RESEARCH COMMUNICATION

Egg Consumption and the Risk of Cancer: a Multisite Case-Control Study in Uruguay

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Abstract

Background: Previous studies have suggested that egg consumption may increase the risk of colorectal cancer and some other cancers. However, the evidence is still limited. To further explore the association between egg intake and cancer risk we conducted a case-control study of 11 cancer sites in Uruguay between 1996 and 2004, including 3,539 cancer cases and 2,032 hospital controls. Results: In the multivariable model with adjustment for age, sex (when applicable), residence, education, income, interviewer, smoking, alcohol intake, BMI, intake of fruits and vegetables, grains, dairy products, total meat and other fatty foods, mate tea and energy, there was a significant increase in the odds of cancers of the oral cavity and pharynx (OR=2.02, 95% CI: 1.19-3.44), upper aerodigestive tract (OR=1.67, 95% CI: 1.17-2.37), colorectum (OR=1.64, 95% CI: 1.02-2.63), lung (OR=1.59, 95% CI: 1.10-2.29), breast (OR=2.86, 95% CI: 1.66-4.92), prostate (OR=1.89, 95% CI: 1.15-3.10), bladder (OR=2.23, 95% CI: 1.30-3.83) and all cancer sites combined (OR=1.71, 95% CI: 1.35-2.17) for a high vs. low egg intake. Conclusions: We found an association between higher intake of eggs and increased risk of several cancers. Further prospective studies of these associations are warranted.

Key Words: Diet - eggs - cancer - epidemiology

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Introduction

A high intake of eggs has been associated with increased risk of colorectal cancer in several previous studies (Steinmetz and Potter, 1994). Some studies have also suggested increased risk of cancers of the oral cavity and pharynx (Zheng et al., 1992a; Levi et al., 1998; Franceschi et al., 1999), esophagus (Gao et al., 1999; Bosetti et al., 2000; Levi et al., 2000), larynx (La Vecchia et al., 1990; De Stefani et al., 1999; Bosetti et al., 2002; Kapil et al., 2005), stomach (Risch et al., 1985; Wu-Williams et al., 1990; Gonzalez et al., 1991; Gao et al., 1999; Nishimoto et al., 2002), lung (Veierod et al., 1997; Darby et al., 2001; Hu et al., 2002; Marchand et al., 2002), bladder (Balbi et al., 2001; Radosavljevic et al., 2005) and kidney (Talamini et al., 1990; Wolk et al., 1996; Hu et al., 2003). However, other studies reported no association (Yu et al., 1988; Knekt et al., 1991; Chow et al., 1992; Ngoan et al., 2002; Ito et al., 2003) or even decreased risk with higher intake of eggs (De Stefani et al., 2004; Wakai et al., 2004) and the report from the World Cancer Research Fund and the American Institute for Cancer Research from 2007 suggested that the evidence was too limited to draw any firm conclusions (World Cancer Research Fund/American Insitute for Cancer Research, 2007). In a previous study we reported elevated risks of several cancers with a western dietary pattern with high loadings of red and processed meat and eggs (De Stefani et al., 2009). Although we have previously reported elevated cancer risks with a high meat intake (Aune et al., 2009) we are not aware of any study of egg intake and multiple cancers. Thus, as part of more detailed investigations of the specific foods and food groups that might be associated with cancer risk we decided to further explore these associations in a case-control study of diet and the risk of eleven different cancers in Uruguay, between 1996 and 2004.

Materials and Methods

Selection of cases

Between 1996 and 2004 we conducted a multisite case-control study including cancers of the oral cavity and pharynx (n=283), esophagus (n=234), stomach (n=275), colon (n=176), rectum (n=185), larynx (n=281), lung (n=931), breast (n=461), prostate (n=345), bladder (n=254) and kidney (n=114). All the cases were <90 years old at diagnosis (age range 23-89 years, mean 63.6 years) and were drawn from the four major public hospitals of Montevideo. A total of 3,744 patients with newly diagnosed and microscopically confirmed primary cancers were considered eligible for the study. In total 205 patients

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refused the interview or were to ill to be interviewed, leaving a final total of 3,539 cases which were included in the study (response rate 94.5%).

