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ORIGINAL CONTRIBUTION

Moderate egg consumption and all-cause and specific-cause mortality in the Spanish European Prospective into Cancer and Nutrition (EPIC-Spain) study

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Abstract

Purpose Dietary guidelines for egg consumption for general population differ among public health agencies. Our aim was to investigate the association between egg intake and both all-cause and specific-cause of mortality in a Mediterranean population.

Methods The European Prospective Investigation into Cancer and Nutrition (EPIC)-Spain cohort included 40,621 men and women aged 29–69 years old in the nineties from 5 Spanish regions. After a mean of 18 years of follow-up, 3,561 deaths were recorded, of which 1,694 were from cancer, 761 from CVD, and 870 from other causes. Data on egg consumption was collected using a validated diet history at recruitment. Cox proportional hazards models, adjusted for confounders, were used in the analyses.

Results The mean (standard deviation) egg consumption was 22.0 g/day (15.8) and 30.9 g/day (23.1) in women and men, respectively. No association was observed between egg consumption and all-cause mortality for the highest vs the lowest quartile (HR 1.01; 95% CI 0.91–1.11; *P* trend = 0.96). Likewise, no association was observed with cancer and cardiovascular diseases mortality. However, an inverse association was found between egg consumption and deaths for other causes (HR 0.76; 95% CI 0.63–0.93; *P* trend = 0.003), particularly for deaths from the nervous system (HR 0.59; 95% CI 0.35–1.00; *P* trend = 0.036). No interaction was detected with the adherence to Mediterranean diet.

Conclusions This study shows no association between moderate egg consumption, up to 1 egg per day, and main causes of mortality in a large free-living Mediterranean population.

Keywords Egg · Intake · Mortality · EPIC-Spain · Cohort

Abbreviations

CVD	Cardiovascular diseases
EPIC	European Prospective Investigation into Cancer and Nutrition
ICD	International Classification of Diseases

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Introduction

The dietary recommendation of egg intake is still a controversial topic for nutritional experts and public health agencies. On one hand, eggs are an inexpensive source of high-quality protein, all B vitamins, folate, fat-soluble vitamins, as well as, several essential minerals that play a fundamental role in basic nutrition. On the other hand, eggs are a main source of cholesterol and relevant of saturated fat that are potentially associated with an increased risk of cardiovascular diseases (CVD) and type 2 diabetes [1].

Dietary guidelines on egg and cholesterol consumption vary among specialist societies, countries, and also differ along the time. The 2010 American Heart Association Dietary Guidelines recommendation to limit consumption of dietary cholesterol to 300 mg per day is not included in the 2015 edition; however, the guidelines state that "individuals should eat as little dietary cholesterol as possible while consuming a healthy eating pattern" [1]. Similarly, the British Heart Foundation recently removed their advice to limit egg consumption to three per week and there is currently no restriction on egg consumption [2]. Some countries, including Thailand, Mexico, New Zealand and Japan, recommend eating eggs regularly as part of a healthy diet for general population [3]. However, the Mediterranean Diet Foundation recommends 3–4 eggs per week, as a good alternative to fish or meat [4]. These recommendations are mostly based on the cholesterol content of eggs. Epidemiological evidence from studies investigating the association between egg consumption and either CVD risk or cardiovascular mortality is in favour of these new recommendations [5], but epidemiological evidence on overall mortality and other causes of death [6–9] is still limited, particularly in Mediterranean populations. Therefore, in the present study, we aimed to evaluate the relationships between egg consumption and all-cause and specific-cause mortality in a large adult Spanish cohort.

Subjects and methods

Study design and population

The European Prospective Investigation into Cancer and Nutrition (EPIC) is an ongoing multi-centric cohort conducted across ten European countries [10]. In the present study, we use data from the Spanish cohort of EPIC, which consists of 41,437 adult participants, aged 29–69 years, enrolled between 1992 and 1996 from 5 Spanish regions: Asturias, Granada, Guipúzcoa, Murcia and Navarra [11]. All participants were apparently healthy volunteers, mostly blood donors, and gave a written informed consent. The study was approved by the Medical Ethical Committee of the Bellvitge University.

