Avian exposure and risk of lung cancer in women in Missouri: population based case-control study

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Abstract

Objective—To investigate the association, previously reported in three European studies, between ownership of pet birds and the risk of lung cancer.

Design—A population based case-control study with a structured questionnaire administered by telephone.

Setting—Missouri, a midwestern state in the United States with a population of about 5 million.

Subjects—All newly diagnosed cases of primary lung cancer in women aged 30–84 years in Missouri from 1 January 1993 to 31 January 1994 reported to the state cancer registry were invited to participate (n = 652); and 629 population based controls.

Main outcome measures—Odds ratios were computed in relation to whether or not the study subject ever kept pet birds, the type of bird kept, and several measures of intensity or duration of exposure. Odds ratios were adjusted for smoking.

Results—The odds ratio (95% confidence interval) for the development of lung cancer associated with keeping pet birds was 0.84 (0.65 to 1.09). The results were similar for the type of pet bird kept, the number of birds kept, the location of the bird in the house, and the duration of ownership.

Conclusion—The keeping of pet birds carries no excess risk for the development of lung cancer.

older were registered with the Health Care Financing Administration. Tissue slides from 627 (86%) were simultaneously reviewed by three pathologists for histological verification by using standard histological classification criteria.^{11–12}

CONTROLS

For women of any race between the ages 30–64 years, names and addresses were randomly selected from files of driving licences. For women between the ages of 65 and 84 years, names and addresses were randomly selected from lists provided by the federal Health Care Financing Administration, which includes an estimated 95% of women of this age group.¹³ Controls were matched to cases by using five year age groups.

Case-control studies of lung cancer typically result in a sample of patients with lung cancer in which nearly all are smokers and a sample of controls in which very few smoke. The extreme imbalance in smoking among cases and controls limits the power of a study to assess subtle effects of smoking as well as interactions of smoking with other risk factors. The two stage randomised recruitment was developed to deal with this problem.^{14–15} An initial screening interview is conducted to obtain information on selected covariates and disease (for this study all cases were enrolled; the randomised procedure was used for selection of controls only). This information is then used to define a random “biased” sampling scheme of subjects on whom further data are collected by using the full interview questionnaire. An important feature of this sampling approach is that standard methods of analysis with commonly available computer software can be adapted for use with ease.

We established a randomised recruitment procedure separately for white, black, and others subjects on the basis of four categories of smoking: those who had never smoked, former smokers, current light to moderate smokers, and heavy smokers. The prospective controls were randomly selected for administration of the full questionnaire on the basis of the sampling probabilities shown in table 1.

Screening interviews were attempted on 4592 potential controls with telephone numbers or complete address information, or both. Of the 3386 controls who were found eligible by screening criteria, 730 subjects were targeted for interview, 700 completed control interviews, and 629 provided information on pet birds and relevant potential confounding exposures (see table 1).

QUESTIONNAIRE DESIGN AND ADMINISTRATION

All interviews obtained information only on the period of life preceding the date of the diagnosis of cancer, and most (>94%) were conducted within seven months of diagnosis. Information on residential history, education, exposure to passive smoking, diet (food frequency questionnaire²), and ownership of pet birds was obtained from a structured questionnaire administered by trained interviewers. For women with lung cancer who could not be interviewed because of death or ill health an interview with a knowledgeable next of kin was obtained (33% of the cases and none of the controls).

Introduction

Previously identified risk factors account for only 36% of the lung cancers among women who have never smoked and 70% of the lung cancers among former smokers in Missouri, highlighting the need for further aetiological research.^{1–6} The observation that keeping birds as pets in the home contributes to indoor pollution⁷ and three subsequent case-control studies with positive results from the Netherlands,⁸ Britain,⁹ and Germany¹⁰ linking bird keeping to an increased risk of lung cancer motivated this population based case-control study among women in Missouri.

