Egg consumption and risk of coronary heart disease and stroke: dose-response meta-analysis of prospective cohort studies

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STUDY QUESTION

Is there a dose-response association between egg consumption and risk of coronary heart disease or stroke?

SUMMARY ANSWER

Consumption of up to one egg per day was not associated with increased risk of coronary heart disease or stroke.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

As a major source of dietary cholesterol, the associations between egg consumption and risk of coronary heart disease and stroke have been examined by several epidemiologic studies, but with inconsistent results.
This meta-analysis found that consumption of up to one egg per day was not associated with increased risk of coronary heart disease or stroke.

Selection criteria for studies

We conducted a literature search of PubMed (Medline) and Embase from January 1966 through June 2012 for prospective cohort studies examining the association between egg consumption and risk of coronary heart disease and stroke. Studies reported relative risks with 95% confidence intervals for at least three quantitative categories of egg intake. We scrutinized references from relevant original papers and review articles to identify further pertinent studies. No language restrictions were imposed.

Primary outcome

Relative risks and 95% confidence intervals of coronary heart disease and stroke for an increment of one egg consumed per day.

Main results and role of chance

Eight articles with 17 reports (nine for coronary heart disease and eight for stroke) were eligible for inclusion in the meta-analysis. There were 3 081 269 person years and 5847 incident cases for the coronary heart disease meta-analysis, and 4 148 095 person years and 7579 incident cases for the stroke meta-analysis. We saw no evidence of a curve linear association between egg consumption and risk of coronary heart disease or stroke (P=0.67 and P=0.27 for non-linearity, respectively). For an increase of one egg consumed per day, summary relative risks were 0.99 (95% confidence interval 0.85 to 1.15; P=0.88 for linear trend; table) for coronary heart disease and 0.91 (0.81 to 1.02; P=0.10 for linear trend) for stroke. Subgroup analyses suggested that increased egg consumption was associated with risk of coronary heart disease in diabetic patients. However, we saw an inverse association between egg consumption and risk of hemorrhagic stroke.

Egg consumption and risk of coronary heart disease and stroke

	Summary relative risk (95% CI)
Increment of one egg consumed per day	
Total coronary heart disease	0.99 (0.85 to 1.15)
Total stroke	0.91 (0.81 to 1.02)
Highest *v* lowest consumption of eggs	
Risk of coronary heart disease in diabetic patients	1.54 (1.14 to 2.09)
Risk of hemorrhagic stroke	0.75 (0.57 to 0.99)

Bias, confounding, and other reasons for caution

Our meta-analysis had several limitations that were inherent in the included epidemiologic studies, such as errors in measurement of egg intake and other dietary habits, which could have attenuated the relation between consumption and risk of coronary heart disease and stroke. In addition, information on the cooking methods of eggs and amount of salt added were not available in the included studies. Moreover, the size of eggs was not uniformly quantified in each study. The results of the subgroup findings were based on a small number of studies, and should be interpreted with caution.

Study funding/potential competing interests

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Concurrent use of diuretics, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers with non-steroidal anti-inflammatory drugs and risk of acute kidney injury: nested case-control study

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STUDY QUESTION

Does the use of diuretics and/or angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers with non-steroidal anti-inflammatory drugs (NSAIDs) increase the risk of acute kidney injury?

SUMMARY ANSWER

A triple therapy combination consisting of diuretics with ACE inhibitors or angiotensin receptor blockers and NSAIDs was associated with an increased risk of acute kidney injury.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Acute kidney injury is a major drug related concern. A double therapy combination consisting of diuretics or ACE inhibitors or angiotensin receptor blockers with NSAIDs was not associated with an increased risk of acute kidney injury, but a triple therapy combination of diuretics and ACE inhibitors or angiotensin receptor blockers with NSAIDs was associated with an increased risk of acute kidney injury, particularly in the first 30 days of treatment.

Participants and setting

This was a nested case-control study using a cohort of patients who were treated with antihypertensive drugs between 1 January 1997 and 31 December 2008, with a follow-up until 31 December 2010, from the UK Clinical Practice Research Datalink linked to the Hospital Episodes Statistics database.

Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination and according to half life of NSAID and duration of use

	Rate ratio (95% CI)	
Current use*	Crude	Adjusted
Diuretics only	Reference	Reference
Diuretics plus NSAIDs	1.16	1.02 (0.81 to 1.28)
ACE inhibitors or ARBs only	Reference	Reference
ACE inhibitors or ARBs plus NSAIDs	0.96	0.89 (0.69 to 1.15)
Diuretics plus ACE inhibitors or ARBs	Reference	Reference
Diuretics plus ACE inhibitors or ARBs plus NSAIDs:	1.34	1.31 (1.12 to 1.53)
NSAID's half life <12 hours†	1.33	1.29 (1.11 to 1.51)
NSAID's half life ≥12 hours†	1.73	1.77 (1.07 to 2.93)
Duration ≤30 days‡	2.00	1.82 (1.35 to 2.46)
Duration 31-60 days‡	1.76	1.63 (1.24 to 2.15)
Duration 61-90 days‡	1.66	1.56 (1.24 to 1.97)
Duration >90 days‡	1.00	1.01 (0.84 to 1.23)

Current users of other antihypertensive drugs and past users of double and triple therapy combinations are not shown but were considered in the regression models.
ACE=angiotensin converting enzyme; ARB=angiotensin receptor blocker; NSAID=non-steroidal anti-inflammatory drug.
*Defined as prescriptions received within 90 days before acute kidney injury event.
†P value for interaction=0.216.
‡Length of exposure to triple therapy combination; P value for interaction <0.001.

