RESEARCH ARTICLE

No Association between Egg Intake and Prostate Cancer Risk: A Meta-analysis

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Abstract

Objective: Egg consumption has been suggested to increase the risk of colorectal and some other cancers. The present study summarized and quantified the current evidence relating dietary intake of eggs and prostate cancer. **Materials and methods**: Literature searches were conducted to identify peer-reviewed manuscripts published up to July 2012. Twenty manuscripts from nine cohort studies and 11 case-control studies were identified. Summary risk estimates with 95% confidence intervals (CIs) were calculated for case-control and cohort studies separately. **Results**: Neither the case-control not the cohort studies showed any association of prostate cancer incidence with egg consumption (case-control studies: odds ratio 1.09, 95% CI 0.86-1.31; cohort studies: relative risk 0.97, 95% CI 0.97-1.07). The results were consistent in subgroup analysis. Furthermore, no association was observed between egg consumption and prostate cancer-specific mortality. **Conclusions**: Our analyses provided no evidence of a significant influence of egg consumption on prostate cancer incidence and mortality. However, more studies, particularly large prospective studies, are needed.

Keywords: Eggs - prostate cancer - meta-analysis

Introduction

Prostate cancer is the most common cancer among men in United States. It is also one of the leading causes of cancer death among men of all races (Siegel et al., 2012). Although age and family history have been established as strong risk factors for prostate cancer, the role of individual dietary factors is not well understood. The large variation in incidence across countries may also suggest the role of lifestyle and dietary factors in its cause (Yu et al., 1991). Eggs are frequently consumed worldwide, supply substantial portions of protein, fat, retinal, riboflavin and iron. Eggs are also unique among foods, given their relatively high content of several substances, such as cholesterol, choline, biotin, and avidin. There is evidence pointing to a possible role of eggs consumption on cancer etiology. A positive association has been observed between eggs consumption and risk of colorectal cancer (Steinmetz et al., 1994). For other cancer sites, there is no established association with eggs. Several studies considered the relation between eggs intake and prostate cancer. Though most of them reported no association, results were often inconsistent. With the aim to investigate the relationship between prostate cancer and eggs consumption, we carried out a meta-analysis of epidemiological studies published up to July 2012.

Materials and Methods

A systematic literature search was carried out in the Medline database, using PubMed, for all studies published in English. We used the following search string in free full-text: (egg or eggs) AND (prostate or prostatic) AND (cancer or carcinoma). The reference lists of all papers of interest were checked to obtain other pertinent publications. For inclusion in this meta-analysis, studies should assess eggs intake in relation to histologically confirmed prostate cancer with informative effect estimates. Cross-sectional and ecologic analyses were excluded.

Figure 1 showed the flowchart for selection of articles. A total of 86 publications were identified in the primary search. Seventy-two articles were excluded after screening the titles and abstracts. We included 12 studies after
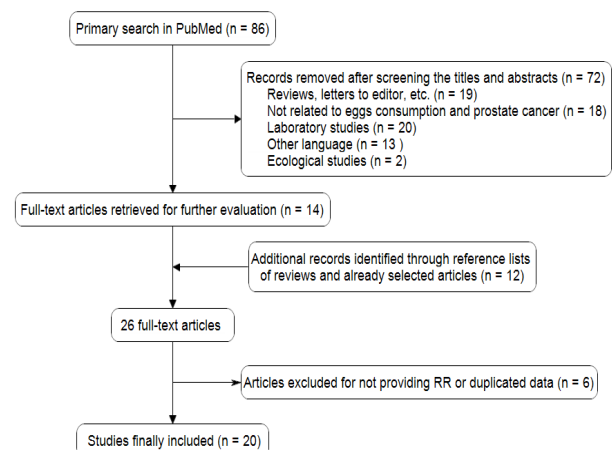

Figure 1. Flowchart of Study Search

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Table 1. Study Characteristics of Published Cohort and Case-control Studies on Eggs Intake and Prostate Cancer