Subjects and methods

CASES

Between 1 January 1993 and 31 January 1994, 783 women with primary lung cancer were reported to the Missouri Cancer Registry. Physicians denied permission to interview 13 of these women, seven did not meet residential eligibility requirements, 19 died and no proxy was available for interview, and 13 refused to be interviewed, which left 731 eligible cases (93%). This group included 64 women who had never smoked, 189 former smokers, 331 current light to moderate smokers (those smoking fewer than 30 cigarettes a day), and 147 heavy smokers (those smoking 30 or more cigarettes a day). Information on pet birds and relevant potential confounding exposures was available for 652 (83%; see table 1). Of these women, 435 (67%) were interviewed by telephone; because of death or serious illness, interviews with the next of kin were obtained for the 217 (33%) other women. Among those under 65 years of age, 86% had a valid Missouri driving licence at the time of diagnosis (see table 1), and all those 65 years or

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Table 1—Characteristics of women with lung cancer and population controls. Figures are numbers (percentages) of subjects

Characteristic	Cases (n = 652)	Controls (n = 629)	Eligible controls (screened)	Selection probability
Age at interview (years):				
<50	47 (7.2)	43 (6.8)		
50-59	115 (17.6)	115 (18.2)		
60-69	232 (35.6)	220 (35.0)		
70-84	258 (39.6)	251 (40.0)		
Smoking and race:				
Never smoked:				
White	49 (7.5)	76 (12.1)	2014	0.04
Black and other	1 (<0.2)	7 (1.1)	113	0.06
Stopped >3 years ago:				
White	151 (23.2)	168 (26.7)	660	0.26
Black and other	11 (1.7)	14 (2.2)	44	0.34
Current smoker ≤30/day (median 20/day):				
White	273 (41.9)	274 (43.6)	443	0.62
Black and other	35 (5.4)	27 (4.3)	38	.70
Current smoker ≥30/day (median 40/day)				
White	124 (19.0)	62 (9.9)	73	1
Black and other	7 (1.1)	1 (0.2)	1	1
Smoking duration (years):				
1-19	23 (3.8)	95 (17.4)		
20-29	65 (10.8)	73 (13.4)		
30-39	143 (23.8)	123 (22.5)		
40-49	199 (33.0)	164 (30.0)		
>50	159 (26.4)	86 (15.7)		
Missing data	13 (2.2)	6 (1.0)		
Type of interview:				
In person	435 (66.7)	629 (100)		
Next of kin	217 (33.3)	0		
Marital status:				
Married	305 (47.0)	351 (55.8)		
Widowed	227 (34.8)	208 (33.1)		
Separated	17 (2.6)	4 (0.6)		
Divorced	94 (14.4)	60 (9.5)		
Never married	9 (1.4)	6 (1.0)		
Education (years):				
<12	247 (37.9)	164 (26.1)		
12	282 (43.3)	290 (46.1)		
>12	115 (17.6)	175 (27.8)		
Unknown	8 (1.2)	0		
Current Missouri driving licence (among women <65 years old)				
No	35 (14)	1 (0.4)		
Yes	215 (86)	215 (99.6)		

ANALYSIS

Crude odds ratios (95% confidence intervals) were computed by using maximum likelihood procedures.^{16 17} In a separate analysis (data not shown) stratified and multivariate adjustment procedures were used to determine if odds ratios were comparable. In the stratified analysis strata were defined by four age groups (<50, 50-59, 60-69, 70-84 years), two categories of race (white, black and other non-white), four categories of smoking (active smoking by pack years: 0-7.5, >7.5-26, >26-45, >45), and for former smokers the number of years since they stopped smoking (>0-9, >9-17, >17-28, >28); these were used to compute "adjusted" odds ratios. In the multivariate analysis the four categories of smoking used in the randomised recruitment—namely, those who had never smoked, former smokers, current light to moderate smokers, and heavy smokers—were used in a multivariate logistic regression model to compute all odds ratios. No differences in odds ratios were observed between the two adjustment procedures, which justified our use of a multivariate technique to compute adjusted odds ratios (see tables 2 and 3). Because strata included the factors used in the randomised recruitment, no special analytic adjustment was required, and the estimated odds ratios and their confidence intervals were unbiased.^{14 15}

Multivariate logistic regression models were used to adjust for potentially confounding variables, including raw vegetable (quarters) and red meat consumption (quarters), age (<50, 50-59, 60-69, 70-84), active

smoking (quarters of pack years), number of years since subjects stopped smoking (quarters), marital status (married, widowed, separated, divorced, never married), education (<12 years, 12 years, >12 years), race (white, not white), ownership of a Missouri driving licence (yes, no), and passive smoking (yes, no).^{14 16} Wald confidence intervals were computed by using the estimated parameter, β , and its standard error (SE), as $\exp \{ \beta \pm 1.96 \times SE(\beta) \}$.

