ORIGINAL ARTICLE

# A case—cohort study of lung cancer in poultry and control workers: occupational findings

Martha Felini,[1] Nikiconia Preacely,[1] Nihita Shah,[1] Anita Christopher,[1] Vishnu Sarda,[2] Mohammed Elfaramawi,[1] Macodou Sall,[3] Saritha Bangara,[1] Subi Gandhi,[1] Eric S Johnson[1]

[1]Department of Epidemiology, UNT Health Sciences Center, Fort Worth, Texas, USA
[2]Department of Biostatistics, UNT Health Sciences Center, Fort Worth, Texas, USA
[3]Tulane University School of Public Health, New Orleans, Louisiana, USA

**Correspondence to**
Professor Eric S Johnson, Department of Epidemiology, School of Public Health, University of North Texas Health Sciences Center, 3500 Camp Bowie Blvd, Fort Worth, TX 76107, USA;
eric.johnson@unthsc.edu

## ABSTRACT

**Objectives** We conducted a mortality study of members of the United Food and Commercial Workers International Union who worked in poultry slaughtering/processing plants, and controls. Excess deaths from cancer at 11 different cancer sites including lung cancer were observed in the poultry workers. The study described here is a pilot case—cohort study of lung cancer nested within the cohort to examine if it is possible, in a larger study to be conducted later, to identify specific potentially carcinogenic occupational exposures in poultry workers.

**Methods** Subjects or the next of kin of deceased subjects were interviewed by phone. Logistic regression ORs and Cox proportional HRs were estimated.

**Results** Elevated risks for poultry exposure were recorded for subjects who (1) killed chickens at work (OR 4.2, 95% CI 1.2 to 14.7; HR 1.8, 95% CI 1.0 to 3.3) and (2) ever had direct contact with chicken blood at work (OR 1.9, 95% CI 1.0 to 3.8; HR 1.3, 95% CI 0.9 to 2.0). These activities are associated with high exposure to oncogenic viruses.

**Conclusion** These results may have important public health implications, since the general population is also exposed to these viruses. Elevated risks were observed for non-poultry-related occupational exposures such as working in a stockyard, working in a chemical plant, use of chemicals to kill moulds, and working in plants where plastic products were manufactured. These preliminary findings indicate that full scale epidemiological studies of adequate statistical power are needed to examine the role of occupational exposures in cancer occurrence in poultry workers.

## INTRODUCTION

Avian leucosis sarcoma viruses (ALSV), reticuloendotheliosis viruses (REV) and Marek's disease virus (MDV) naturally infect chickens and turkeys and commonly cause cancer in these birds.[1] Some subtypes of ALSV and REV are among the most potent cancer-causing agents known, and can induce cancer in chickens and turkeys within a week of exposure.[2] Humans are commonly exposed to these viruses since exposure occurs not only occupationally (poultry workers, veterinarians, laboratory workers, cooks, restaurant workers, etc) but also in the general population through contact with or eating poultry and poultry products including eggs,[2] and from inoculation with vaccines grown in eggs.[3] In a survey of eggs

---

**What this paper adds**

- ► Cohort studies have recorded an excess risk of lung cancer in workers in poultry slaughtering and processing plants, but the occupational exposures responsible for the excess are not known.
- ► This paper provides clear evidence, for the first time, linking the excess lung cancer risk in these workers to jobs associated with a high risk of exposure to oncogenic viruses, after adjusting for tobacco smoking and other confounders.
- ► There is a need to confirm these findings and also to examine the role of other potentially carcinogenic exposures in the industry that this study was not able to investigate because of insufficient statistical power.
- ► Sufficient evidence is provided in the study to warrant consideration of steps to reduce potentially carcinogenic exposures in this occupational group.

---

displayed for sale in a random sample of supermarkets in the New Orleans metropolitan area, 14% of eggs were positive for endogenous and exogenous ALSV (ie, at least one egg in a carton of a dozen eggs).[4 5] Similarly, it has been reported that virtually all stocks of measles and mumps vaccines currently in use in the US are contaminated with endogenous ALSV.[3] Thus, exposure in humans is widespread, and a high prevalence of antibodies to ALSV, REV and MDV has been reported not only in poultry workers but also in the general population, in some but not all studies.[6—10] Therefore, it is of interest whether these viruses can also cause cancer in humans.

We conducted mortality studies of three cohorts of workers in poultry slaughtering and processing plants located in seven states in the US.[11—16] Workers in poultry slaughtering and processing plants have one of the highest human exposures to these viruses, and so, if these viruses cause cancer in humans, are an ideal group for investigation. The results from these studies[11—16] indicate that deaths from cancer at 11 different cancer sites including deaths from cancer of the trachea, bronchus and lung (henceforth referred to simply as lung cancer) occur in excess in poultry workers. However, because non-occupational factors and other

potentially carcinogenic occupational exposures were not investigated, it was not possible to determine the role of oncogenic poultry viruses. The other potentially carcinogenic exposures that occur in poultry plants include: (1) fumes containing polycyclic aromatic hydrocarbons (PAH), benzene and phthalates that are emitted from the wrapping machine[17-19]; (2) PAH emitted from the smokehouse during the smoking of poultry[20]; (3) heterocyclic amines emitted during the frying or cooking of poultry[21 22]; and (4) nitrosamines formed during the curing of poultry.[22-24] A nested case—control design would be appropriate for such investigations. However, before embarking on a full scale study of this type, we conducted a feasibility case—cohort study of a few of the excess cancers to determine if a large scale study would be worthwhile to establish the possible occupational exposures responsible. We report here the findings for lung cancer obtained in this pilot case—cohort study.