Authors	Publication year	Study design	Study period	Country	Cases/Subjects	Highest vs lowest	Variables of adjustment	Cruciferous vegetables assessment
Snowdon et al.	1984	Cohort	1960-1980	USA	97/6763	≥ 3 days/wk vs < 1 day/wk	Age	Questionnaire
Mills et al.	1989	Cohort	1976-1982	USA	150/65593 (person-yr)	≥ 3 times/wk vs < 1 time/wk	Age	Questionnaire
Severson et al.	1989	Cohort	1965-1986	Hawaii	174/7999	≥ 5 times/wk vs ≤ 1 time/wk	Age	Interview
Hsing et al	1990	Cohort	1966-1986	USA	149/17663	> 21 times/month vs < 4 times/month	Age and tobacco use	Questionnaire
Le Vecchia et al	1991	Hospital-based case-control study	1985-1989	Italy	96/388	High vs low intake	Age, area of residence, education and BMI	Interview
Le Marchand et al.	1994	Cohort	1975-1989	Hawaii	198/20316	The highest vs lowest quantile	Age, ethnicity, and income by proportional hazards regression.	Interview
Ewings et al.	1996	Hospital-based case-control study	1989-1991	UK	159/484	> 1 times/day vs < 2 time/wk	Age	Interview
Gronberg et al.	1996	Population-based case-control study	1967-1970	Sweden	406/1624	Great vs no or small part	Age	Questionnaire
Jain et al.	1999	Population-based case-control study	1990-1992	Canada	617/1253	> 28.5 g/day vs < 7.2 g/day	Log total energy, vasectomy, age, ever-smoked, marital status, study area, body mass index, education, ever-used multivitamin supplements in 1 yr before diagnosis/interview, area of study, and log-converted amounts for grains, fruit, vegetables, total plants, total carotenoids, folic acid, dietary fiber, conjugated linoleic acid, vitamin E, vitamin C, retinol, total fat, and linoleic acid.	Interview
Sung et al.	1999	Hospital-based case-control study	1995-1996	China	80/240	Yes vs no	Age and admission data	Interview
Schuurman et al.	1999	Cohort	1986-1992	Netherland	642/58279	The highest vs lowest tertile	Age, family history of prostate cancer and socioeconomic status (local and advanced)	Questionnaire
Allen et al.	2004	Cohort	1963-1996	Japan	196/252602 (person-yr)	Almost daily vs < 2 time/wk	Age, calendar period, city of residence, radiation dose and education level	Questionnaire
Bosetti et al.	2004	Hospital-based case-control study	1991-2002	Italy	1294/2745	The highest vs lowest tertile	Age, study center, years of education, social class, BMI, family history of prostate cancer and total calorie intake	Interview
Sonoda et al.	2004	Hospital-based case-control study	1986-1992	Japan	140/280	≥ 100 g/day vs ≤ 28.5 g/day	Age, cigarette smoking and energy intake	Interview
Chen et al.	2005	Hospital-based case-control study	1996-1998	China	237/718	≥ moderate vs less/none	Age and BMI	Interview
Allen et al.	2008	Cohort	1989-2004	Europe	2727/142251	The highest vs lowest quintile	Age, education, marital status, height, weight and energy intake	Questionnaire
Ukoli et al.	2009	Hospital-and population-based case-control study	Not clear	Nigeria	56/324	The highest vs lowest quartile	Age and education	Interview
Tyagi et al.	2010	Population-based case-control study	1998-2000	India	303/909	Yes vs no	Age	Interview
Richman et al.	2011	Cohort	1994-2008	USA	199/306715	≥ 2.5 times/wk vs < 0.5 time/wk	Age, energy, BMI, smoking, vigorous activity, and lycopene intake	Questionnaire
Deneo-Pellegrini et al.	2012	Hospital-based case-control study	1996-2004	Uruguay	326/1814	The highest vs lowest tertile	Age, residence, urban/rural status, education, BMI, family history, and total energy intake	Interview

