Table S2 Observational Studies of an Association of Egg Consumption with Cardiovascular Events (based on Food Frequency Questionnaires)

Study	Population	Egg Intake	Population characteristics	Event ascertainment	Findings
Hu JAMA 1999[1] Health Professionals Follow-up Study (HPFS) and Nurses' Health Study (NHS)	HPFS: 37,851 males, ages 40-75 excluded men with diabetes, CVD, cancer or high cholesterol at baseline NHS: 80,082 women	5 intake categories: <1, 1, 2-4, 5-6 per week or ≥1 per day HPFS: mean egg intake/d 2.3/wk in 1986 1.6/wk in 1990 6.3% consumed ≥1/d Fully adjusted models included age, energy intake, tobacco and alcohol use, BMI, history of HTN, vitamin use, consumption of whole milk, fish, beef as main dish, chicken, or cereal. NHS also adjusted for menopausal status, post-menopausal hormone use and exercise. NHS: 2.8/wk in 1980 1.4 /wk in 1990 8.9% consumed ≥1 per day		Primary outcome for HPFS and NHS incident CHD and stroke Based on participant report, then adjudicated with hospital records	HPFS: Mean follow-up 8 yrs CHD with >1 egg/day vs <1 egg/wk RR 1.08 (95% CI, 0.79-1.48) Among men with diabetes RR 2.02 (95% CI 1.05-3.87; P=.04 for trend) Stroke RR 1.07 (95% CI, 0.66-1.75) NHS: mean follow-up 14 yrs CHD RR 0.82 (95% CI, 0.60-1.13) Among women with diabetes RR 1.49 (95% CI, 0.88-2.52; *P* = .008 for trend) Stroke: RR 0.89 (95% CI, 0.60-1.3

Sauvaget Int J Epi 2003[2] Hiroshima/Nagasaki Life Span Study	40,349 males and females enrolled in 1979	4 intake categories never, <once/week, 2–4 times/week, and 'almost daily 29.6% consumed eggs almost daily Fully-adjusted model included age, sex, smoking status, alcohol intake, BMI, education, diabetes, hypertension, radiation dose, study center			Mean follow-up 16 yrs Daily egg intake vs no egg intake Stroke Mortality HR 0.70 (0.51, 0.95); Similar decreased risk with those who consumed <once a wk and 2-4 times/wk
Nakamura Br J Nutr 2006[3] Japan Public Health Center-based prospective study	90,735 participants 1 cohort in 1990 and 2nd cohort in 1993 ages 40-59 in 4 prefectures, and 40-69 in 5 prefectures	4 intake categories <1 d/wk, 1–2 d/wk, 3–4 d/wk and almost every day 31% consumed eggs almost everyday Fully adjusted model included age at baseline, sex, BMI, diabetes, hypertension, cigarette smoking, alcohol intake, use of cholesterol-lowering drugs, dietary intake categories of meat (beef and pork), fish (fresh and dry), vegetables, fruits, whether or not intended to avoid cholesterol-rich diets, and cohort effects		Endpoint CHD death and nonfatal MI Participant report on 5- and 10-year follow-up questionnaire, adjudicated with medical records; also performed systematic search for death certificates	Cohort 1: follow-up 11 yrs Cohort 2: follow-up 8 yrs CHD Events No significant association with egg intake Prevalence of HTN lower in the group with highest egg consumption; intake of fruit, vegetables, fish and meat also higher than groups with lower consumption of eggs