## METHODS

The source population was identified from the records of (1) the United Food and Commercial Workers (UFCW) Meatcutters' Union in Baltimore, Maryland (six poultry plants), (2) the UFCW Poultry Union in Marshall, Missouri (six poultry plants) and (3) the UFCW Union Pension Fund in Chicago, Illinois, covering 11 poultry plants in six states. The subjects consisted of 30 411 workers who were exposed to poultry through employment in these 23 poultry slaughtering and processing plants located in seven states (Maryland, Missouri, Alaska, Arkansas, Louisiana, Maine and Texas). In addition, a heterogeneous group of 16 408 non-poultry plant workers from nine states (Maryland, Florida, Illinois, Indiana, Massachusetts, New Jersey, Ohio, Pennsylvania and Texas) who were also members of the UFCW Baltimore union or other UFCW unions and worked in companies that handled seafood, soft drinks, cheese or oriental food or manufactured metal containers, etc, was also studied. The combined cohort of 46 819 poultry and non-poultry individuals worked anytime between 1 July 1949 and 31 December 1989, and were initially followed up from 1 July 1949 to 31 December 1989. Follow-up methods included retrieving information from the National Death Index, Pension Benefit Information, Inc., state Departments of Motor Vehicles or Vital Records, obituaries and/or the US Postal Service, personal contact by telephone and mail, and internet tracing methods.

Of the 46 819 individuals, 2915 had died by the end of 1989. The remaining 43 904 who were alive as of 1 January 1990 constitute the base population for the study reported here, and were followed-up from 1 January 1990 until the end of December 2003, using the methods described above. Since no new subjects were added after 1 January 1990, and all subjects lost to follow-up were assumed alive at the end of the study, this group of subjects alive as of 1 January 1990 was essentially a closed cohort. Cases consisted of 1218 subjects who had died of cancer at 11 different cancer sites, but for the present report were defined as all 552 deaths from lung cancer (ICD-9 162, and ICD-10 C34) that newly occurred in the base population between 1 January 1990 and 31 December 2003. The comparison group for the lung cancer cases was a subcohort that consisted of 1516 subjects randomly sampled from the base population, some of whom later died during the study period.

Because this was a feasibility study, exhaustive attempts were not made to identify study subjects or their next of kin. Since the addresses and phone numbers of study subjects in union records were not available for the pilot study, tracing methods consisted of simply looking up the location of the plant, company or union the study subject was associated with, and

calling all persons with the subject's name in a telephone directory for that location until the study subject was identified. For deceased subjects, we retrieved their death certificates, and used all names and addresses listed in the death certificate to identify the names and addresses of relatives using internet sources such as Public Eye/Public, http://records.com and http://ancestry.com. Once contact was made with the correct person, if the study subject was deceased, the next of kin was administered a questionnaire over the phone, to obtain information on the deceased study subject. Live study subjects in the subcohort (controls) were administered the questionnaire directly.

The questionnaire sought information on the usual demographic variables of race, gender, date of birth and date of death. A detailed list of questions (selected questions are shown in table 1) on occupations and industries under the following major headings were included: (1) occupational poultry-specific exposures; (2) mixed occupational poultry and meat and meat-related exposures; (3) working or living on a farm; (4) occupational exposure to seafood; (5) killing food animals other than poultry; (6) applying chemicals at work; and (7) working in occupations and industries outside the poultry and meat sectors. The risk associated with each job exposure was calculated for ever/never responses. All questions on specific occupations included dates and duration of employment. Among those with occupational exposures only, limited dose—response relationships were examined, categorised on <1—4 years versus 5 or more years of duration of exposure. There were also detailed non-occupational questions on lifestyle, medical history, diet, medication use, family history of medical conditions, radiation exposures, immunisations and miscellaneous, but these non-occupational exposures are not considered here.

To obtain information on the reliability of responses from proxies, the questionnaire was administered to a small subset of seven pairs consisting of a live control study subject and their next of kin.

Potential confounders abstracted from the telephone interview or death certificate included age, birth cohort, gender, ever smoking (yes, no) and union location. The main analyses consisted of logistic regression and Cox regression in which gender, age and tobacco smoking were adjusted for simultaneously. Adjusting additionally for birth cohort and union location did not change the main results, and these variables were not included in the final models for the main analyses. However, union location was included in secondary analyses.

Using the SAS PROC LOGISTIC procedure in SAS 9.1, logistic regression models were initially fit to the data. Because the control group was a random sample of the base population, the ORs obtained estimate the RR without the need for the rare disease assumption.[25] ORs and their associated 95% CIs were estimated independently for each job exposure. In the Cox regression analysis, HRs (rate ratios) were estimated using the SAS PHREG procedure. Subjects entered the study at the age attained on 1 January 1990 (time variable) and the failure time for formation of a risk set was the age at death of a lung cancer case. At failure time, a risk set was formed consisting of the case and all available controls at risk at that time. All failures were included, whether they occurred in the subcohort or not. A case outside the subcohort is not at risk until just before its failure and is therefore not included in earlier risk sets.

The protocols for both the original cohort study and this pilot case—cohort study were reviewed and approved by the Human Subjects Committee (Institutional Review Board) of the University of North Texas Health Science Center.