Follow-up and mortality ascertainment

Date and vital status were obtained through record linkage with the Spanish National Statistics Institute (Instituto Nacional de Estadística). Cause of death was coded using International Classification of Diseases (ICD)-10; coding I00-I99 for CVD, C00-C99 for cancer, and remaining codes (including benign tumours classified as D1-D48, diseases of the nervous system G00-G99, diseases of the respiratory system J00-J99, and diseases of the digestive system K00-K95) for other causes. For this analysis, the follow-up for vital status was completed between December 2011 and December 2013 depending on the centre. After the exclusion of 816 subjects because of implausible dietary information (the lowest and highest 1% of the ratio of total energy intake to energy requirement), the final population studied consisted of 40,621 subjects, among whom 3,561 died during the follow-up period.

Dietary and lifestyle data

Habitual food intake of the previous year was collected at the baseline using a computerised version of a validated dietary history questionnaire and was administered by trained interviewers [12–14]. The portion sizes of each food consumed (g/day) were assessed by means of a photo series, natural units, and household measures. The edible weight of a standard egg was considered 50 g. The EPIC Nutrient DataBase (ENDB), a country-specific food-composition database, was used to estimate each participant's total energy intake (kcal/d) and daily nutrient intake [15]. The Mediterranean score (0–18 points) was used to estimate the level of adherence to the Mediterranean diet, as previously applied in EPIC studies [16]. Briefly, six components presumed to reflect the Mediterranean Diet (vegetables, fruits and nuts, legumes, fish and seafood, cereals, and olive oil) and two components presumed not to reflect the Mediterranean Diet (dairy products and meat), were calculated as a function of energy density (g/day/2000 kcal) and divided into tertiles. Alcohol was scored as a dichotomous variable, assigning 2 for moderate consumers (range: 5–25 g/day for women and 10–50 g/day for men) and 0 for subjects outside (above or below) the sex-specific range.

An interviewer-administered lifestyle questionnaire was used to collect information on sociodemographic and lifestyle factors, including history of tobacco consumption and alcohol intake, physical activity and reproductive and medical history (including medication use and history of diseases such as diabetes, cancer and CVD). Weight and height were measured by trained personnel at recruitment [10].

Statistical analyses

Data on egg consumption was analysed both as a categorical (sex-specific quartiles) and as a continuous variable (per 1 egg/week). Trend tests were calculated on the basis of quartile-based scores 1–4 used as continuous variables. Additionally, egg consumption was also included in the statistical models as nutrient density (g/2000 kcal per day) [17].

Associations between egg consumption and primary (all-cause mortality) and secondary endpoints (main specific causes of mortality) were assessed by means of the hazard ratio (HR) and the corresponding 95% confidence interval (CI) estimated by a multivariable Cox proportional hazards models. Exploratory analyses were performed to investigate the subclasses of causes of death, if the main class was significant. The assumption of proportional hazards over time was assessed by a test based on scaled Schoenfeld residuals. Age was used as the primary time variable, with age at recruitment as the entry time, and age at the date of death or the end of follow-up (whichever came first) as the exit time. Raw model was stratified by age at recruitment (5 years intervals), sex and centre. Multivariable model was additionally adjusted for covariates that were selected a priori because of their known influence on overall mortality risk; smoking status and intensity (never, former from ≤ 10 years, former from 11 to 20 years, former from > 20 years, current 1–15 cigarettes/day, current 16–25 cigarettes/day, current > 25 cigarettes/day, occasional smoker, current not specified, and not specified), body mass index (BMI; < 25, 25–29.9, and ≥ 30 kg/m^2), lifetime alcohol intake never consumer, former consumer, low (≤ 10 g/day for women or ≤ 15 g/day for men), moderate (> 10–20 g/day for women or > 15–30 g/day for men), high (> 20 g/day for women or > 30 g/day for men)], education level (no formal education, primary school, technical or professional training, secondary school, university, and unspecified), physical activity (inactive, moderately inactive, moderately active, and active) [18], total energy intake (kcal/day), Mediterranean diet score (continuous). A category of "unspecified" was created to include the missing values of the lifestyle variables. The association between egg consumption and specific-cause mortality was estimated using a competing risk analysis for Cox regression models [19].