Qureshi Med Sci Monit 2007[4] National Health and Nutrition Examination I (1971-1975)	follow-up through the 1992 exam 9,734 males and females Mean age 48.1-51.9	3 intake categories <1 egg/wk, 1-6/wk, and ≥6/wk 20% reported consuming ≥6/wk Multivariate analysis adjusted for age, gender, race/ethnicity, systolic blood pressure, serum cholesterol, BMI, DM, cigarette smoking, and education		Outcomes coronary artery disease events and stroke	CHD, Stroke or Mortality: No association with egg intake Among adults with diabetes with ≥6/wk RR of CHD 1.9 (95% CI 1.0–3.5)
Djousse and Gaziano. Am J Clin Nutr 2008[5] Physicians' Health Study I	Observational study within Physicians' Health Study I, a 2x2 factorial design to study low-dose aspirin and β-carotene for the primary prevention of CVD and cancer among US male physicians; 21,327 participants included in the current analysis	Detailed questionnaire, stratified consumption into groups: <1, 1, 2–4, 5–6, and ≥7 eggs/wk The final multivariate model controlled for hypercholesterolemia, parental history of premature MI, diabetes, atrial fibrillation, consumption of breakfast cereal, alcohol, vegetables, use of multivitamins and physical activity	Mean age at baseline 53.7±9.5 years 8.1% consumed ≥7 eggs/wk	Outcomes CHD, stroke, all-cause mortality Based on participant report and confirmation with hospital records	-no significant association with egg consumption and MI or stroke -significant association with all-cause mortality in men who consumed ≥7 eggs/wk, HR 1.23 (95% CI, 1.11-1.36) -risk of death was stronger in men with diabetes in highest vs lowest category of egg consumption (HR: 2.01; 95% CI 1.26, 3.20); *P* for interaction 0.09
Djousse and Gaziano Circulation 2008[6] Physicians' Health Study I	Observational study within Physicians' Health Study I	Detailed questionnaire, stratified consumption into groups: <1, 1, 2–4, 5–6 per week, and 1/day or ≥2/day The multivariate model controlled for age, BMI,	6.9% consumed 1/day and 1.2% consumed ≥2/day Egg consumption declined over time; 23.5% reported no egg consumption	Primary outcome: heart failure Based on participant report, including responses to a HF questionnaire with detailed questions about	-Mean follow-up 20.4 years -There was a significant association of high egg intake with incident heart failure. Compared to adults who consume <1 egg/wk HR of heart

		smoking, alcohol consumption, DM, hypertension, atrial fibrillation, hypercholesterolemia, physical activity, and history of valvular heart disease Used time-dependent Cox regression models to update reported egg consumption at 24, 48, 72, 96, and 120 months	at 10-year follow-up versus 6.9% at baseline; egg consumption of >1 per day decreased from 8.1% at baseline to 2.1% after 10 years of follow-up.	time and place of HF diagnosis, clinical signs and symptoms, medical treatment, and diagnostic methods (echocardiography, angiography, and radionuclide imaging)	failure for those who consumed 1/day 1.28 (95 CI, 1.02–1.61), and ≥2/day 1.64 (95% CI, 1.08–2.49) -no interaction with diabetes status or after excluding adults with antecedent MI -lacked power to evaluate association among adults with antecedent MI
Nettleton J Am Diet Assoc 2008[7] Atherosclerosis Risk in Communities Study (ARIC)	14,153 participants without prevalent HF at baseline	66-item FFQ administered at baseline (1987–1989) and Exam 3 (1993–1995); thereafter, intake was based on averaged baseline and Exam 3 responses Fully adjusted model included energy intake, age; sex; race; study center; education, smoking status, smoking intensity, physical activity level, and alcohol consumption; and baseline history of CVD [coronary heart disease and stroke], diabetes, hypertension, intakes of whole grains, high-fat dairy, fruits/vegetables, fish,	Mean age 53.9 among those without and 57 among those with incident HF Mean egg intake among those without HF 0.29 eggs/day Mean egg intake among those with heart failure 0.36 eggs/day	Primary outcome: hospitalized or fatal heart failure Review of county death certificates and local hospital discharge lists and defined according to the International Classification of Diseases Codes (ICD-9 or ICD-10). Incident HF was defined as first HF hospitalization (428, ICD-9) or any death where the death certificate included an HF code (428, ICD-9 and I50, ICD-10). Nonhospitalized, nonfatal HF was not captured	Mean follow-up 13 years Greater intake of eggs associated with RR of heart failure (RR per 1 serving/day=1.23 [95% CI, 1.08-1.41]) No interaction with diabetes status or presence of other risk factors