**Table 1** Poultry-associated occupational exposures: associations with lung cancer mortality, 1990—2003

| | Cases (n=125) | Controls (n=152) | Adjusted logistic regression ORs* OR (95% CI) | Adjusted Cox proportional HRs† HR (95% CI) |
|---|---|---|---|---|
| Poultry-specific exposures | | | | |
| Ever killed chickens/birds at work | 115 | 151 | 4.2 (1.2 to 14.7)‡ | 1.8 (1.0 to 3.3)‡ |
| Ever worked on a commercial poultry farm | 66 | 102 | 2.9 (0.9 to 9.1) | 1.6 (0.9 to 2.9) |
| Ever had direct contact with chicken/bird blood at work | 109 | 150 | 1.9 (1.0 to 3.8)‡ | 1.3 (0.9 to 2.0) |
| Ever worked catching live chickens/birds | 120 | 152 | 1.6 (0.6 to 4.2) | 1.2 (0.7 to 2.1) |
| Ever loaded and unloaded chickens/birds from trucks | 117 | 151 | 1.3 (0.5 to 3.8) | 1.5 (0.8 to 2.9) |
| Ever handled eggs of chicken/birds at work | 115 | 151 | 1.4 (0.6 to 2.9) | 1.2 (0.8 to 1.9) |
| Ever worked where poultry waste was used or handled | 62 | 102 | 0.8 (0.2 to 1.8) | 0.9 (0.5 to 1.6) |
| Ever spread chicken/bird waste as manure | 111 | 151 | 0.7 (0.2 to 3.0) | 1.0 (0.5 to 2.2) |
| Ever had a job related to cock fighting | 124 | 151 | 0.7 (0.0 to 137.0) | 0.4 (0.0 to 2.7) |
| Ever had contact with or handled unwrapped raw chicken/birds at work | 108 | 150 | 0.6 (0.3 to 1.3) | 0.8 (0.5 to 1.4) |
| Ever worked where poultry was deboned | 63 | 101 | 0.3 (0.1 to 0.8) | 0.4 (0.2 to 0.7) |
| Ever worked in a plant where raw poultry was processed and packed in plastic | 65 | 103 | 0.3 (0.1 to 0.8) | 0.4 (0.2 to 0.7) |
| Mixed poultry and meat exposures | | | | |
| Ever worked in a stockyard where animals were held before slaughter | 60 | 103 | 7.4 (0.8 to 64.4) | 1.9 (0.9 to 4.0) |
| Ever worked in the meat department of a grocery store/supermarket handling raw meat | 70 | 104 | 3.1 (0.3 to 35.4) | 1.6 (0.5 to 4.4) |
| Ever worked in a deli department | 70 | 104 | — | 1.4 (0.3 to 6.0) |
| Ever worked as a butcher (killing animals) | 120 | 150 | 2.7 (0.4 to 18.8) | 0.8 (0.3 to 2.3) |
| Ever worked as a meat cutter (not killing animals) | 116 | 150 | 0.7 (0.3 to 1.7) | 0.7 (0.4 to 1.2) |
| Other potentially carcinogenic exposures in poultry plants | | | | |
| Ever involved in smoking meat at work | 115 | 149 | 1.2 (0.1 to 16.2) | 0.8 (0.2 to 3.2) |
| Ever involved in curing meat | 114 | 149 | 0.9 (0.1 to 6.3) | 0.6 (0.2 to 1.8) |
| Ever worked in a plant where poultry were partly or wholly cooked | 62 | 103 | 0.6 (0.2 to 1.5) | 0.8 (0.4 to 1.4) |
| Ever complained of fumes or smoke while wrapping chickens/meat at work | 113 | 149 | 0.5 (0.1 to 1.4) | 0.6 (0.3 to 1.3) |
| Non-poultry occupational exposures | | | | |
| Ever used chemicals to kill moulds | 113 | 147 | 7.3 (1.1 to 50.0)‡ | 3.2 (1.3 to 8.0)‡ |
| Ever worked in a chemical plant | 115 | 148 | 5.2 (0.5 to 52.2) | 2.6 (1.1 to 6.5)‡ |
| Ever applied chemicals to fences at work | 113 | 147 | 3.4 (0.3 to 36.0) | 1.5 (0.5 to 4.1) |
| Ever sprayed or applied insecticides at work | 114 | 146 | 3.3 (0.5 to 20.9) | 0.9 (0.4 to 2.0) |
| Ever worked where exposure to petrol, kerosene or heating fuels occurred | 110 | 148 | 3.1 (0.9 to 11.0) | 1.6 (0.9 to 2.9) |
| Ever worked in a textile plant | 114 | 148 | 2.8 (0.5 to 16.1) | 2.1 (0.8 to 5.1) |
| Ever worked in forestry | 116 | 149 | 2.5 (0.2 to 27.5) | 0.8 (0.3 to 1.9) |
| Ever worked where plastics or plastic products were manufactured | 109 | 148 | 2.1 (0.4 to 10.0) | 3.2 (1.4 to 7.6)‡ |
| Ever worked in a petrol station or petrol storage facility | 113 | 148 | 2.0 (0.7 to 5.8) | 1.1 (0.7 to 2.0) |
| Ever worked where asbestos was handled | 109 | 147 | 2.0 (0.4 to 9.0) | 1.6 (0.6 to 4.1) |
| Ever sprayed weed killer on a farm | 113 | 147 | 1.6 (0.4 to 6.7) | 0.9 (0.4 to 1.8) |

Age- and gender-adjusted OR for ever smoked tobacco 7.1 (95% CI 2.8 to 18.0).
Age- and gender-adjusted HR for ever smoked tobacco 3.7 (95% CI 1.8 to 7.4).
*ORs were adjusted for smoking, gender and age by the logistic regression method.
†HRs were adjusted for smoking, gender and age by the Cox proportional hazard method.
‡Significant at the 95% CI.