Selection of controls

In the same time period and in the same hospitals, 2,117 patients <90 years old (age range 22-89 years, mean 62.3 years) with non-neoplastic diseases not related to smoking or drinking and without recent changes in their diet were considered eligible for the study. Eighty five patients refused the interview, leaving a final total of 2,032 controls (response rate 96.0%). These patients presented with the following diseases: eye disorders (21.2%), abdominal hernia (20.8%), injuries and accidents (19.1%), venous diseases (5.5%), acute appendicitis (5.5%), diseases of the skin (6.7%), hydatid cyst (5.0 %), urinary system diseases (4.7%) and various other conditions (11.5%). The controls were not matched to the cases on any factors.

Interviews and questionnaire

The participants were interviewed by two trained social workers in the hospitals shortly after admittance, using a structured questionnaire (there were no proxy interviews). The questionnaire included sections on: 1) socio-demographic characteristics (age, sex, residence, education); 2) occupational history (type of job and duration in each job); 3) self-reported height and weight five years before the date of the interview; 4) a history of cancer in first degree relatives; 5) tobacco smoking (age at start, age at quitting, number of cigarettes smoked per day, type of tobacco, type of cigarettes, inhalation practices); 6) alcohol drinking (age at start, age of quit, number of glasses drunk per day or week, type of alcoholic beverage); 7) mate, coffee and tea consumption (age at start, age of quit, number of cups or liters ingested per day); and 8) a detailed food frequency questionnaire (FFQ) on the intake of 64 food items which covered the dietary intake one year before diagnosis. This FFQ was considered as representative of the Uruguayan diet and allowed for the estimation of total energy intake. Although the FFQ has not been validated, it has been tested for reproducibility with reasonable results and the correlation coefficient between the two assessments of egg intake was 0.45 (Ronco et al., 2006). Egg intake was categorized by weekly frequency of intake with the following cut points using non-consumers as the reference group: 0 eggs per week, >0-3.5, >3.5. The median in each category was 0, 2 and 6 eggs per week.

Statistical methods

We used unconditional logistic regression to estimate odds ratios for increasing intake of eggs compared with the lowest referent category. We used a multivariable model including the following covariates: age (continuous), sex (when applicable), residence (urban/rural), education (continuous), income (continuous), interviewer, smoking status (never smokers, former smokers, current smokers), age at starting smoking (continuous), cigarettes per day (continuous), years since quitting smoking (continuous), duration of smoking (continuous), alcohol intake (0, 1-60, 61-120, 121-240, ≥241 ml/d), intake of fruits and vegetables (continuous), grains (continuous), dairy products (continuous), total meat (continuous), other fatty foods (continuous), mate drinking status (never drinkers, former drinkers, current drinkers), energy intake (continuous), and BMI (continuous). Potential confounders were included in the multivariate model based on a review of the literature and from comparisons of cases vs. controls and/or whether they altered the risk estimate 10% or more. To address the possibility of residual confounding from other dietary factors we also conducted analyses with further adjustment for several other variables including legumes, fiber, coffee, and tea and with separate adjustment for red meat, processed meat, poultry and fish and for fruits and vegetables. To assess whether dietary cholesterol might account for part of the association between egg intake and cancer risk we conducted exploratory analyses with additional adjustment for cholesterol intake. Tests for linear trend were calculated by entering the categorical variables as continuous parameters in the models. Possible interactions between egg intake and age, sex, fruits and vegetables, total meat, smoking status or alcohol intake

Table 1. Socio-demographic Characteristics and Selected Risk Factors among Cases and Controls (Values are means (standard deviations), except for sex (%))