Design, size, and duration

A cohort of 487 372 users of antihypertensive drugs was followed for an average of 5.9 years. All incident cases of acute kidney injury were identified and each was matched to up to 10 controls on age, sex, calendar year of cohort entry, prevalent user status, and duration of follow-up. The index date was defined as the date of the acute kidney injury for the case and its matched controls.

Primary outcome(s), risks, exposures

Exposure was defined as use of double or triple therapy combination occurring in the 90 day period before the index date, then examined in terms of half life of NSAID and duration of use.

Main results and the role of chance

We matched 2215 cases (incidence rate 7/10 000 person years) of acute kidney injury diagnosed during follow-up to 21 993 controls. Overall, current use of a double therapy combination of an antihypertensive drug with NSAIDs was not associated with an increased rate of acute kidney injury. Current use of a triple therapy combination of diuretics and ACE inhibitors or angiotensin receptor blockers with NSAIDs was associated with an increased rate of acute kidney injury (rate ratio 1.31, 95% confidence interval 1.12 to 1.53), which was driven by the first 90 days of use, with an almost twofold increase in risk in the first 30 days of use (1.82, 1.35 to 2.46).

Bias, confounding, and other reasons for caution

The database does not record over the counter use of NSAIDs. This could have led to a possible underestimation of the observed risks.

Generalisability to other populations

The results of this study can be generalised to populations exposed to antihypertensive drugs.

Study funding/potential competing interests

This study was funded in part by the Drug Safety and Effectiveness Network, the Canadian Institutes of Health Research, and the Canada Foundation for Innovation. SS has received research grants and participated in advisory board meetings or as a speaker at conferences for AstraZeneca, Boehringer-Ingelheim, GlaxoSmithKline, Novartis, Pfizer, and Merck. SJN has received speakers' honorariums from Baxter Healthcare and Merck Frosst.

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Evaluation of interventions to reduce air pollution from biomass smoke on mortality in Launceston, Australia: retrospective analysis of daily mortality, 1994-2007

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STUDY QUESTION

Was an intervention to reduce outdoor smoke pollution from domestic wood heaters associated with reductions in mortality?

SUMMARY ANSWER

Decreased biomass smoke was associated with reduced annual all cause mortality in males and with reduced cardiovascular and respiratory mortality during winter months.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Despite a large amount of published research on the adverse health effects of air pollution, few studies have investigated shifts in health outcomes associated with public health interventions to improve ambient air quality. In Launceston, Tasmania, coordinated interventions to reduce pollution from domestic wood heaters substantially improved winter air quality. The period of improved air quality was associated with an overall trend towards reduced mortality.

Participants and setting

The intervention population at the 2001 census included 67 000 residents of central Launceston, Australia, where interventions to reduce outdoor pollution from domestic wood heaters were implemented from July 2001. These included community education campaigns, enforcement of environmental regulations, and a programme of wood heater replacement. The control population included 148 000 residents of central Hobart, a comparable city where no specific air quality interventions were implemented.

Percentage change* in all cause, cardiovascular, and respiratory mortality in Launceston and Hobart, Tasmania, from January 1994-May 2001 to June 2001-November 2007. Years 2001-7 correspond with period of improved air quality after a series of coordinated interventions in Launceston

	Launceston (intervention)		Hobart (control)	
	Per cent change (95% CI)	P value	Per cent change (95% CI)	P value
All year—males and females combined				
All cause mortality	−2.7 (−8.7 to 3.7)	0.40	1.4 (−3.0 to 6.0)	0.54
Cardiovascular mortality	−4.9 (−15.5 to 7.0)	0.40	0.9 (−7.1 to 9.6)	0.83
Respiratory mortality	−8.5 (−23.2 to 9.0)	0.32	4.8 (−7.4 to 18.6)	0.50
All year—males				
All cause mortality	−11.4 (−19.2 to −2.9)	0.01	0.7 (−5.4 to 7.2)	0.82
Cardiovascular mortality	−17.9 (−30.6 to −2.8)	0.02	−7.1 (−16.8 to 3.8)	0.19
Respiratory mortality	−22.8 (−40.6 to 0.3)	0.05	3.4 (−13.1 to 24.4)	0.67
All year—females				
All cause mortality	2.7 (−5.3 to 11.4)	0.52	−0.7 (−6.3 to 5.2)	0.80
Cardiovascular mortality	2.3 (−12.2 to 19.3)	0.77	3.6 (−7.6 to 16.2)	0.54
Respiratory mortality	1.0 (−18.9 to 24.4)	0.96	−1.4 (−15.5 to 15.1)	0.86
Wintertime—males and females combined				
All cause mortality	2.2 (−14.1 to 11.3)	0.73	−2.0 (−10.2 to 6.9)	0.64
Cardiovascular mortality	−19.6 (−36.3 to 1.5)	0.06	−7.0 (−20.8 to 9.2)	0.38
Respiratory mortality	−27.9 (−49.5 to 3.1)	0.07	8.0 (−16.9 to 40.4)	0.60

*Adjusted for age structure, meteorological conditions, and secular mortality trends in Tasmania.