## RESULTS

Altogether, 374 of 1218 cases (31%) of cancer at any of the 11 cancer sites of interest were traced within the short time available for the pilot study, and a telephone interview was successfully obtained for 300 of those traced (80%), 125 of whom had lung cancer. Similarly, 214 of 1516 subjects (14%) in the subcohort were traced, and interviews were obtained for 152 (71%), two of whom were counted as both a case and a control in the logistic regression analysis. We report here on the 125 lung cancer cases that occurred in the base population between 1 January 1990 and 31 December 2003, and the 152 control subjects in the subcohort. Overall, 77 of the 125 lung cancer cases, and 115 of the 152 controls worked in poultry plants, and thus had potential exposure to the oncogenic poultry viruses. The results obtained when the analysis was restricted to these 192 subjects were very similar to those obtained for the 277 subjects, and are therefore not shown.

Comparison of demographic variables for the 552 lung cancer cases that occurred in the base population between 1 January 1990 and 31 December 2003 with those for the 125 subjects who died from lung cancer showed that the distributions were unremarkable (table 2). Information on race was not available for live controls selected but not interviewed. Importantly, response rate was not significantly related to exposure status (percentage with poultry exposure), since among the lung cancer cases, the percentage of poultry workers was 60% for those interviewed versus 53% for all cases; and among controls it was 80% for interviewed subjects versus 69% for all controls (table 2).

A comparison of the responses of the seven live control subjects and those of their next of kin showed that of the 245 direct questions with a dichotomous option in the questionnaire (Yes/No), agreement between the two was 100% for 44% of the questions, 80—99% for 30% of the questions, 60—79% for 18% of the questions and <60% for 8% of the questions.

### Occupational exposure to poultry
The age and gender adjusted OR for ever smoked tobacco was 7.1 (95% CI 2.8 to 18.0) and the HR was 3.7 (95% CI 1.8 to 7.4). Table 1 gives a detailed summary of the main results for age-,

**Table 2** Demographic and baseline characteristics of cases and controls

| | Lung cancer cases | | Controls | |
|---|---|---|---|---|
| | Total (n = 552) | Interviewed (n = 125) | Total (n = 1516) | Interviewed (n = 152) |
| **Race** | | | | |
| White | 394 (74%) | 104 (83%) | NA | 108 (80%) |
| Non-white | 141 (26%) | 21 (17%) | NA | 27 (20%) |
| Unknown | 17 | 0 | NA | 19 |
| Total | 552 | 125 | 1516 | 152 |
| **Gender** | | | | |
| Female | 245 (45%) | 48 (38%) | 768 (51%) | 82 (58%) |
| Male | 304 (55%) | 77 (62%) | 724 (49%) | 60 (42%) |
| Unknown | 3 | 0 | 24 | 10 |
| Total | 552 | 125 | 1516 | 152 |
| **Age** | | | | |
| ≤50 years | 99 (19%) | 17 (14%) | 570 (42%) | 47 (34%) |
| >50 years | 429 (81%) | 108 (86%) | 776 (58%) | 93 (66%) |
| Unknown | 24 | 0 | 170 | 12 |
| Total | 552 | 125 | 1516 | 152 |
| **Type of worker** | | | | |
| Poultry | 290 (53%) | 75 (60%) | 792 (69%) | 111 (80%) |
| Non-poultry | 262 (47%) | 50 (40%) | 363 (31%) | 27 (20%) |
| Unknown | 0 | 0 | 361 | 14 |
| Total | 552 | 125 | 1516 | 152 |
| **Smoking status** | | | | |
| Ever | NA | 110 (92%) | NA | 96 (65%) |
| Never | NA | 9 (8%) | NA | 51 (35%) |
| Unknown | NA | 6 | NA | 5 |
| Total | 552 | 125 | 1516 | 152 |
| **Location of source union** | | | | |
| Chicago, Illinois | 350 (63%) | 98 (78%) | 925 (61%) | 113 (75%) |
| Marshall, Missouri | 69 (13%) | 18 (15%) | 308 (20%) | 36 (24%) |
| Baltimore, Maryland | 133 (24%) | 9 (7%) | 283 (19%) | 2 (1%) |
| Unknown | 0 | 0 | 0 | 1 |
| Total | 552 | 125 | 1516 | 152 |

gender- and smoking-adjusted lung cancer mortality associated with occupational activities or conditions with the highest risks in the study (whether statistically significant or not), including those known to be associated with lung cancer.[26]

Statistically significantly elevated risks related to poultry and meat were recorded for (1) subjects who killed chickens or birds at work (OR 4.2, 95% CI 1.2 to 14.7; HR 1.8, 95% CI 1.0 to 3.3) and (2) subjects who ever had contact with chicken or bird blood at work (OR 1.9, 95% CI 1.0 to 3.8; HR 1.3, 95% CI 0.9 to 2.0). Occupational exposure to eggs seems to be associated with only a slightly increased risk of lung cancer, if at all. Significantly depressed risks were observed for ever working in a plant where raw poultry was processed and packed in plastic bags and for ever working where poultry was deboned.

No significant association was observed for working on any type of animal or crop farm. The risk for working on a commercial poultry farm was elevated and almost significant.

### Mixed poultry and meat exposures
The risks associated with working in a stockyard, working in the meat or deli department of a grocery store and working as a butcher (killing animals) are elevated but not statistically significant (table 1).