Results

The median age of all women in our study was 67 years. We observed several significant differences between the two groups (table 1). Fewer women with lung cancer had completed high school or college and had a current Missouri driving licence. Other factors observed in this study or in other studies reported in literature that could act as confounding variables included consumption of vegetables and red meat and intensity of smoking or passive smoking. The adjusted odds ratios included these variables in the logistic model to mitigate confounding.

After we controlled for potential confounding variables we observed no excess risk of lung cancer among those who kept birds compared with those who did not keep birds (table 2). Nor was there any excess risk for bird keeping observed in any strata of smoking or difference if the analysis excluded interviews with next of kin (adjusted odds ratio 0.98; 95% confidence interval 0.74 to 1.28). There was no excess risk among those who kept any specific species of birds. Pet birds kept in the bedrooms of those women who developed lung cancer⁹ conferred no additional risk, in fact a reduction in risk was seen among owners of parakeets (budgerigar) and canaries who kept the birds in their bedroom. A significantly reduced risk of lung cancer was also observed among those who personally raised chickens, turkeys, ducks, or other birds. Owners of cats also seemed to be at a reduced risk of lung cancer compared with those who had never owned a cat; this reduced risk was also observed if the analysis excluded interviews with next of kin (0.74; 0.56 to 0.98). No excess or reduced risk was observed among owners of any other pets. When we examined duration of bird ownership and number of birds kept no association was observed (table 3).

Discussion

In Missouri, no excess risk of lung cancer was found among subjects in any exposure group based on duration, intensity, or type of bird kept. In fact, among those who personally raised chickens or other farm fowl a significant reduction of risk was observed. This lower risk of lung cancer has previously been observed among farmers in the United States and around the world.¹⁸ The apparent protective effect of keeping parakeets or canaries in the bedroom is based on very small numbers and may be a statistical artefact. The protective effect of keeping cats is based on larger numbers and cannot be explained on the basis of smoking, dietary intake, or the socioeconomic variables available to us at this time.

These observations were made in the context of a large population based case-control study with several important strengths—namely, high participation rates, relatively few proxy interviews, information on many other potential risk factors, and a large proportion of the population who kept birds. The observations were consistent across categories of smoking and whether the analysis included or excluded interviews with next of kin. Three explanations are possible.

Firstly, as suggested by Modigh *et al*,¹⁹ the positive results from the earlier European studies may be the result of bias caused by the confounding influence of

Table 2—Odds ratios (confidence intervals) for lung cancer according to exposure to birds and other animals