Plausible effect modification by sex, centre, age at recruitment (< 45 years, 45–54 years, and ≥ 55 years), BMI (< 25, 25–29.9, ≥ 30 kg/m^2), smoking status (never, former, current), lifetime alcohol (never, former, current low, current moderate, and current high), and adherence to Mediterranean diet (≤ 7, 8–10, and 11–18) were explored by modelling interaction terms between each of these separate variables and egg consumption, and tested using the log-likelihood ratio test. In addition, risk of all-cause mortality in relation to egg consumption (1 egg/week) was examined in analyses stratified by these cohort subgroups.

Sensitivity analyses were carried out by additional adjustment for total dietary cholesterol, or the presence of diabetes, hyperlipidaemia, and hypertension. Additional models were created excluding participants with prevalent chronic diseases at recruitment (coronary heart disease, stroke, diabetes mellitus, and cancer), and excluding deaths in the first 2 years of follow-up to avoid the possibility of reverse causality. Finally, we conducted analysis censoring data at 9 years of follow-up to check if the associations were maintained with shorter follow-ups, since we were not able to control for potential changes in the diet of participants during the follow-up. All statistical analyses were conducted using R 3.2.1 software (R Foundation for Statistical Computing, Vienna, Austria). Competing risk analysis was done using the packages crrSC [20].

Results

The cohort of 40,621 participants was followed-up for a mean of 18.4 years, during which time 3561 deaths were recorded; 1694 from cancer, 761 from CVD, 870 from other causes (including 130, 163 and 112 from diseases of the nervous, respiratory and digestive systems, respectively), and 236 exitus had missing information on cause of death. The mean (standard deviation) egg consumption was 22.0 g/day (15.8) and 30.9 g/day (23.1) in women and men, respectively (*P* value = 0.001) (Supplementary table 1). The mean intake of egg caloric density was 24.3 g/2000 kcal per day (17.9) and 24.2 g/2000 kcal per day (17.6) in women and men, respectively (*P* value = 0.76). The percentage of non-egg consumers was 5.7% for women and 5.2% for men. The egg intake in this population was low to moderate; only 9.9% and 2.4% consumed ≥ 1 and ≥ 1.5 egg/day, respectively. Subjects in the highest quartile of egg consumption were younger, more physically active, more likely to be current smokers, consume more total energy, and had less prevalent chronic diseases compare to those in lowest quartile (Table 1). Individuals in the highest quartile of egg intake consume more legumes, olive oil, cereals and meat than those in the lowest quartile. Men only in the fourth quartile have also a lower intake of fruit and a higher intake of alcohol compared to those in the first one (Supplementary table 2).

In the adjusted Cox models, no association between egg consumption and all-cause mortality was observed either evaluating the extreme quartiles (HR 1.01; 95% CI 0.91–1.11; *P* trend = 0.96) or the continuous variable (HR 1.00; 95% CI 0.99–1.01) (Table 2). Models using the energy-adjustment method (g/2000 kcal per day) did not alter the results appreciably between extreme quartiles (HR 1.03; 95% CI 0.94–1.13; *P* trend = 0.52). No association was also found between egg intake and either cancer or CVD deaths in competing risk models. Null results were observed with CVD mortality subtypes (e.g., ischaemic heart diseases and cerebrovascular diseases). A statistically significant inverse association between extreme quartiles of egg consumption and other causes of death was detected (HR 0.76; 95% CI 0.63–0.93; *P* trend = 0.003), especially with deaths from diseases of the nervous system (HR 0.59; 95% CI 0.35–1.00; *P* trend = 0.036), but not for those from diseases of the digestive or respiratory systems (Table 2). Relationships between egg consumption and specific-cause mortality were also analysed using the traditional Cox models and the results were almost identical (data not shown).