reviewing reference lists of retrieved articles or preceding reviews. After closer examination of full text, four articles did not report risk estimates on the relation between eggs intake and prostate cancer and were no longer considered. One case-control study published partly duplicated data in three different articles, and we selected the recent one with largest sample size (Deneo-Pellegrini et al., 2012). Finally, the remaining 20 publications were retained for the meta-analysis (Snowdon et al., 1984; Mills et al., 1989; Severson et al., 1989; Hsing et al., 1990; La Vecchia et al., 1991; Le Marchand et al., 1994; Ewings et al., 1996; Gronberg et al., 1996; Jain et al., 1999; Schuurman et al., 1999; Sung et al., 1999; Allen et al., 2004; Bosetti et al., 2004; Sonoda et al., 2004; Chen et al., 2005; Allen et al., 2008; Ukoli et al., 2009; Tyagi et al., 2010; Richman et al., 2011; Deneo-Pellegrini et al., 2012).

We reviewed all the studies and abstracted the information as follows: the name of the first author, the year of publication, study design, country, period of enrolment (case–control studies) and/or of follow-up (cohort studies), number of subjects, covariates adjusted for in the analysis, odds ratios (ORs) or relative risk (RRs) for highest vs lowest level of consumption and exposure assessment. When available, we used multivariate-adjusted risk estimates.

We estimated the summary association between eggs consumption and prostate cancer incidence in case-control and cohort studies separately. Subgroup analyses were performed according to geographical regions, time of PSA screening (Using 1994 as the cutoff for after which time most men were screened for PSA). In addition, we performed analyses for the association of eggs consumption with high-stage and fatal prostate cancer. We calculated summary estimates using the fixed or random effects models depending on heterogeneity between studies. Heterogeneity between studies was assessed using the Cochrane Q test and I^2 score. We conducted sensitivity analyses by excluding each study at a time from the meta-analysis. Publication bias was assessed using the tests of Egger and Begg. Statistical significance was considered while $p < 0.05$. We performed all statistical analyses with

Stata v.11.0 (StataCorp, College Station, TX).

Results

Table 1 reports the main characteristics of the 20 studies included in the meta-analysis. There were 11 case–control studies and 9 cohort studies. Of all studies reviewed, three cohort studies presented RR estimates for fatal prostate cancer (Snowdon et al., 1984; Hsing et al., 1990; Richman et al., 2011). Seven studies were conducted in US/Canada (Snowdon et al., 1984; Mills et al., 1989; Severson et al., 1989; Hsing et al., 1990; Le Marchand et al., 1994; Jain et al., 1999; Richman et al., 2011), six in Europe (La Vecchia et al., 1991; Ewings et al., 1996; Gronberg et al., 1996; Schuurman et al., 1999; Bosetti et al., 2004; Allen et al., 2008), five in Asia (Sung et al., 1999; Allen et al., 2004; Sonoda et al., 2004; Chen et al., 2005; Tyagi et al., 2010), one in Negeria (Ukoli et al., 2009) and one in Uruguay (Deneo-Pellegrini et al., 2012). Overall, this meta-analysis included 5791 cases of prostate cancer, and most studies suggested a non-significant relationship between eggs consumption and prostate cancer.

Case-control studies

Based on data from 11 case-cohort studies (La Vecchia et al., 1991; Ewings et al., 1996; Gronberg et al., 1996; Jain et al., 1999; Sung et al., 1999; Bosetti et al., 2004; Sonoda et al., 2004; Chen et al., 2005; Ukoli et al., 2009; Tyagi et al., 2010; Deneo-Pellegrini et al., 2012), we found no association between high intake of eggs and risk of prostate cancer (OR 1.09, 95% CI 0.89-1.31) (Figure 2). There was a significant heterogeneity between studies (p = 0.022, I^2 = 52.2%). Pooled ORs from the sensitivity analysis ranged from 1.04 (95% CI, 0.87, 1.21) after excluding Deneo-Pellegrini et al. (Deneo-Pellegrini et al., 2012) to 1.14 (95% CI, 0.92-1.36) after excluding Le vecchia et al. (1991), which indicated that no study significantly influenced the pooled estimate. After the removal of the study by Deneo-Pellegrini et al. (2012), the p value for heterogeneity was no longer statistically significant (p = 0.217, I^2 = 24.6%). The Begg (p = 0.533)