Cancer	Number	Age (years)	Men (%)	Smoking (Cig./d)	Ethanol (ml/d)	Fruits, vegetables (g/d)	Meat (g/d)	Eggs (times/week)
Oral cavity, pharynx	283	59.9 (9.7)	96.8	27.6 (15.9)	213.1 (222.5)	335.7 (155.3)	258.7 (108.7)	2.7 (2.6)
Esophagus	234	66.3 (10.3)	78.6	22.2 (18.8)	122.9 (195.7)	317.7 (146.6)	238.0 (99.8)	2.4 (3.0)
Larynx	281	62.1 (10.0)	97.5	32.6 (21.3)	194.0 (231.6)	327.8 (141.8)	265.0 (101.4)	2.5 (2.8)
Upper aerodigestive	798	62.5 (10.3)	91.7	27.8 (19.2)	179.9 (221.3)	327.6 (148.1)	254.9 (104.1)	2.5 (2.8)
Stomach	275	65.5 (11.2)	69.3	16.0 (17.7)	85.4 (140.2)	342.9 (143.9)	230.1 (99.2)	2.0 (2.7)
Colon	176	64.3 (11.9)	49.4	13.7 (19.0)	45.7 (127.1)	322.5 (153.7)	220.2 (92.0)	2.5 (2.9)
Rectum	185	66.3 (10.2)	68.6	14.8 (17.2)	70.3 (119.3)	335.0 (171.4)	235.1 (98.6)	2.3 (3.7)
Colorectum	361	65.3 (11.1)	59.3	14.2 (18.0)	58.3 (123.6)	328.9 (162.9)	227.8 (95.6)	2.4 (3.3)
Lung	931	62.0 (10.0)	94.0	31.6 (19.8)	135.9 (185.6)	317.8 (169.7)	232.6 (100.6)	2.7 (3.3)
Breast	461	59.7 (13.1)	0.0	4.1 (8.7)	12.1 (51.5)	282.5 (157.5)	198.1 (82.1)	2.1 (1.9)
Prostate	345	70.6 (7.3)	100.0	18.0 (18.5)	96.4 (165.9)	347.1 (163.8)	205.1 (94.3)	2.5 (2.4)
Bladder	254	66.9 (10.0)	88.2	19.3 (18.0)	83.7 (129.7)	348.5 (190.0)	220.2 (112.7)	2.9 (3.1)
Kidney	114	60.6 (11.8)	67.5	15.6 (16.3)	78.0 (162.8)	323.5 (163.6)	201.5 (103.8)	2.0 (2.0)
All cases	3,539	63.6 (11.0)	75.1	21.4 (20.1)	108.4 (176.6)	323.7 (162.6)	227.9 (100.7)	2.5 (2.9)
Controls	2,032	62.3 (12.8)	64.8	13.5 (15.8)	75.3 (147.4)	329.8 (156.0)	195.8 (87.1)	2.3 (4.3)

Table 2. Egg Intake and Odds of Various Cancers[1]

Cutoffs (medians)	0 (0) eggs/wk		>0-3.5 eggs/wk (2)		>3.5 eggs/wk (6)		P for trend
Cancer site	Cases	OR	Cases	OR (95% CI)	Cases	OR (95% CI)	
Oral cavity, pharynx	29	1.00 (ref.)	180	0.78 (0.50-1.24)	74	2.02 (1.19-3.44)	<0.0001
Esophagus	26	1.00 (ref.)	162	1.10 (0.71-1.73)	46	1.69 (0.98-2.93)	0.05
Larynx	32	1.00 (ref.)	193	0.75 (0.49-1.16)	56	1.17 (0.69-1.97)	0.35
Upper aerodigestive	87	1.00 (ref.)	535	0.90 (0.67-1.20)	176	1.67 (1.17-2.37)	0.001
Stomach	34	1.00 (ref.)	205	0.93 (0.62-1.39)	36	1.19 (0.69-2.04)	0.55
Colon	18	1.00 (ref.)	120	1.60 (0.94-2.72)	38	3.21 (1.68-6.11)	<0.0001
Rectum	23	1.00 (ref.)	137	1.20 (0.74-1.95)	25	0.90 (0.48-1.72)	0.71
Colorectum	41	1.00 (ref.)	257	1.29 (0.89-1.87)	63	1.64 (1.02-2.63)	0.05
Lung	89	1.00 (ref.)	654	1.28 (0.95-1.72)	188	1.59 (1.10-2.29)	0.018
Breast	52	1.00 (ref.)	346	1.74 (1.20-2.52)	63	2.86 (1.66-4.92)	<0.0001
Prostate	35	1.00 (ref.)	243	1.25 (0.83-1.88)	67	1.89 (1.15-3.10)	0.01
Bladder	27	1.00 (ref.)	157	1.22 (0.77-1.93)	70	2.23 (1.30-3.83)	0.001
Kidney	19	1.00 (ref.)	80	0.97 (0.56-1.66)	15	0.82 (0.38-1.75)	0.60
All sites	384	1.00 (ref.)	2,477	1.16 (0.97-1.39)	678	1.71 (1.35-2.17)	<0.0001
Controls	286	(156/130 m/w[2])	1,522	(1016/506)	224	(174/50)	

[1]Multivariable model: age, sex, residence, education, income, interviewer, smoking status, age at starting smoking, cigarettes per day, years since quitting smoking, duration of smoking, alcohol intake, intake of fruits and vegetables, grains, dairy foods, total meat, other fatty foods, mate drinking status, energy intake, BMI; [2]m/w, men/women

were assessed by including cross product terms in the multivariable models. A two-tailed P-value of <0.05 was considered to be statistically significant. All statistical analyses were conducted using STATA version 9.1.