### Other potentially carcinogenic exposures in poultry slaughtering/processing plants
Of the four other potentially carcinogenic exposures which occur in poultry slaughtering and processing plants that are

associated with (1) smoking of poultry, (2) curing of poultry, (3) frying/cooking of poultry, and (4) use of the wrapping machine, the risks for surrogates of these exposures were not significantly elevated (table 1).

### Non-poultry occupational exposures
Occupational use of chemicals to kill mould, working in a chemical plant and working where plastic or plastic products are manufactured, were all associated with significantly elevated risks of lung cancer (tables 1 and 3). Risks associated with several other occupational exposures that are known risk factors for lung cancer were also elevated, but the ORs or HRs were not statistically significant (table 1).

### Results obtained after controlling for additionally identified potential risk factors
For each major risk factor identified in table 1, we attempted whenever possible to obtain a risk estimate after adjusting for other identified possible risk factors (tables 3–5). Insufficient sample size limited the number of factors that could be adjusted for simultaneously.

### Risk associated with killing chickens, catching live chickens at work and direct contact with chicken blood
The risks associated with killing chickens and to a lesser extent catching live chickens and contact with chicken blood appear to persist even after controlling for tobacco smoking, age, union

**Table 3** Lung cancer risk for selected occupational exposures, adjusted additionally for history of stockyard work and union location, 1990–2003

| | HRs (95% CI) |
|---|---|
| Occupational exposures | |
| Ever killed chickens at work | 2.2 (1.0 to 4.9) |
| Ever had direct contact with chicken blood at work | 1.4 (0.7 to 2.7) |
| Ever caught live chickens at work | 1.7 (0.8 to 3.5) |

*Adjusted for smoking, age, gender, history of stockyard work and union location.

**Table 5** Adjusted lung cancer mortality associated with ever using wrapping machines to wrap meat at work by gender, 1990–2003

| | Females HR (95% CI)* | Males HR (95% CI)* |
|---|---|---|
| Ever used wrapping machines to wrap meat at work | | |
| Adjusted additionally for history of working in a deli department | 1.7 (0.6 to 4.5) | 0.3 (0.1 to 1.5) |
| Adjusted additionally for history of working in a meat department | 1.6 (0.6 to 4.2) | 0.3 (0.1 to 1.5) |

*Adjusted for smoking, age and union location.

location and history of working in a stockyard (table 3), and after controlling for the use of chemicals to kill mould at work (not shown).

### Risk associated with working in a stockyard

Working in a stockyard appears to be associated with an increased risk of lung cancer even after controlling jointly for tobacco smoking, age, gender and one of the following occupational exposures: killing chickens at work, catching live birds or direct contact with chicken blood at work (tables 1 and 4(1)). The risk associated with working in a stockyard was also independent of the risk associated with eating various types of meat (not shown) and is not affected by tobacco smoking status (table 4(2)).

### Risk associated with exposure to a wrapping machine

Exposure to wrapping machine fumes that contain carcinogenic PAH, benzene and phthalates has been shown to be associated with lung cancer risk[17–19 27] in poultry and meat plants and in the deli or meat departments of supermarkets/grocery stores. In the deli and meat departments, wrapping is principally carried out by women, and fumes emitted from the wrapping machine are the only potentially carcinogenic exposure apart from exposure to oncogenic viruses. It is seen in table 1 that the risk associated with working in the meat or deli department of a supermarket appears elevated, although not statistically significant. In table 5, it is similarly seen that the risk for ever use of the wrapping machine while adjusting for age, smoking, union location and work in the deli or meat department of a supermarket was elevated for women but not for men. Also, the risk associated with working in the meat or deli department of a supermarket appears elevated after adjusting for tobacco smoking and each of the major risk factors found in this study (not shown).

In the analysis by duration of exposure, it was possible to obtain results for only some of the identified possible risk factors of interest. For the poultry-related exposures, in nearly all instances, exposure for 5 or more years was associated with

**Table 4** Lung cancer risk for working in stockyards, adjusted for tobacco smoking, age, gender, union location and selected occupational exposures

| | HRs (95% CI) |
|---|---|
| (1) Working in stockyards | |
| Adjusted additionally for ever killed chickens/birds at work | 1.6 (0.7 to 3.6)* |
| Adjusted additionally for ever caught live chickens at work | 1.8 (0.8 to 4.2)* |
| Adjusted additionally for ever had direct contact with chicken blood at work | 1.7 (0.7 to 3.9)* |
| (2) Working in stockyards | |
| Adjusted for age among ever smokers | 1.8 (0.8 to 4.2)† |
| Adjusted for age among never smokers | 2.0 (0.1 to 36.9)† |

*Adjusted for age, smoking, gender and union location.
†Adjusted for age, smoking and gender.

higher ORs or higher HRs than exposure for <5 years (data not shown). However, the value of this exercise was limited by the lack of statistical power.

The study also provided valuable information on the prevalence of exposure to the main carcinogenic agents in the poultry industry: (1) high exposure to oncogenic viruses captured by (a) working in a stockyard, (b) slaughtering of poultry, (c) working on a commercial poultry farm, (d) catching live chickens at work, (e) working as a butcher, and (f) contact with chicken blood at work; 7%, 7%, 21%, 14%, 3% and 38% of workers, respectively, were engaged in these activities; (2) exposure to fumes from the wrapping machine, captured by (a) working in the deli department of a supermarket, and (b) working in the meat department of a supermarket; 3%, 4% and 12% of workers, respectively, complained of fumes from a wrapping machine; (3) exposure to smoke in the smokehouse captured by (a) working in a plant where poultry was smoked, and (b) involvement in smoking meat at work; 3% and 2% of workers, respectively, were affected; (4) curing of poultry captured by ever being involved in curing meat at work; 3% of workers were exposed; and (5) exposure to heterocyclic amines and PAH during frying of poultry captured by working in a place where poultry was partly or wholly cooked; 37% of workers were exposed. These prevalence estimates will be useful in power calculations for any proposed large scale study, bearing in mind that some of the questions should be modified in a new questionnaire.