		nuts, eggs, and red/processed meat			
Zazpe Eur J Clin Nutr 2011[8] Seguimiento Universidad de Navarra (SUN) Project	Prospective cohort study of 14,185 adults in Spain, all participants are university graduates, >50% are health professionals	136-item FFQ Egg consumption stratified into 4 groups: <1/wk, 1/wk, 2–4/wk and ≥4/week Fully adjusted model included age, sex, and baseline total energy intake, adherence to the Mediterranean food pattern, alcohol intake, BMI, smoking status, physical activity during leisure, family history of CVD years, self-reported diabetes, self-reported hypertension and self-reported hypercholesterolemia	Mean age 38.4 10.9% consumed ≥4 eggs/week	CVD defined as a composite of fatal or nonfatal MI, fatal or nonfatal stroke	Mean follow-up 5.8 years No significant association in the whole cohort with egg consumption and CVD events HR for CVD for the highest egg consumption category vs lowest egg category among participants age ≤56 and >56 years were, respectively, HR: 0.47 (95% CI: 0.11–2.05) and 2.94 (95% CI: 0.93–9.30). P-value for interaction (likelihood ratio test) was 0.075
Bernstein Stroke 2012[9] Health Professionals Follow-up Study and Nurses' Health Study	Health Professionals Follow-up Study and Nurses' Health Study	FFQ Compared protein sources and risk of stroke Model adjusted for age and calendar time, and included dietary protein sources, and also intakes of total energy, cereal fiber, alcohol, fruit and vegetables servings/day), trans, or unsaturated fatty acids, and potential nondietary confounding variables, which were	Egg consumption stratified into quintiles	Stroke	2 041 679 person-years of follow-up from 1980 through 2006 in the NHS, and 833 660 person-years of follow-up from 1986 through 2008 in the HFPS

		updated biennially: body mass index, physical exercise, cigarette smoking, menopausal status in women, parental history of early myocardial infarction (age <60 years), years of multivitamin use, vitamin E supplement use, and aspirin use			
Chagas Atherosclerosis 2012[10]	382 adults referred for coronary angiogram at The Center for Cardiovascular Diagnosis and Intervention, São Lucas Hospital (Porto Alegre, Brazil)	Egg consumption was divided into three categories: less than one egg a week; one egg a week; and more than one egg a week model of multiple linear regression was completed using the FS as the dependent variable and the other variables (socio-demographic data, cardiovascular risk factors and egg consumption) as the independent variables	Direct personal interviews	Atherosclerotic burden on coronary angiogram graded by Freisinger score	Egg consumption f more than 1 egg/wk inversely associated with atherosclerotic burden
Goldberg Atherosclerosis 2013[11] Northern Manhattan Study (NOMAS)	1429 participants	207-item FFQ Egg consumption never or <1/month, 1/month, 2-3/month, 1/week, 2/week, 3-4/week, 5-6/week, 1/day, 2/day Fully adjusted model included age, sex, vascular risk factors (BMI, diabetes, hypertension, LDL cholesterol, HDL cholesterol, triglycerides, cholesterol-lowering medication use, moderate alcohol use, moderate-heavy physical activity, smoking, and education level), total daily kilocalories consumed and the Mediterranean-style diet	5% of participants consumed >2eggs/week	Carotid intima media thickness a combined incident vascular event (incident stroke, MI, or vascular death)	Increasing egg consumption was inversely associated with CIMT, plaque presence, thickness, and area, in models adjusted for demographics, vascular risk factors and diet. For every additional egg consumed per week, the risk of plaque decreased by 11% (95% CI 3%-18%)

		score. history of stroke among siblings, history of MI among siblings, daily consumption of saturated fat, unsaturated fat, protein and carbohydrates			no association between egg consumption and vascular events
Robbins ESPEN-J 2014[12] the NHLBI Family Heart Study	1848 participants	588 families were chosen at random (with 2673 subjects) and 566 families were selected based on higher than expected risk of CHD (3037 subjects) clinical evaluation (between 1993-1995), CAC testing Model was adjusted for age, sex, field center, BMI, smoking, alcohol intake, physical activity, income, bacon consumption, history of hypertension and diabetes	staff-administered semi-quantitative food frequency questionnaire	Coronary artery calcium	no association between egg consumption and prevalent CAC
Haring PLoS One 2014[13] Atherosclerosis Risk in Communities Study (ARIC)	12,066 participants	FFQ at baseline (1987-1999), then 6 years later Model adjusted for age, sex, ARIC study center, total energy intake, smoking, education, systolic blood pressure, use of antihypertensive medication, HDLc, total cholesterol, use of lipid lowering medication, body mass index (kg/m2), waist-to-hip ratio, alcohol	In top quintile median consumption was 1 egg/day	Coronary heart disease	median follow-up of 22 years, through December 31, 2010 no association of egg intake and CHD risk