Table 2. Summary of Pooled Risk Estimates of Eggs Intake with Prostate Cancer by Geographical Region, Time of PSA Introduction, and Clinical Characteristic

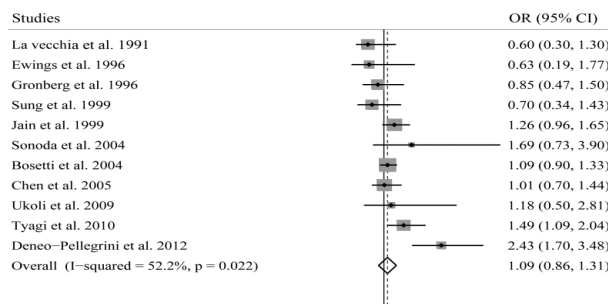|	Case-control studies			Cohort studies		
	No. of studies	Pooled RR (95% CI)	Heterogeneity (I² score)	No. of studies	Pooled RR (95% CI)	Heterogeneity (I² score)
All studies	11	1.09 (0.86, 1.31)	0.022 (52.2%)	6	0.97 (0.87, 1.07)	0.441 (0)
North America	1	1.26 (0.96, 1.64)	-	3	0.95 (0.70, 1.20)	0.126 (51.6%)
Europe	4	0.90 (0.65, 1.16)	0.239 (28.9%)	2	0.96 (0.85, 1.07)	1.000 (0)
Asia	4	1.11 (0.73, 1.49)	0.144 (44.6%)	1	1.14 (0.79, 1.65)	-
Uruguay	1	2.43 (1.54, 3.32)	-	-	-	-
Negeria	1	1.18 (0.50, 2.81)	-	-	-	-
Before 1994	5	0.93 (0.60, 1.27)	0.164 (38.6%)	4	0.97 (0.75, 1.19)	0.247 (27.6%)
After 1994	4	1.32 (0.76, 1.87)	0.005 (76.9%)	-	-	-
Advanced cancer	-	-	-	1	0.70 (0.53-0.93)	-
Fatal cancer	-	-	-	3	1.33 (0.72, 1.95)	0.142 (48.8%)

Figure 2. Pooled Results for 11 Case-control Studies of Eggs Consumption and Prostate Cancer Incidence
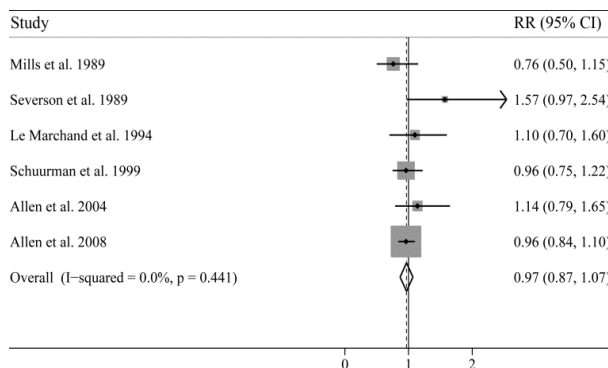

Figure 3. Pooled Results for 6 Cohort Studies of Eggs Consumption and Prostate Cancer Incidence

and Egger (p = 0.151) tests, as well as visual inspection of the funnel plot (not shown), did not suggest a publication bias.

Considering the geographic area, the pooled OR was 0.90 (95% CI, 0.65–1.16) in European studies and 1.11 (95% CI 0.73–1.49) in Asian studies and 1.09 (95% CI 0.74–1.62) in Asian studies. Only one study was included in three other regions and should be interpreted cautiously. In the subgroup analysis by PSA era, no statistical significant association between eggs consumption and prostate cancer was observed for studies conducted before or after 1994, although the summary OR seemed to be higher for the latter (Table 2).

Cohort studies

Data from 6 cohort studies (Mills et al., 1989; Severson et al., 1989; Le Marchand et al., 1994; Schuurman et al., 1999; Allen et al., 2004; Allen et al., 2008) showed no association between a high eggs intake and prostate cancer

incidence (RR 0.97, 95% CI 0.97-1.07) (Figure 3). The results were homogeneous. There was no indication of publication bias from Begg's (p = 0.452) or Egger's (p = 0.401) test.

