27)	2.27 (1.28-4.03)
7+/week	581	1.23 (1.11-1.37)	1.22 (1.09 –1.35)		68	1.55 (1.00-2.40)	2.01 (1.26-3.20)
P for linear trend		<0.0001	<0.0001			0.009	0.0005
P for interaction model 1*				0.029			
P for interaction model 2†				0.09			

*Adjusted for age, body mass index (continuous), smoking (never, past and current smokers), and history of hypertension.

†Adjusted as in model 1 plus vitamin intake, alcohol consumption (<1, 1-4, 5-6, 7+ drinks/week), vegetable consumption (<3, 3-4, 5-6, 7-13, 14+ servings/week), breakfast cereal (0, 1, 2-6, 7+ servings/week), physical activity (<1, 1, 2-4, 5+/week), treatment arm (4 groups) atrial fibrillation (yes/no), hypercholesterolemia (yes/no), and parental history of premature myocardial infarction (yes/no).