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Poultry workers are at a great risk of exposure to potentially harmful transmissible agents which can cause cancer in poultry; yet there are few epidemiological studies that examine the association of occupation and illnesses experienced by these workers. Workers in poultry slaughtering and processing plants are well suited to investigate the effect of exposure to poultry oncogenic agents because they have one of the highest human exposures to these agents. Additionally, there is a need to investigate the effect of exposure to carcinogenic chemicals formed during the packaging and preparation of poultry. The preparations of poultry via smoking, and frying are additional exposures that release carcinogens which may be involved in lung cancer risk among poultry workers. Union records from several unions belonging to the United Food & Commercial Workers International Union for the years 1949-1989 were used to identify a cohort of workers once employed in poultry slaughtering and processing plants. The current research investigated whether certain occupational exposures were associated with lung cancer mortality among these workers. The research employed a case cohort design that provided individual level occupational and lifestyle data for workers who died with lung cancer between 1990 and 2003 compared to a sub-cohort of individuals randomly sampled from the entire cohort.

It is anticipated that by identifying potentially harmful exposures in this industry, future research may focus on developing methods to alleviate them among poultry

workers. The results of this study will provide public health professionals and the poultry industry with new information on the occupational exposures not previously explored in relation to lung cancer mortality among poultry slaughtering/processing plant workers.

LUNG CANCER RISK AMONG WORKERS IN POULTRY SLAUGHTERING AND PROCESSING PLANTS: A PILOT STUDY

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CHAPTER 1

INTRODUCTION

Statement of the Problem

Many dangerous exposures that impact industrial illnesses and diseases similarly affect the general population. Members of the workforce, however, tend to be better suited to investigate certain associations between exposures and diseases because (a) the study population is usually well defined; (b) good records are available to determine exposed from unexposed; (c) exposure information is available at the individual level; (d) information is recorded on demographic variables; (e) date of first exposure is available, therefore latency is easier to investigate, and changes that have occurred in exposures over time; (f) better exposure gradient is available from non-exposed to extremely high exposures; and (g) workers have prolonged and consistent contact with the health hazard. The scope of occupational health issues is broad and there is a need for industry specific research that examines possible exposure-related morbidity and mortality.

Occupational epidemiological studies are important to identify risk factors to occupational diseases. Possible carcinogenic exposures in the poultry industry include a host of microbial, chemical, and other potentially dangerous agents. Exposure to occupational hazards in meat industries which slaughter and process pork, beef, lamb, and other livestock animals are similar to the occupational exposures of the poultry industry. An increased risk of lung cancer has been reported in several studies in the meat industry. Several studies have consistently shown excesses of lung cancer among meat industry workers (Boffetta et al., 2000; Coggon, Pannett, Pippard, & Winter, 1989; Fox, Lynge, & Malker, 1982; Griffith, 1982; Guberan, Usel, Raymond, & Fioretta, 1993; Jöckel, Ahrens, Jahn, Pohlabeln, & Bolm-Audorff, 2004; Johnson, 1991, 1994a; Johnson, Dalmas, Noss, & Matanoski, 1995; Johnson, Fischman, Matanoski, & Diamond, 1986a, 1986b; Kristensen & Lynge, 1993; Lynge, Andersen, & Kristensen, 1983; McLean, Cheng, t Mannetje, Woodward, & Pearce, 2004; Reif, Pearce, & Fraser, 1989). However there is no strong evidence in the literature of precise etiologic factors. A few studies of the meat industry (Besson, Banks, & Boffetta, 2006; Coggon & Wield, 1995; Gustavsson, Fellenius, & Hogstedt, 1987; Johnson, Shorter, Rider, & Jiles, 1997; Milham, 1982) found no risk of lung cancer associated with occupational exposures. Although previous research (Johnson, Dalmas, Noss, & Matanoski, 1995)has identified possible hazardous exposures in the meat industry, no study has comprehensively explored the occupational risk of lung cancer in the poultry industry.

Purpose

Employees of poultry slaughtering/processing plants constitute one of the lowest paid groups of workers in the United States and they typically belong to the lowest socioeconomic stratum (Quandt et al., 2006). As a result, they experience the worst health outcomes due to host of factors related to poverty including poor work conditions, lack of health insurance, and lack of access to quality health care. The current study investigates lung cancer mortality, after controlling for confounders, in three cohorts of workers who were members of any one of several local unions belonging to the United

Food & Commercial Workers International Union (UFCW) which drew their membership from geographically diverse areas of the United States. The base population included subject who were employed in poultry slaughtering and processing plants as well as a comparison group from fish plants, canning/bottling, or dairy industries. Poultry slaughtering and processing plants from the cohort will be examined separately to ascertain poultry industry specific exposure information.

Research Objectives

Objective 1: To identify the specific occupational task exposures within the poultry industry that can explain the excess risk of lung cancer mortality among poultry workers.