Design, size, and duration

The study period was 1994-2007. Changes in daily mortality between the 6.5 year periods before and after the intervention were assessed with an age stratified time series analysis with Poisson regression models adjusted for the effects of temperature, humidity, day of week, respiratory epidemics, and secular mortality trends.

Main results and the role of chance

The mean annual number of deaths from all non-accidental causes in Launceston was 577, of which 42% (243) were from cardiovascular causes and 9% (54) from respiratory causes. Particulate pollution with particle size <10 µm diameter (PM_{10}) during winter fell from a mean of 42 µg/m^3 during 1994-2000 to 26 µg/m^3 during 2001-7. The period of improved air quality was associated with small non-significant reductions in annual mortality. The observed reductions were larger and significant for males. There were reductions in cardiovascular and respiratory mortality of borderline significance in wintertime. There were no significant mortality changes in the control city of Hobart.

Bias, confounding, and other reasons for caution

An important limitation was the relatively small study population, which reduced the statistical power of our study. Although the magnitude of most associations was relatively large, confidence intervals were wide. This was especially the case for respiratory mortality, which comprised just 10% of all deaths.

Models were adjusted for measurable confounders such as age, temperature, humidity, and respiratory epidemics. To account for the influence of secular mortality trends, we included smoothed daily mortality data from the rest of Tasmania. The entire state has similar distributions of health outcomes, socioeconomic status, and demographic structure, so temporal changes in the prevalence of population risk factors such as smoking and diabetes were probably representative of Launceston.

Generalisability to other populations

This is a population based study, and the results are likely to be generalisable to populations with a similar sociodemographic structure and comparable environmental exposures

Study funding/potential competing interests

This study was supported by the Australian Research Council (LP0882048), the Tasmanian Government Department of Health and Human Services, and the Environment Protection Authority Tasmania.

Presentation of continuous outcomes in randomised trials: an observational study

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STUDY QUESTION

What percentage of available data for continuous primary outcomes is presented in randomised trials published in high impact factor medical journals?

SUMMARY ANSWER

When adjusted for the number of patients in the trial, studies report a median 3.5% (interquartile range 3–7%) of the available data for the best reported primary outcome; a small percentage of the data.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Selective reporting can lead to bias and has been partially addressed by trial registration. Incomplete reporting can also lead to bias and has not yet been fully characterised or addressed. We show that, even for the best reported outcome, only a small fraction of the available data is reported.

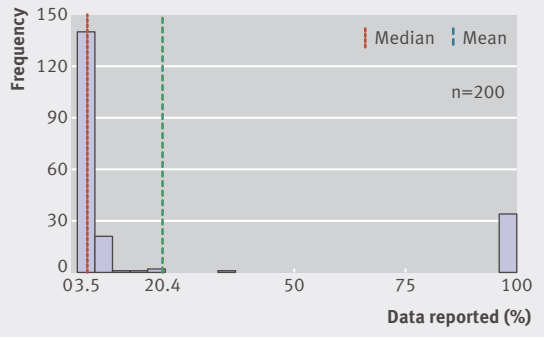
Participants and setting

A random sample of randomised controlled trials that had a continuous primary outcome and were published in six high impact factor general journals and 14 high impact factor specialty journals between 2007 and 2009.

Design

Cross sectional structured survey of 10 randomly selected eligible papers from 20 high impact medical journals. Continuous outcomes were defined as outcomes that could have at least five unique values.

Percentage of data reported for the best reported outcome in each of the 200 papers in this study



Primary outcome(s)

We calculated the ratio of the amount of data reported to the amount of data that could have been reported about the study's primary outcome, expressed as a percentage. For example, a two arm trial with 100 patients per arm that reported two sample sizes, two means, and two standard deviations reported 6/200 data elements (1.5%), but if that paper included a scatterplot with 200 points it would score 200/200 (100%).

Main results and the role of chance

As shown in the figure, papers either presented a small fraction of data or completely reported the best reported outcome (17% of all papers). Complete reporting was typically achieved with high data density figures such as scatterplots, histograms, and survival curves, and was seldom achieved when the data were reported in low density figures (such as bar graphs), tables, or text alone.

Note that if our paper reported only the mean (standard deviation) or median (interquartile range), readers would be deprived of the knowledge that the distribution of results is reverse-J shaped (figure).

Bias, confounding, and other reasons for caution

There is no consensus about how much data should be reported, and there is no validated measure of the amount of data reported. However, we believe that our metric is a straightforward means of measuring this quantity.

Generalisability to other populations

This study sampled high impact factor journals. We have no reason to believe that reporting would be higher in lower impact factor journals, and it may well be lower.

Study funding/potential competing interests

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