In addition to tobacco smoking, this study also confirmed known established non-occupational risk factors for lung cancer (not shown), such as ingestion of various types of meat, and their methods of preparation, radiation, etc.[26]

### DISCUSSION

The study reported here is important despite its preliminary nature, because it includes a group with the highest human exposure to these viruses. Furthermore, the cohorts studied are the only ones to have provided information on cause-specific mortality in poultry workers or subjects exposed to poultry. We selected for study *all* cases that occurred in the cohort, and the control group was a *random* sample of the cohort. Thus there should be minimal selection bias in how study subjects were initially recruited into the study. Also, once traced, the proportion of responders who provided an interview was quite high (80% in cases and 71% in controls). Furthermore, interviewed subjects were similar to the base population regarding demographic variables and proportion exposed to poultry.

Similarly, the limited comparison of responses from seven live subjects with those of their next of kin indicates that responses given by the proxies in this study were reliable for the vast majority of questions, with good to excellent agreement for over 90% of the questions, and hence response bias between live control subjects and the next of kin of deceased cases and controls is not likely to have been serious.

The diagnosis of lung cancer was based on underlying cause of death as coded in the death certificate. The confirmation and detection rates for cancer of the trachea, bronchus and lung coded as underlying cause are very high (94% and 95%, respectively),[28] and thus misclassification of the disease is likely to be insignificant.

A major advantage is that subjects in the study all belong to the same UFCW International Union, and constitute a very homogeneous group by virtue of their being in the lowest socioeconomic stratum, with salaries of poultry workers at minimum wage levels. Hence, factors that may be confounding across different socioeconomic groups are unlikely to be operative here.

### Exposure to oncogenic viruses

For occupational poultry exposures, the highest RRs were observed for workers who had contact with live poultry and killed poultry at work, had contact chicken/bird blood and worked on commercial poultry farms. These relationships also persisted in the analysis restricted to poultry workers only (not shown) and after controlling for important occupational risk factors identified in this study. Similarly, working in a stockyard where exposure to live animals occurs, was associated with an apparent increased risk of lung cancer, even after controlling for occupational risk factors. These activities are believed to be associated with high exposure to zoonotic microbial agents, including oncogenic poultry, cattle, pig and sheep viruses. We suspect, therefore, that the high risks associated with these jobs probably result from exposure to the oncogenic viruses of food animals in general, including those of poultry (ALSV, REV and MDV), since no other known potentially carcinogenic occupational exposures are associated with these activities. This finding is consistent with the relationship observed between lung cancer risk and exposure to live cattle, pigs and sheep in another study, where one of the highest risks reported (between six and sevenfold) was also for working in a stockyard and slaughtering animals, even after adjusting for tobacco smoking.[29] It is also consistent with the increased lung cancer risk associated with freshly slaughtered pigs or exposure to other live animals.[30–33]

### Exposure to fumes during wrapping

The risk for working in the deli department, with potential exposure to fumes from the 'hot wire' wrapping machine, was slightly elevated and consistent with the elevated risk for working in the meat department of a supermarket (table 1). As mentioned above, the increased risks associated with both these activities appeared to hold after controlling for activities associated with high oncogenic virus exposure (table 6), thus indicating that additional risk is associated with these exposures beyond exposure to oncogenic viruses. The meat departments of supermarkets consist of the deli department where workers (mostly women) wrap and sell *cooked* meat, and the meat room where meatcutters (usually men) cut *raw* meat, working side-by-side in the same room with meatwrappers (women) who wrap the freshly cut *raw* meat. Thus, wrapping meat is the primary, if not the only, activity carried out by women in the deli section and meat room. The observation that the risk of lung cancer was increased approximately twofold for women wrapping meat and poultry in the deli or meat department of supermarkets, while it was not for men who were mainly cutting meat (table 5), suggests that wrapping meat and poultry and exposure to fumes from the wrapping machine are also possibly related to the excess lung cancer occurrence. Prior to 1976, exposure to these fumes was significant and caused meat wrapper's asthma and chronic bronchitis in supermarket wrappers (typically women). These fumes contain PAH, benzene and phthalates which are carcinogenic, and the irritant hydrogen chloride.[17–19] After 1975, with modification of the wrapping machines, exposure to such fumes was markedly reduced and was no longer an acute problem. An excess risk of lung cancer among women in supermarkets has been previously reported in our mortality study of the Baltimore cohort of workers exposed to cattle, pigs, sheep and poultry, and the risk was also shown to decrease after 1975.[27] The only other study to investigate these fumes also reported an elevated risk of lung cancer for this exposure.[34] Unexpectedly, the risk obtained for *complaining* about fumes and smoke at work from the wrapping machine was 0.5 or 0.6. A possible reason for this discrepancy is that, as noted earlier, proxies did not seem able to provide reliable information on whether subjects who used the machine were actually exposed to fumes or had trouble with the fumes, since complaining of fumes during wrapping was noted to be one of the few questions for which there was poor agreement (40%) between the responses of the live workers and their next of kin, while the agreement for working in the deli or meat department was 100%.