Results

Sociodemographic characteristics and selected risk factors of the cases and the controls are shown in Table 1. Compared with the controls, the cases were in general older (p=0.0001 with t-test, not shown in the Table), they also smoked more (p<0.0001) and had a higher intake of alcohol (p<0.0001), meat (p<0.0001) and eggs (p<0.0001), but the intake of fruits and vegetables was not significantly different (p=0.18).

Table 3. Egg Intake and Odds of all Cancers Combined Stratified by Selected Covariates

	Eggs	>0-3.5 eggs/wk[2] OR (95% CI)	>3.5 eggs/wk[2] OR (95% CI)	P
Age	≤50 yrs	1.32 (0.83-2.12)	2.24 (1.21-4.17)	0.64
	>50 yr	1.15 (0.94-1.40)	1.65 (1.27-2.14)	
Sex	Men	1.00 (0.80-1.26)	1.42 (1.06-1.89)	0.17
	Women	1.47 (1.09-1.98)	2.48 (1.55-3.96)	
Fruits, vegetables				
	<246.9 g/d	1.23 (0.92-1.66)	2.49 (1.58-3.91)	0.031
	246.9-365.4	0.98 (0.71-1.37)	1.48 (0.95-2.31)	
	>365.4	1.27 (0.92-1.75)	1.59 (1.08-2.35)	
Meat	≤154.1 g/d	1.54 (1.12-2.11)	1.83 (1.13-2.96)	0.21
	>154.1-217.5	1.00 (0.73-1.38)	1.56 (1.02-2.39)	
	>217.5	0.94 (0.68-1.31)	1.62 (1.09-2.40)	
Smoking				
	Never	1.28 (0.95-1.72)	2.30 (1.46-3.61)	0.11
	Former	1.42 (0.99-2.04)	1.72 (1.08-2.75)	
	Current	0.92 (0.68-1.24)	1.39 (0.95-2.02)	
Alcohol				
	Nondrinker	1.44 (1.12-1.85)	2.20 (1.52-3.19)	0.31
	1-120 ml/d	0.99 (0.71-1.39)	1.32 (0.87-1.99)	
	121+ ml/d	0.89 (0.57-1.38)	1.56 (0.89-2.73)	

[1]Multivariable model: age, sex, residence, education, income, interviewer, smoking status, age at starting smoking, years since quitting smoking, cigarettes per day, duration of smoking, alcohol intake, intake of intake of fruits and vegetables, grains, dairy foods, total meat, other fatty foods, mate drinking status, energy intake, BMI; [2]Reference category is 0 eggs/wk

In the multivariable model, the highest vs. the lowest intake of eggs was associated with an increased odds of cancers of the oral cavity and pharynx (OR=2.02, 95% CI: 1.19-3.44; p_{trend}<0.0001), esophagus (OR=1.69, 95% CI: 0.98-2.93; p_{trend}=0.05), upper aerodigestive tract (includes oral cavity, pharynx, esophagus, larynx) (OR=1.67, 95% CI: 1.17-2.37; p_{trend}=0.001), colon (OR=3.21, 95% CI: 1.68-6.11; p_{trend}<0.0001) and colon and rectum combined (OR=1.64, 95% CI: 1.02-2.63; p_{trend}=0.05), lung (OR=1.59, 95% CI: 1.10-2.29; p_{trend}=0.018), breast (OR=2.86, 95% CI: 1.66-4.92; p_{trend}<0.0001), prostate (OR=1.89, 95% CI: 1.15-3.10; p_{trend}=0.01), bladder (OR=2.23, 95% CI: 1.30-3.83; p_{trend}=0.001), and all cancers combined (OR=1.71, 95% CI: 1.35-2.17; p_{trend}<0.0001) (Table 2). We also had information on intake of fried and boiled eggs in this study and the results were in general similarly elevated both with intake of boiled and fried eggs (results not shown).

There was a stronger association in the age and sex-adjusted model for all sites combined (OR=2.13, 95% CI: 1.71-2.65, for the highest vs. the lowest intake, results not shown) than in the multivariable model (OR=1.71, 95% CI: 1.35-2.17). However, when we further adjusted for intake of legumes, fiber, coffee, tea and separately for red meat, processed meat, poultry and fish and separately for fruits and vegetables, the OR for all cancer sites combined was not materially changed (OR=1.70, 95% CI: 1.33-2.17, for the highest vs. the lowest intake, results not shown). As an exploratory analysis, further adjustment for cholesterol intake strengthened the association (OR=1.98, 95% CI: 1.45-2.71, results not shown).