Characteristic	Cases†	Controls†	Odds ratio (95% confidence interval)	
			Crude	Adjusted
Contact with pet bird for ≥6 months (all smoking categories combined):	256	258	0.95 (0.76 to 1.20)	0.84 (0.65 to 1.09)‡
Never smoked	22	30	1.36 (0.63 to 2.97)	1.15 (0.48 to 2.74)§
Former smoker	67	80	0.91 (0.58 to 1.43)	0.85 (0.53 to 1.37)§
Light to moderate smoker	118	118	1.00 (0.71 to 1.40)	0.92 (0.65 to 1.32)§
Heavy smoker	49	30	0.66 (0.34 to 1.28)	0.57 (0.27 to 1.18)§
Contact with pet dog for ≥6 months	554	545	0.94 (0.67 to 1.31)	0.95 (0.65 to 1.38)‡
Contact with pet cat for ≥6 months	265	322	0.67 (0.53 to 0.84)*	0.66 (0.52 to 0.86)*‡
Contact with other animal pets for ≥6 months	85	96	0.85 (0.61 to 1.18)	0.85 (0.59 to 1.21)‡
Contact with any pet for ≥6 months	587	580	0.90 (0.58 to 1.38)	0.87 (0.55 to 1.39)‡
Type of pet bird kept:				
Parrot	12	9	1.31 (0.51 to 3.40)	1.31 (0.49 to 3.48)‡
Parakeet	188	194	0.93 (0.72 to 1.19)	0.87 (0.66 to 1.13)‡
Kept in bedroom	7	21	0.32 (0.12 to 0.80)*	0.31 (0.12 to 0.80)*‡
Canary	66	65	0.99 (0.68 to 1.45)	0.92 (0.62 to 1.38)‡
Kept in bedroom	3	5	0.59 (0.11 to 2.82)	0.21 (0.05 to 0.97)*‡
Other pet birds	52	44	1.20 (0.78 to 1.85)	0.87 (0.55 to 1.39)‡
Kept in bedroom	4	5	0.80 (0.18 to 3.42)	0.52 (0.13 to 2.13)‡
Parents kept chickens, turkeys, ducks, or other birds during subject's childhood	360	373	0.93 (0.74 to 1.17)	0.83 (0.64 to 1.07)‡
Subject had some responsibility for them such as gathering eggs, feeding	279	286	0.99 (0.78 to 1.24)	0.84 (0.65 to 1.08)‡
Subject kept chickens, turkeys, ducks, or other birds	135	167	0.74 (0.57 to 0.97)*	0.52 (0.38 to 0.71)*

*P<0.05.

†Cases and controls reported here used in calculation of crude odds ratio, slightly smaller counts were used in calculation of adjusted odds ratio because of missing data.

‡Adjusted for consumption of raw vegetable (quarters), red meat (quarters), age (<50, 50-59, 60-69, 70-84), smoking (quarters of pack years), number of years since smoking cessation (quarters), marital status (married, widowed, separated, divorced, never married), education (<12, 12, >12 years), race (white, not white), driving licence (yes, no), and passive smoking (yes, no).

§Adjusted for raw vegetables, red meat, age, marital status, education, race, driving licence, and passive smoking.

Table 3—Odds ratios* (95% confidence intervals) for lung cancer according to duration and intensity of exposure to pet birds

Exposure	No of subjects	Odds ratio (95% confidence interval)	P value for linear trend test
Duration (total years of regular contact):			
None	355	1	
1-9	182	0.80 (0.61 to 1.04)	
10-82	57	1.13 (0.72 to 1.78)	0.63
Intensity (maximum No of birds kept):			
None	355	1	
1	159	0.88 (0.67 to 1.17)	
2	55	0.77 (0.49 to 1.20)	
≥3 (median 5)	26	0.91 (0.48 to 1.74)	0.39

*Adjusted for consumption of raw vegetables (quarters), red meat (quarters), age (<50, 50-59, 60-69, 70-84), smoking (quarters of pack years), years since smoking cessation (quarters), marital status (married, widowed, separated, divorced, never married), education (<12, 12, >12 years), race (white, not white), driving licence (yes, no), and passive smoking (yes, no).

higher prevalence rates of pet bird ownership among the lower socioeconomic classes, who have higher rates of lung cancer.

Secondly, the intensity of exposure may be greater in the Netherlands, Britain, and Germany than in Missouri or Sweden.¹⁷ While this does not seem to be the case on the basis of the number of pets owned or the duration of pet ownership, which seem quite similar, it may be due to different practices of bird keeping not yet made clear in the published literature.

Thirdly, the association reported may not be due intrinsically to the birds, which are somewhat com-

Key messages

- Three previous European studies found an association between keeping pet birds and an increased risk of lung cancer
- A population based case-control study of lung cancer among women in Missouri was conducted with detailed questions about the duration of bird ownership, the number and type of birds owned, and where in the home the birds were kept
- The study in Missouri was larger than previously conducted studies and had extensive information on other risk factors for lung cancer
- No excess risk was found with any measure of exposure to birds
- The association previously reported may not be due intrinsically to birds

parable among the countries studied, but rather to an infection or infestation of the birds that varies by country.

The inconsistency in results between this study and those in the Netherlands, Great Britain, and Germany precludes immediate public health recommendations, but it does suggest the need for further investigations to help explain the disparity in risk among countries.

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