With regard to the other potentially carcinogenic occupational exposures in poultry plants associated with frying, curing and smoking of poultry,[35–38] the study did not have sufficient power to adequately assess these exposures, although smoking of poultry seems to be associated with some increased risk, while curing is not.

It should be pointed out that the risk estimates given in this study were obtained by comparing subjects exposed to a given occupational poultry-related task with those not exposed to that task who were nevertheless exposed to poultry from performing other poultry-related tasks. Thus, for each assessment of risk for a given poultry task, the comparison group is not truly unexposed. Hence, the risk estimates given in this study for poultry-associated tasks or exposures are conservative.

For non-poultry occupational exposures, an increased risk of lung cancer was found for the following exposures: (1) use of chemicals to kill moulds (eg, chlorophenols, captafol); (2) working in a chemical plant (eg, vinyl chloride); (3) applying chemicals to fences (eg, chlorophenols); (4) spraying and applying of insecticides and weed killers (eg, chlordane, heptachlor, DDT, dichlorvos and phenoxyacetic acid herbicides); (5) work with exposure to petrol (eg, in a petrol station or storage facility, diesel fumes, benzene, etc); (6) asbestos; and (7) plastic manufacturing (eg, vinyl chloride). These findings are consistent with the those in the literature as these activities are all known to involve exposure to established carcinogens in animals or humans.[39 40]

The choice of presenting risk as an RR or a rate ratio, as in the logistic and Cox regression, respectively, is somewhat arbitrary, and because of this we chose to present both. The point estimates obtained by the Cox regression were consistently more conservative and precise than those obtained by logistic regression. It has been reported that the agreement between OR and HR estimates is the product of the length of follow-up, the frequency of the outcome, and the strength of the association. Thus the greater the risk, the more divergent the two estimates,[41] as is suggested in table 1.

In summary, these findings should be interpreted with caution, bearing in mind that this is a feasibility study. However, the study successfully achieved its objectives. It showed that a full scale case—cohort study of cancers occurring in excess in our poultry cohorts can be conducted without serious selection

or response bias, and that valid results can be obtained. In spite of its limitations, especially the lack of statistical power to adequately control for confounding factors other than those examined, the study confirmed established associations and also showed that the workers at highest risk of developing occupationally-induced lung cancer in the poultry industry are among those who have the highest exposure to poultry and other food animal oncogenic viruses. This finding may have important implications for the general population which is also exposed to these viruses, and needs to be adequately investigated.