		intake, Baecke's physical activity score, leisure-related physical activity, carbohydrate, fiber and magnesium intake			
Choi Atherosclerosis 2015[14]	23,417 adults referred for coronary artery calcium testing at Kangbuk Samsung Hospital Total Healthcare Centers, South Korea (March 2011 to April 2013	102-item FFQ Egg consumption divided into 5 categories < 1, 1 < 2, 2 < 4, 4 < 7, and ≥7 eggs/wk Fully adjusted models included age, sex, study center, education, physical activity, smoking, BMI, parental history of CHD, self-reported history of hypertension, alcohol consumption, and consumption of total energy, fruits, vegetables, and red and processed meats. Additional adjustment then made for lipids, HOMA-IR, glucose. 3rd model included adjustment for cholesterol intake.	Median age 41, 78.6% male 5.2% consumed ≥7 eggs/wk Mean egg consumption 2.1 per week Prevalence of CAC>0 was 11.6%	Coronary artery calcium score measured at the time of the FFQ	Prevalence ratio of CAC 1-100 vs 0 was 1.20 (0.97-1.47) among adults who consumed ≥7 eggs/wk vs none Prevalence ratio for CAC>100 was 1.75 (1.14-2.68) Association between egg consumption and CAC scores was stronger in participants with low vegetable intake compared to those with high vegetable intake (P for interaction =0.02) borderline significance for interaction with BMI, p=0.05
Larsson Am J Clin Nutr 2015[15] Cohort of Swedish Men	37,766 men (Cohort of Swedish Men) and 32,805 women (Swedish Mammography Cohort)	FFQ 8 predefined frequency categories: never, 1–3/mo, 1–2/wk, 3–4/wk,	-Mean ±SD egg consumption was 1.4 ± 1.6/wk in men and	Swedish National Patient Register [includes inpatient and outpatient (non-primary	13 years of follow-up -no statistically significant association between egg

And Swedish Mammography Cohort		5–6/wk, 1/d, 2/d, or ≥3/d.	1.4 ± 1.4/wk in women. Only 2.7% of men and 2.1% of women consumed ≥1 eggs/d.	care) data] and the Swedish Cause of Death Register (also includes nonhospitalized cases)	consumption and MI or any stroke type in either men or women; -no association with HF in women. - in men, consumption daily egg (>1/d) was associated with HF (RR: 1.30; 95% CI: 1.01, 1.67).
Virtanen Am J Clin Nutr 2016[16] Kuopio Ischaemic Heart Disease Risk Factor Study	1032 men aged 42–60 y in Eastern Finland, baseline exam 1984–1989 Association of egg intake with CIMT and CHD was stratified with APOE4 genotype, given strong associations between the presence of APOE4 and high cholesterol levels	Guided 4-day food record Egg consumption variable represents total egg consumption, including eggs in mixed dishes and recipes Fully-adjusted model included age, examination year, and energy intake, BMI (kg/m2), diabetes, hypertension, family history of CHD, smoking, education years, leisure-time physical activity, and intake of alcohol, PUFAs (% of energy), SFAs (% of energy), dietary fiber (g/d), and fruit, berries, and vegetables	Mean age 51.4-52.3 Mean egg intake ≈4 medium-sized eggs/wk 15% consumed ≥1egg/day 28.6% had the ApoE 3/4 phenotype and 3.9% had the 4/4 phenotype Men with a higher egg intake were more physically active and less likely to smoke and to have diabetes. They also had higher intakes of energy, fiber, and saturated fat and a lower polyunsaturated fat intake.	Outcomes: Carotid intima media thickness, CHD events **CIMT**: Measured in right and left common carotid arteries (CCAs) in a 1.0-1.5-cm section at the distal end of the CCA, proximal to the carotid bulb **CHD**: Data on fatal and nonfatal CHD events from the beginning of the study to the end of the year 2012 were obtained by computer linkage to the national hospital discharge and death certificate registers	Mean follow-up 20.8 years No association of egg intake and CIMT in the whole cohort or stratified by ApoE subtype no significant associations between egg intake and CAD risk in the whole study population or in the analyses stratified by the ApoE4 phenotype each 1 additional egg (55 g)/d was associated with a HR of 1.17 (95% CI:0.85, 1.61) in the ApoE4 noncarriers and an HR of 0.93 (95% CI: 0.50, 1.72) in the ApoE4 carriers (P-interaction = 0.34)