No significant effect modification of the association between egg consumption and overall mortality was observed across categories of potential confounders, as

Table 1 Baseline characteristics according to quartiles of egg consumption in men and women in EPIC-Spain cohort

Baseline characteristics	Women ($n = 25,298$)				Men ($n = 15,323$)			
	Q1 ($n = 6,539$)	Q2 ($n = 6,137$)	Q3 ($n = 6,330$)	Q4 ($n = 6,292$)	Q1 ($n = 3,996$)	Q2 ($n = 3,677$)	Q3 ($n = 3,819$)	Q4 ($n = 3,831$)
Egg consumption (g/day), cutoff	< 10.8	10.8–19.9	20.0–30.4	> 30.4	< 14.4	14.4–26.8	26.9–42.6	> 42.6
Age at recruitment (years)	50.3 (8.7)	48.2 (8.4)	47.7 (8.2)	47.3 (7.9)	51.9 (7.5)	50.6 (7.2)	50.4 (7.2)	50.1 (6.8)
BMI (kg/m^2)	28.4 (4.7)	28.0 (4.61)	28.0 (4.7)	28.2 (4.8)	28.4 (3.3)	28.3 (3.4)	28.3 (3.4)	28.6 (3.5)
Educational level (%)[a]								
No formal education	47.0	40.0	36.8	33.4	29.5	26.0	24.7	25.5
Primary school	32.6	37.3	42.1	45.9	32.9	35.5	38.6	42.6
Technical or professional training	4.9	5.7	5.4	5.7	11.2	13.3	13.6	13.2
Secondary school	5.3	5.8	5.6	5.5	8.0	7.9	8.2	7.8
Universitary degree	9.4	10.4	9.6	8.5	17.7	16.9	14.3	10.4
Physical activity (%)								
Inactive	49.9	49.6	48.9	46.0	24.8	21.6	21.2	19.0
Moderately inactive	34.7	35.0	35.3	35.8	31.7	30.7	30.1	27.4
Moderately active	11.1	11.7	11.4	13.7	24.3	25.6	26.3	31.2
Active	4.3	3.7	4.4	4.4	19.1	22.2	22.4	22.4
Smoking status (%)[a]								
Never	73.9	71.4	71.5	69.1	27.7	29.1	29.7	30.5
Former	9.4	10.0	9.8	10.1	35.3	31.0	29.6	26.2
Current	16.7	18.6	18.6	20.8	36.9	39.9	40.7	43.3
Menopausal status (%)								
Pre-menopause	42.8	53.2	57.2	59.1	–	–	–	–
Post-menopause	41.1	31.6	28.3	27.3	–	–	–	–
Peri-menopause	8.8	10.1	9.9	9.6	–	–	–	–
Surgical menopause	7.2	5.1	4.6	4.0	–	–	–	–
Myocardial infarct (%)[a]	0.4	0.3	0.1	0.1	1.9	0.9	0.3	0.3
Stroke (%)[a]	0.8	0.6	0.5	0.3	0.8	0.5	0.4	0.5
Hyperlipidaemia (%)[a]	26.7	17.8	11.8	9.4	38.1	27.5	21.8	17.5
Hypertension (%)[a]	23.6	19.4	18.0	17.1	23.0	21.6	20.2	20.1
Diabetes (%)[a]	6.5	4.5	3.9	3.3	7.4	6.5	4.6	4.6
Cancer (%)[a]	1.2	1.1	1.2	0.9	0.6	0.3	0.5	0.5
Lifetime alcohol (%)								
Never	39.4	34.6	34.3	32.3	3.9	4.0	3.7	3.0
Former	17.1	17.2	16.1	16.0	13.8	10.0	10.0	9.1
Current low[b]	32.0	34.3	34.0	32.8	29.4	29.1	27.8	24.2
Current moderate[b]	7.4	8.5	9.4	11.0	20.5	20.5	18.6	18.5
Current high[b]	4.1	5.4	6.2	7.8	32.4	36.4	39.8	45.1
Adherence to Mediterranean diet (%)								
Low (rMED ≤ 7)	36.2	37.1	37.9	41.3	26.3	27.3	30.7	34.0
Medium (rMED 8–10)	41.1	39.5	41.6	41.3	38.9	41.0	40.7	41.7
High (rMED ≥ 11)	22.7	23.3	20.5	17.5	34.8	31.7	28.6	24.3
Total energy (kcal/day)	1678 (478)	1829 (498)	1914 (503)	2029 (525)	2346 (606)	2493 (602)	2618 (613)	2823 (656)