## REFERENCES

1. **Saif YM,** John Barnes H, Fadly AM, et al. Diseases of Poultry. Ames, IA: Iowa State Press, 2003.
2. **Johnson ES.** Poultry oncogenic retroviruses and humans. Cancer Detect Prev 1994;**18**:9—30.
3. **Tsang SX,** Switzer WM, Shanmugam V, et al. Evidence of avian leucosis virus subgroup E and endogenous avian virus in measles and mumps vaccines derived from chicken cells: investigation of transmission to vaccine recipients. J Virol 1999;**73**:5843—51.
4. **Pham TD,** Spencer JL, Johnson ES. Detection of avian leukosis virus in albumen of chicken eggs using reverse transcription polymerase chain reaction. J Virol Methods 1999;**78**:1—11.
5. **Pham TD,** Spencer JL, Traina-Dorge VL, et al. Detection of exogenous and endogenous avian leukosis virus in commercial chicken eggs using reverse transcription and polymerase chain reaction assay. Avian Pathol 1999;**28**:385—92.
6. **Johnson ES,** Overby L, Philpot R. Detection of antibodies to avian leukosis/sarcoma viruses (ALSV) and reticuloendotheliosis viruses (REV) in humans, by Western blot assay. Cancer Detect Prev 1995a;**19**:472—86.
7. **Johnson ES,** Nicholson LG, Durack DT. Detection of antibodies to avian leukosis/sarcoma viruses (ALSV) and reticuloendotheliosis viruses (REV) in humans, by enzyme-linked immunosorbent assay (ELISA). Cancer Detect Prev 1995b;**19**:394—404.
8. **Choudat D,** Dambrine G, Delemotte B, et al. Occupational exposure to poultry and prevalence of antibodies against Marek's disease virus and avian leukosis retroviruses. Occup Environ Med 1996;**53**:403—10.
9. **Hussain AI,** Shanmugam V, Switzer WM, et al. Lack of evidence of endogenous avian leukosis virus and endogenous avian retrovirus transmission to measles mumps rubella vaccine recipients. Emerg Infect Dis 2001;**7**:66—72.
10. **Hussain AI,** Johnson JA, da Silva-Freire M, et al. Identification and characterization of avian retroviruses in chicken embryo-derived yellow fever vaccibes. Investigation of transmission to vaccine recipients. J Virol 2003;**77**:1105—11.
11. **Johnson ES,** Fischman HR, Matonski GM, et al. Cancer occurrence in women in the meat industry. Br J Ind Med 1986;**43**:597—604.
12. **Johnson ES,** Shorter C, Rider B, et al. Mortality from cancer and other diseases in poultry slaughtering/processing plants. Int J Epidemiol 1997;**26**:1142—9.
13. **Netto GF,** Johnson ES. Mortality in workers in poultry slaughtering/processing plants: the Missouri poultry cohort study. Occup Environ Med 2003;**60**:784—8.
14. **Johnson ES,** Zhou Y, Yau CL, et al. Mortality from malignant diseases—update of the Baltimore union poultry cohort. Cancer Causes Control 2009;**21**:215—21.
15. **Johnson ES,** Ndetan H, Zhou Y, et al. Update of cancer and non-cancer mortality in the Missouri poultry cohort. Am J Ind Med 2011;**54**:49—54.
16. **Johnson ES,** Ndetan H, Lo K-M. Cancer mortality in poultry slaughtering/processing plant workers belonging to a union pension fund. Environ Res 2010;**110**:588—94.
17. **Pauli G,** Bessot JC, Kopferschmitt MC, et al. Meat wrapper's asthma: identification of the causal agent. Clin Allergy 1980;**10**:263—9.
18. **Vandervort R,** Brooks SM. Polyvinyl chloride film thermal decomposition products as an occupational illness. I. Environmental exposures and toxicology. J Occup Med 1977;**19**:188—91.
19. **Johnson ES,** Halabi S, Netto G, et al. Detection of low level benzene exposure in supermarket wrappers by urinary muconic acid. Biomarkers 1999;**4**:106—17.
20. **Nordholm L,** Espensen I, Jensen HS, et al. Polycyclic aromatic hydrocarbons in smokehouses. Scand J Work Environ Health 1986;**12**:614—18.
21. **Vainiotalo S,** Matveinen K. Cooking fumes as a hygienic problem in the food and catering industries. Am Ind Hyg Assoc J 1993;**54**:376—82.
22. **Jakszyn P,** Agudo A, Ibanez R, et al. Development of a food database of nitrosamines, heterocyclic amines, and polycyclic aromatic hydrocarbons. J Nutr 2004;**134**:2011—14.
23. **Sen NP,** Miles WF, Donaldson B, et al. Formation of nitrosamines in meat curing mixture. Nature 1973;**45**:104—5.
24. **Sen NP,** Donaldson B, Charbonneau C, et al. Effect of additives on the formation of nitrosamines in meat curing mixtures containing spices and nitrite. J Agric Food Chem 1974;**22**:1125—30.
25. **Rothman KJ,** Greenland S, eds. Modern Epidemiology. Philadelphia, PA: Lippincott & Raven, 1998.
26. **Adami H-O,** Hunter D, Trichopoulos D, eds. Textbook of Cancer Epidemiology. New York: Oxford University Press, 2002.
27. **Johnson ES.** Cancer mortality among workers in the meat department of supermarkets. Occup Environ Med 1994;**51**:541—7.
28. **Percy C,** Stanek E 3rd, Gloeckler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health 1981;**71**:242—50.
29. **Johnson ES.** Nested case-control study of lung cancer in the meat industry. J Natl Cancer Inst 1991;**83**:1337—9.
30. **Guberan E,** Usel M, Raymond L, et al. Mortality and incidence of cancer among a cohort of self-employed butchers from Geneva and their wives. Br J Ind Med 1993;**50**:1008—16.
31. **Coggon D,** Pannett B, Pippard EC, et al. Lung cancer in the meat industry. Br J Ind Med 1989;**46**:188—91.
32. **McLean D,** Cheng S, 't Mannetje A, et al. Mortality and cancer incidence in New Zealand meatworkers. Occup Environ Med 2004;**61**:541—7.
33. **Durusoy R,** Bofetta P, Mannetje A, et al. Lung cancer risk and occupational exposure to meat and live animals. Int J Cancer 2006;**118**:2543—7.
34. **Fritschi L,** Fenwick S, Bulsara M. Mortality and cancer incidence in a cohort of meatworkers. Occup Environ Med 2003;**60**:E4.
35. **Sinha R,** Kulldorff M, Curtin J, et al. Fried well-done red meat and risk of lung cancer in women (United States). Cancer Causes Control 1998;**9**:621—30.
36. **Deneo-Pellegrini H,** De Stefani E, Ronco A, et al. Meat consumption and risk of lung cancer; a case-control study from Uruguay. Lung Cancer 1996;**14**:195—205.
37. **Lam TK,** Cross AJ, Consonni D, et al. Intakes of red meat, processed meat, and meat mutagens increase lung cancer risk. Cancer Res 2009;**69**:932—9.
38. **Alavanja MC,** Field RW, Sinha R, et al. Lung cancer risk and red meat consumption among Iowan women. Lung Cancer 2001;**34**:37—46.
39. **International Agency for Research on Cancer.** Occupational exposures in insecticide application, and some pesticides. IARC Monogr Eval Carcinog Risks Hum 1991;**53**:5—586.
40. **International Agency for Research on Cancer.** Overall evaluations of carcinogenicity: an updating of IARC Monographs volumes 1 to 42. IARC Monogr Eval Carcinog Risks Hum Suppl 1987;**7**:1—440.
41. **Symons MJ,** Moore DT. Hazard rate ratio and prospective epidemiological studies. J Clin Epidemiol 2002;**55**:893—9.

# A case–cohort study of lung cancer in poultry and control workers: occupational findings

Martha Felini, Nikiconia Preacely, Nihita Shah, et al.

Updated information and services can be found at:

http://oem.bmj.com/content/69/3/191.full.html

*These include:*

| | |
|---|---|
| **References** | This article cites 38 articles, 10 of which can be accessed free at:<br>http://oem.bmj.com/content/69/3/191.full.html#ref-list-1 |
| **Email alerting service** | Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article. |

| | |
|---|---|
| **Topic Collections** | Articles on similar topics can be found in the following collections<br><br>Other exposures (526 articles) |

**Notes**

To request permissions go to:

http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:

http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:

http://group.bmj.com/subscribe/