Stratified analysis showed that the elevated risk with egg intake persisted in most subgroups (Table 3). There were higher ORs among younger persons vs. older persons, among women vs. men, among those with a low intake of fruits and vegetables vs. a high intake and among

never smokers vs. current smokers and among non-drinkers of alcohol vs. those with a high alcohol intake, but only the interaction with fruit and vegetable intake was statistically significant (p=0.03).

Discussion

Our results suggest that a high intake of eggs increases the risk of several cancers. We found a positive association between egg intake and cancers of the oral cavity and pharynx, consistent with several previous case-control studies (Zheng et al., 1992a; Levi et al., 1998; Franceschi et al., 1999; De Stefani et al., 2005). Our study also suggested an elevated risk of esophageal cancer with higher egg intake, although the estimate was not statistically significant, while previous case-control studies found either positive associations (Gao et al., 1999; Bosetti et al., 2000; Levi et al., 2000), no associations (Yu et al., 1988; De Stefani et al., 1999) or inverse associations (Tavani et al., 1994). We found no association between egg intake and laryngeal cancer while most previous case-control studies reported non-significant increases with higher intake (La Vecchia et al., 1990; Zheng et al., 1992b; De Stefani et al., 1999; Bosetti et al., 2002; Kapil et al., 2005). We also found no association between egg intake and stomach cancer consistent with two case-control studies (Hoshiyama and Sasaba, 1992; Ito et al., 2003) and a cohort study (Ngoan et al., 2002), but not with other case-control studies (Risch et al., 1985; Wu-Williams et al., 1990; Gao et al., 1999).

We observed a strong increase in the risk of colon cancer with higher intake of eggs, but there was no association with rectal cancer. Most previous case-control (Le Marchand et al., 1997; Boutron-Ruault et al., 1999; Chiu et al., 2003; Hu et al., 2007a; 2007b) and cohort studies (Phillips and Snowdon, 1985; Hsing et al., 1998; Jarvinen et al., 2001; Sanjoaquin et al., 2004; Lee et al., 2009) and a review (Steinmetz and Potter, 1994) suggested significant or non-significant increases in the risk of colorectal cancer with higher egg intake. Further, a pooled analysis of case-control studies found an increased risk of colorectal cancer with a high intake of cholesterol (of which eggs are a major dietary source) (Howe et al., 1997). Several case-control studies (Goodman et al., 1992; Darby et al., 2001; Hu et al., 2002; Marchand et al., 2002) and a cohort study (Veierod et al., 1997) found significant or non-significant positive associations between egg intake and lung cancer, however, two other cohort studies reported no clear association (Knekt et al., 1991; Chow et al., 1992).

Previous studies of egg intake and breast cancer risk have shown mixed results with most published case-control (Dai et al., 2002; Hermann et al., 2002; Hirose et al., 2003) and cohort studies (Mills et al., 1989b; Key et al., 1999) reporting no association between egg intake and breast cancer, while a pooled analysis of cohort studies reported a positive association (Missmer et al., 2002). Our study is consistent with the pooled analysis in finding a positive association, although our result is considerably stronger. Most, but not all (Ross et al., 1987; Vena et al., 1992; Walker et al., 1992; Radosavljevic et al., 2005) previous studies reported no association between the intake of eggs and prostate (Mills et al., 1989a; Severson et al., 1989; Schuurman et al., 1999;Hsing et al., 1990; Le Marchand et al., 1994; Allen et al., 2004; 2008) or bladder cancer (Steineck et al., 1990; Chyou et al., 1993; Nagano et al., 2000; Sakauchi et al., 2004; Wakai et al., 2004), while our study showed a significant positive association with both these cancers. We found no significant association between egg intake and kidney cancer while previous studies reported non-significant elevations in risk (Talamini et al., 1990; Wolk et al., 1996; Hu et al., 2003). A recent cohort study reported an elevated risk of total cancer incidence with a RR of 1.07 (95% CI: 1.01-1.13) per 10 grams of eggs per day (Benetou et al., 2008), in line with our results of an elevated risk of all cancer sites (included in this study) combined, although it should be noted that our estimate for all cancer sites combined is not equal to total cancer incidence since we did not have information on all cancer sites.