Table 1 (continued)

Values are means and standard deviations

[a]Missing values in women: education level (0.77%), smoking status (0.06%), myocardial infarct (0.07%), stroke (0.12%), hyperlipidaemia (0.55%), hypertension (0.15%), diabetes (0.18%), cancer (0.55%)

[b]Missing values in men: education level (0.52%), smoking status (0.05%), myocardial infarct (0.08%), stroke (0.08%), hyperlipidaemia (0.37%), hypertension (0.15%), diabetes (0.18%), cancer (0.46%)

[c]Current low (≤ 10 g/day for women or ≤ 15 g/day for men), moderate (> 10–20 g/day for women or > 15–30 g/day for men), high (> 20 g/day for women or > 30 g/day for men)

Table 2 Adjusted hazard ratios (HRs) and 95% confidence interval (CI) for mortality according to egg consumption in the EPIC-Spain cohort

	Quartile 1 HR (95% CI)	Quartile 2 HR (95% CI)	Quartile 3 HR (95% CI)	Quartile 4 HR (95% CI)	*P* trend	Continuous (eggs/week) HR (95% CI)
All-cause mortality (no. of deaths)	1061	881	837	782		3561
Crude	1 (ref)	1.05 (0.96, 1.15)	0.99 (0.91, 1.09)	0.99 (0.90, 1.09)	0.70	1.00 (0.99, 1.01)
Multivariate	1 (ref)	1.08 (0.99, 1.18)	1.02 (0.93, 1.12)	1.01 (0.91, 1.11)	0.96	1.00 (0.99, 1.01)
Specific-cause mortality (in competing risk)						
Cancer (no. of deaths)	471	411	403	409		1694
Crude	1 (ref)	1.04 (0.91, 1.19)	1.00 (0.87, 1.14)	1.06 (0.93, 1.22)	0.50	1.01 (0.99, 1.03)
Multivariate	1 (ref)	1.07 (0.93, 1.22)	1.04 (0.90, 1.19)	1.11 (0.96, 1.28)	0.23	1.01 (1.00, 1.03)
Cardiovascular diseases (no. of deaths)	239	189	179	154		761
Crude	1 (ref)	1.05 (0.87, 1.28)	1.03 (0.84, 1.25)	0.98 (0.80, 1.22)	0.91	0.99 (0.97, 1.02)
Multivariate	1 (ref)	1.11 (0.91, 1.34)	1.10 (0.90, 1.34)	1.07 (0.86, 1.32)	0.49	1.00 (0.98, 1.03)
Ischaemic heart diseases (no. of deaths)	104	81	74	55		314
Crude	1 (ref)	1.00 (0.75, 1.34)	0.94 (0.69, 1.27)	0.77 (0.55, 1.07)	0.13	0.97 (0.93, 1.01)
Multivariate	1 (ref)	1.06 (0.79, 1.43)	1.01 (0.75, 1.37)	0.85 (0.60, 1.19)	0.40	0.98 (0.94, 1.03)
Cerebrovascular diseases (no. of deaths)	58	46	41	39		184
Crude	1 (ref)	1.08 (0.73, 1.60)	0.99 (0.66, 1.47)	1.05 (0.69, 1.61)	0.92	1.00 (0.95, 1.05)
Multivariate	1 (ref)	1.14 (0.77, 1.69)	1.01 (0.67, 1.53)	1.07 (0.69, 1.66)	0.86	1.00 (0.95, 1.05)
Other causes (no. of deaths)	292	222	189	167		870
Crude	1 (ref)	0.98 (0.82, 1.17)	0.84 (0.70, 1.01)	0.79 (0.65, 0.96)	0.007	0.97 (0.94, 0.99)
Multivariate	1 (ref)	0.98 (0.82, 1.17)	0.83 (0.69, 1.01)	0.76 (0.63, 0.93)	0.003	0.96 (0.93, 0.99)
Nervous system diseases (no. of deaths)	46	34	29	21		130
Crude	1 (ref)	0.95 (0.61, 1.48)	0.79 (0.50, 1.26)	0.61 (0.36, 1.04)	0.05	0.91 (0.84, 0.98)
Multivariate	1 (ref)	0.96 (0.61, 1.49)	0.78 (0.49, 1.25)	0.59 (0.35, 1.00)	0.036	0.90 (0.84, 0.97)
Respiratory system diseases (no. of deaths)	69	33	33	28		163
Crude	1 (ref)	0.65 (0.42, 0.99)	0.69 (0.45, 1.06)	0.65 (0.41, 1.03)	0.055	0.95 (0.89, 1.01)
Multivariate	1 (ref)	0.67 (0.44, 1.04)	0.72 (0.47, 1.11)	0.67 (0.42, 1.07)	0.084	0.95 (0.90, 1.02)
Digestive system diseases (no. of deaths)	29	32	28	23		112
Crude	1 (ref)	1.43 (0.86, 2.40)	1.29 (0.75, 2.19)	1.16 (0.66, 2.04)	0.62	1.04 (0.97, 1.11)
Multivariate	1 (ref)	1.50 (0.89, 2.52)	1.31 (0.76, 2.26)	1.17 (0.66, 2.07)	0.61	1.04 (0.97, 1.11)