A subgroup analysis was also performed according to different regions. We found that the non-significant relationships between prostate cancer and eggs consumption were consistent in all geographical areas. The pooled RR was not statistically significant before introduction of PSA test. No cohort began enrolling patients after 1994.

Advanced prostate cancer

The only cohort study (Schuurman et al., 1999) to report RR estimates based on tumor stage reported eggs consumption to have a significant negative association with high-stage prostate cancer (RR 0.70, 95% CI 0.53-0.93).

Prostate cancer–specific mortality

Pooling the results of the 3 studies (Snowdon et al., 1984; Hsing et al., 1990; Richman et al., 2011) showed no association of high eggs consumption with fatal disease (RR:1.33; 95% CI: 0.72-1.95). There is a weak heterogeneity between studies (p = 0.142, I² = 48.8%).

Discussion

Previous studies have suggested that eggs consumption may increase the risk of colorectal cancer and some other cancers (Steinmetz et al., 1994; Aune et al., 2009). In the present meta-analysis, we found no statistically significant positive association between high intake of eggs and risk of prostate cancer. Furthermore, our findings for lethal prostate cancer also suggested no association with high consumption of eggs. To our knowledge, this is the first meta-analysis to evaluate the relationship between them.

Several factors contributed to the stability of our findings. First, the results were generally homogeneous. No heterogeneity was detected in cohort studies but some heterogeneity in case-control studies. However, when the study (Deneo-Pellegrini et al., 2012) conducted in Uruguay with the highest effect estimates was excluded, the results for case-control studies became homogeneous, and the pooled OR was not significantly changed. Second,

the findings were consistent across the subgroup analyses, regardless of regions and PSA screening. Third, for the two established risk factors, all studies included in this meta-analysis provided risk estimates adjusted for age, but only 2 case-control studies and 1 cohort study controlled for a family history of prostate cancer in their analyses. It is unlikely that is a strong confounder because a family history of prostate cancer is not strongly related to eggs consumption, it could not be a strong confounder for association for them.

A mechanistic role of eggs intake in the etiology of prostate cancer is plausible. Eggs are an important source of cholesterol and choline, both of which are highly concentrated in prostate cancer cells. Cholesterol homeostasis is disrupted in malignant cells, leading to accumulation of cholesterol, which is a precursor of androgen and may alter signaling pathways to promote cancer progression (Freeman et al., 2004; Dillard et al., 2008). Choline is essential for a variety of cell functions involved in cancer growth and progression. Malignant prostate cells have higher choline concentrations than do healthy cells, and choline kinase is overexpressed in prostate cancer (Glunde et al., 2006; Ramirez de Molina et al., 2008). Blood concentrations of cholesterol and choline have been positively associated with risk of advanced prostate cancer (Platz et al., 2008; Johansson et al., 2009). However, in our study, eggs consumption was associated with a lower incidence of advanced prostate cancer, and no association was observed with fatal prostate cancer, while these results need to be interpreted with caution because of the few studies available. Another plausible mechanism through which eggs could increase the risk of prostate cancer include the effect of calcium in prostatic epithelium, which was the only mineral presented a significant increased risk of prostate cancer (Gao et al., 2005; Huncharek et al., 2008).

Our study has several limitations. First, as a meta-analysis of observational data, our results are prone to recall and selection bias inherent in the original studies. Second, eggs are generally not the main focus of the included studies. Although analysis of total eggs consumption was based on many studies, fewer studies were available for the secondary outcomes of advanced and lethal disease. Also, eggs intake may include eggs prepared in a number of methods, such as fried eggs, which may increase risk of prostate cancer by higher intake of fat. Third, because of limited resources, we only searched PubMed, and collected papers in English, which may lead to publication bias, even though no significant evidence of publication bias was observed.

In conclusion, this meta-analysis of epidemiological studies provides evidence on the absence of any association between eggs intake and prostate cancer risk. Given the relatively small number of cohort studies included in this meta-analysis, larger prospective studies are needed to confirm this association in the future.

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