As to the mechanism that may explain a possible detrimental effect of egg intake upon cancer risk the most plausible explanation involves the high cholesterol content of eggs. Higher intake of cholesterol has been shown to increase the formation of secondary bile acids in both humans and animals (Cruse et al., 1979; Hiramatsu et al., 1983) and to enhance the induction of colorectal tumors in animal models (Sakaguchi et al., 1986). One cohort study reported a positive association between egg intake and colorectal adenomas, precursors of colorectal cancer (Cho et al., 2007). Further, other experimental data suggested that cholesterol intake also could enhance the formation of lung tumors (Kimura and Sumiyoshi, 2007). Cholesterol is a precursor of steroid hormones and might affect breast cancer risk through the formation of estrogens. Experimental studies of cholesterol feeding and mammary tumor development have, however, provided mixed results, with some showing an adverse effect (Klurfeld and Kritchevsky, 1981; Nakayama et al., 1993), while others found a protective effect (el-Sohemy et al., 1996). Our finding that adjustment for cholesterol intake slightly strengthened the association between egg intake and cancer risk suggests that other factors than cholesterol may account for the positive associations we observed. Eggs can also be a source of heterocyclic amines which are formed during high temperature cooking (Layton et al., 1995), however, this mechanism is unlikely to explain much of the elevated risk because most of the results were similarly elevated for both fried eggs and boiled eggs. As for the other cancer sites, we are currently not able to point to a biologically plausible mechanism.

Higher intakes of eggs could also be a marker of a less healthy diet and this seemed to be the case in our study. More frequent intakes of eggs was associated with higher intakes of total, red and processed meat which have been consistent risk factors for several cancer sites in the Uruguayan population (Aune et al., 2009). Furthermore, egg consumers also tended to smoke more and use more alcohol. However, adjustment for alcohol and smoking did not materially affect the effect estimates and adjustment for total meat intake strengthened rather than attenuated the association between egg intake and cancer

risk. Also, the finding that the results persisted among never smokers, non-drinkers of alcohol and among those with a low intake of meat and high intake of fruit and vegetables intake suggest that residual confounding from these factors does not explain the findings. We were not able to adjust for physical activity which is an important risk factor for several cancer sites. We cannot exclude the possibility that residual confounding from other dietary factors or unknown or unmeasured factors could explain the associations we observed. Nevertheless, when we further adjusted the results for other food groups and nutrients including legumes, tea, coffee, fiber and separately for fish, poultry, red and processed meat, and separately for fruits and vegetables, the results remained similar.

Our study has several potential limitations; as with any case-control study we cannot rule out the possibility of recall or selection bias. If the controls either consume or report their egg consumption differently than the general population biased results may occur. Participation rates were very high, thus minimizing the potential for selective participation according to lifestyle practices. Recall bias is a potential problem in all case-control studies because of the retrospective assessment of diet while selection bias may be a problem particularly in hospital-based case-control studies, if the dietary factor investigated somehow is related to the diseases of the controls. The participants in this study were generally of low socioeconomic status, with minimal knowledge about the role of diet in affecting cancer risk and there has been little or no focus on egg intake as a risk factor for cancer in the media. Although a reduction in the intake of eggs and cholesterol has been recommended for cardiovascular disease patients, we are not aware of medical advice to limit egg intake among persons with any of the disorders who served as the control group in this study. Thus, although dietary changes after diagnosis may influence recall of past diet, there is little reason to believe that the hospitalized controls in this study have decreased their egg intake following their diagnosis and that such a dietary change have led to an underestimation of egg intake. These points should make recall bias and selection bias less likely, but nevertheless, we cannot exclude the possibility that such biases partly may explain some of our findings. Since we investigated egg intake and multiple cancers, some of our findings may have been due to chance. Because of the lack of information on other cancer sites, we were not able to investigate the association between egg intake and other cancers potentially related to egg intake (Shu et al., 1993; Pirozzo et al., 2002; Purdue et al., 2004; Zheng et al., 2004; Genkinger et al., 2006).

Our study has several strengths as well; the relatively large dietary variation in the Uruguayan population increased the power to detect significant associations. Adjustment for a number of potentially important confounding factors did not substantially alter the results. To our knowledge this is the first multisite case-control study of egg consumption and cancer risk. Our finding of a dose-response relationship between egg consumption and increased cancer risk suggest an underlying biological effect of egg intake on cancer risk, although we cannot exclude other potential explanations for the results.

In conclusion our study provides evidence for an adverse effect of egg consumption upon cancer risk. It is unclear whether these findings are real or whether egg intake simply is a marker of a cancer-prone diet and other lifestyle factors. Further prospective investigations of these associations are warranted.

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