Cutoff points are based on sex–specific quartiles of total egg intake: men (< 14.4, 14.4–26.8, 26.9–42.6, > 42.6), women (< 10.8, 10.8–19.9, 20–30.4, > 30.4)

Crude model stratified by centre, age at recruitment in 5 year categories and sex

Multivariable model additionally adjusted for smoking intensity, BMI, lifetime alcohol intake, education level, physical activity, energy intake, and adherence to Mediterranean diet derived from the analyses comparing models with or without interaction terms between egg consumption (as a continuous variable) and each category of the variable of interest (Supplementary table 3), except for BMI (P for interaction = 0.038). However, the association between egg intake and all-cause mortality was not statistically significant for any of the BMI categories.

In the sensitivity analysis, the results with overall mortality were almost identical: (1) additionally adjusting for total dietary cholesterol (HR 1.03 95% CI 0.92–1.16; *P* trend = 0.71); (2) further adjusting for hypertension, hyperlipidaemia and diabetes at baseline (HR 1.04; 95% CI 0.94–1.14; *P* trend = 0.60); (3) excluding 2,684 subjects with prevalent chronic diseases (HR 1.02; 95% CI 0.91–1.13; *P* trend = 0.94); and (4) excluding 109 participants who died in the first 2 years of follow-up (HR 1.01; 95% CI 0.91–1.11; *P* trend = 0.89); (5) censoring data at 9 years of follow-up and therefore only considering 905 deaths (HR 0.98; 95% CI 0.81–1.19; *P* trend = 0.83).

Discussion

To our knowledge, this is the first large prospective cohort that has evaluated the association between egg consumption and mortality in a Mediterranean population. We found that moderate egg consumption, up to 1 egg/day, was not associated with a higher all-cause and main specific-cause mortality risk. We cannot properly evaluate the effect with higher intakes of egg (> 1 egg/day or > 7 eggs/week), because in the present study there was only a small proportion (< 10%) of participants consuming larger amounts.