Diez-Espino Clinical Nutrition 2017[17] PREvention conDIeta MEDiterranea (PREDIMED)	Observational study within the PREvention conDIeta MEDiterranea (PREDIMED) randomized controlled trial; in 7,216 adults ages 55-80 in Spain at high cardiovascular risk; compared standard advice about Mediterranean diet vs enrichment with extra virgin olive oil or nuts	Annual 137-item FFQ 3 categories of egg consumption: <2 (low), 2-4, >4 eggs/week (high) fully adjusted model included adjustment for Mediterranean diet score, alcohol intake, and total energy intake	-34.8% consumed <2 eggs/wk; 62.3% consumed 2-4 eggs/wk; 2.9% consumed >4 eggs/wk -adults reporting >4 eggs/week were younger, had higher physical activity and education level, total energy and alcohol intake; more likely to be male, current smokers, less likely to take insulin than adults reporting <2 eggs/week	Primary endpoint composite MI, stroke and death from CVD; ascertained by participant report, contacts with general practitioners of participants, yearly review of medical records, and National Death Index	Mean follow-up 5.8 years; -no significant association between high and low consumption (HR 0.96, 95% CI 0.33-2.76) -no interaction with diabetes status
Farvid. Am J Prev Med. 2017[18] The Golestan Cohort Study in Iran	Prospective cohort study of 42,403 adults in Iran	116-item FFQ Multivariate models were adjusted for age, gender, place of residence, marital status, educational level, ethnicity, cigarette smoking, opium use, BMI, systolic blood pressure, family history of cancer, occupational physical activity, medication, wealth score, alcohol consumption, and total energy intake, fruit and vegetable or total grain intake, intake of low-fat dairy foods	Median egg intake in the highest quartile 0.48 eggs/day	Outcomes: death due to CHD, stroke or CVD Deaths were reported by family members, friends, or local health workers during annual telephone calls. When a death was reported, a physician visited the house to complete a validated verbal autopsy questionnaire by interviewing the next of kin. Relevant medical documents including medical charts, radiography and pathology reports, and hospital discharge reports were gathered from the hospitals	Median follow-up 8 years Higher egg consumption was associated with a lower all-cause mortality risk (HR [highest versus lowest] =0.88, 95% CI=0.79, 0.97, p trend=0.03 Substituting one serving/day of eggs for one serving/day of total red meat was associated with a lower risk of all-cause mortality (HR=0.65, 95% CI=0.43, 0.98 No association between egg consumption and CVD, CHD or stroke

Nakamura Eur J Clin Nutr 2018[19] The National Survey on Circulatory Disorders, Japan (NIPPON DATA)	4,686 woman randomly selected in Japan in 1990, age≥30	31-item FFQ Egg consumption stratified into 5 groups: <1/w, ≈1–2/w, ≈1/2d, ≈1/d, and ≥2/d Fully adjusted models included age, BMI, hypertension, DM, cigarette smoking, and alcohol intake, therapy for dyslipidemia, and intake of fiber, meat, and sodium	29.6% consumed 1 egg/day, <1% consumed 2/day Mean age of women who consumed 1 egg/day 52.2 ± 14.3 Mean BMI 22.7 ± 3.2 kg/m^2 Prevalence of DM 4.7%; HTN 38.9%	Primary outcome cardiovascular mortality National Vital Statistics, Japan; based on ICD-9 codes	Follow-up 15 years No significant association with egg intake and CVD mortality; HRfor CVD death with 1-2 eggs/wk vs 1/day 1.16 (0.81–1.67)

Abbreviations: HPFS—Health Professionals Follow-up Study; NHS—Nurses' Health Study; BMI—Body Mass Index; HTN—hypertension; CHD—Coronary Heart Disease; RR—Relative Risk; HR—Hazard Ratio; MI—myocardial infarction; DM—diabetes mellitus; CI—Confidence Interval; HF—Heart Failure; FFQ—Food Frequency Questionnaire; CVD—cardiovascular disease; CIMT—carotid intima-media thickness; NHLBI—National Heart Lung and Blood Institute; CAC—coronary artery calcium; ICD-9—International Classification of Disease, version 9;

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