Similar to us, no association between egg consumption and overall mortality was observed in two cohorts, with the highest category of egg intake much higher (≥ 14 eggs/week) in a Japanese study [8] and slightly higher (≥ 5 eggs/week) in a UK study [6] than in ours. However, in a cohort from Iran, a 12% reduction of overall mortality was found comparing extreme quartiles (median intake 3.5 vs 0 egg/week) [7]; whereas in a US cohort a 23% increase of all-cause mortality was observed comparing extreme groups (≥ 7 vs < 1 egg/week) [9]. Inconsistencies in the results might be due to differences in the range of egg consumption or differences in dietary patterns related with different amounts of egg consumption. Indeed, in the new dietary guidelines, egg intake is regularly included as part of a healthy eating, but the recommendation should be probably different in Westernized diets, such as in the US.

Many epidemiological studies have investigated the association between egg consumption and both CVD risk and cardiovascular mortality. Two meta-analyses basically showed null associations, such as in our study [5, 21]; although a higher risk of CVD comorbidity among diabetic patients was suggested [5]. In a Mediterranean population, egg intake was neither associated with CVD risk in general population [22] nor population at high cardiovascular risk, with or without type 2 diabetes [23].

In the present study, no association was observed between egg consumption and overall cancer mortality, such as in the Japanese study [8]. However, in the Iran-based cohort, a statistically significant inverse relationship was found [7]. Regarding cancer risk, null results were observed for most of the cancer sites [24]; although in a recent meta-analysis, egg consumption was associated with a higher risk of breast, ovarian and fatal prostate tumours [25].

Surprisingly, per each egg/week consumed a 4% decreased risk in other causes of death was found in the current study. It was mainly due to the inverse association with deaths from the nervous system, predominantly Alzheimer's (39%) and Parkinson's (15%) diseases, for which the risk reduction reached 10%. To our knowledge, only few studies have investigated the relationships between egg consumption and risk of neurodegenerative diseases. A Finish cohort found no association between both dietary cholesterol and egg intakes and dementia or Alzheimer's disease risks; although moderate egg consumption was associated with better performance on several neuropsycological tests [26]. Eggs are a rich source of choline [27] and an interesting source of lutein and zeaxanthin [28], which may have protective effects on cognition across the lifespan [29]. Low plasma free choline levels were associated with poor cognitive performance, especially in addition to low vitamin B_{12} or high methylmalonic acid concentrations in a Norwegian cross-sectional study [30]. Moreover, plasma concentrations of lutein and zeaxanthin were directly associated with better cognitive performances in a cross-sectional analysis in the small 3-City Bordeaux cohort [31]. However, our results should be interpreted with caution, since the causes of death included in this group were heterogeneous and the biological plausibility is still uncertain. Therefore, further prospective studies are warranted to evaluate the suggested association with the risk of incident neurodegenerative diseases, instead of its mortality risk.

The strengths of this study are that we are using prospective data of a well-known Mediterranean cohort (the EPIC-Spain study) with a large sample size and a number of deaths, the long period of follow-up, and the high variability in the dietary exposure among subjects. In addition, we were able to control for a wide variety of relevant confounders. This study also has several potential limitations. Our results may be influenced by measurement errors that may have attenuated our findings, although a validated dietary history questionnaire was used [12–14]. In addition, dietary and lifestyle information was available only at baseline, and therefore, we cannot evaluate changes over follow-up, although the results were similar when data was censored at 9 years of follow-up. Finally, modification of diet in the years previous to death or after chronic disease ascertainment is probable, but the exclusions of either deaths occurred in the first 2 years of the follow-up or prevalent cases of chronic diseases at recruitment did not modify our findings.

In conclusion, this large prospective study shows no association between moderate egg consumption, up to 1 egg/day, and all-cause and main specific causes (cancer and CVD) of mortality in a Mediterranean population. Our results are in line with previous studies and with the updated dietary guidelines from American and British Heart Associations allowing up to 1 egg/day within a healthy dietary pattern, like the Mediterranean diet.

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Author contributions RZ-R designed the research; VC and RC performed the statistical analysis; RZ-R drafted the manuscript; MLR, M-JS, MR-B, J-JS-C, OM, LG, PA, CN, MDC, JMH, AB, EA, CM-I, AA contributed to the design of the study, data collection, and quality control and analysis. All authors read, critically reviewed and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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