This study objective was accomplished by conducting a series of univatiate, bivariate and multivariable analyses of occupational task exposures in the poultry industry hypothesized to be associated with excess lung cancer mortality. Confounding and effect measure modification were assessed using Mantel-Haenszel stratified analyses. Unconditional logistic regression models were used to predict the probability of lung cancer mortality based upon occupational task exposures in the poultry industry. Independent variables that were important predictors of occupational task related exposures on lung cancer mortality were retained in the final models.

Research Question 1A: What is the risk of lung cancer mortality among workers exposed to transmissible agents?

Research Question 1B: What is the risk of lung cancer mortality among workers exposed to nitrosamines formed during the curing of poultry?

Research Question 1C: What is the relationship between lung cancer mortality among workers exposed to carcinogenic smokehouse emissions?

Research Question 1D: What is the relationship between lung cancer mortality among workers exposed to fumes emitted from the thermal decomposition of plastic during the wrapping and labeling of poultry products?

Objective 2: To investigate the occurrence of lung cancer mortality according to places of work that handled poultry.

This study objective was accomplished by evaluating places of employment that handled poultry association with lung cancer mortality. Logistic regression models were used to calculate odds ratios and control for major confounding factors, tobacco smoking and time of employment.

Research Question 2A: Which places of employment in the poultry industry continue to have the elevated risks of lung cancer mortality after controlling for major confounding factors?

Delimitations

The current study had a few delimitations. The cohort was restricted to union workers belonging to the UFCW between July 1949 and December 1989. Only lung cancer deaths reported from January 1, 1990 - December 31, 2003 were included in the study to reduce possible information bias from the respondents. Lung cancer was ascertained from the cause of death listed in the National Death Index using International Classification of Diseases 9th and 10th revisions. Only proxies and controls with telephones were surveyed in for the study.

Assumptions

The following were made for the purposes of this study:

- The cohort studied was representative of US poultry workers.
- All lung cancer deaths occurring in the cohort were identified.
- Next of kin proxies' responses were accurate and complete.

Conceptual Definitions

Case. A deceased member of the cohort with lung cancer (ICD 162, C33 or C34) reported as the cause of death.

Control. A member of the sub-cohort defined as a random sample of the cohort.

Transmissible agents. Prions, viruses, bacteria, protozoa, etc. that are known to cause malignant and non-malignant disease in animals (Johnson, 2005).

Marek's disease virus. A highly oncogenic alpha herpes virus that induces T-cell lymphomas in poultry (Petherbridge et al., 2004).

Poultry oncogenic retroviruses. Groups of either avian leukosis and sarcoma viruses(ALSV), reticuloendotheliosis viruses (REV) which are highly prevalent in chickens and turkeys and naturally cause tumors in them (Johnson, 1994b).

Nitrosamines. Group of compounds not naturally present in foods but generated during cooking or preservation (Jakszyn et al., 2004).

Carcinogen. Any substance, agent, or exposure which causes cancer development.

Processing plant. Facility where poultry products are prepared for commercial distribution.

Slaughtering plant. Facility where poultry is killed for commercial purposes.

Occupational task. Job specific duties and responsibilities.

Occupational carcinogens. Known or suspected occupational agents that may cause tumors or cancer.

Meat worker. An individual that handles cattle, pigs, or sheep in an occupational setting.

Poultry worker. An individual that handles chickens, turkeys, ducks, or other birds in an occupational setting

Next of kin proxy. Family member or close acquaintance of deceased subject who is knowledgeable of the deceased subject's lifestyle, medical and work histories that was willing to respond to the study's questionnaire.

Union membership. Workers who are a member of any one of several local unions belonging to the United Food and Commercial Workers International Union at any time between July 1949 and December 1989 regardless of length of membership or employment.

Lung cancer. Any malignant disease of the lung inclusive of small cell lung cancer, non-small cell lung cancer or mixed small cell/large cell cancer.

Tracing. Identification of study subjects through the use of Internet-based software or public records searches.

Significance of the Study

Occupational epidemiology is an integral division of public health. The contribution of occupational epidemiology is important because its research and findings aide in the identification of causal agents which influence the occurrence of occupational diseases among exposed workers. Hazardous working conditions remain significant problems in the meat and poultry industries. The workforce of slaughtering, packing, and distributing poultry in the United States is larger and more diverse than it was in the past. Shifts from family farm producers to large-scale production and mechanization have led to safety, health, and environmental contamination concerns (Levy, Wegman, Baron, & Solas, 2006). Unions however have been instrumental in directing attention to occupational safety and health issues through hiring health professionals, developing workplace health and safety committees, and by supporting epidemiological studies. Unfortunately, poultry worker membership in unions is not as abundant as it was in the past. Due to changing demographics in the workforce and changes in the work activities, the industry has transformed from a relatively high paid group of unionized workers to one that is dominated primarily by immigrant workers who have low union membership, extremely high turnover rates, and are low paid (Levy, et.al).

An excess of lung cancer has been consistently reported in the literature in the meat industry, yet many of these investigations have not been able to control for major confounding factors. Lung cancer mortality has never been investigated in the poultry industry, apart from two cohort studies by Johnson et al.(1997), and Netto et al.(2003). Further research is needed in this area that controls for confounding factors, particularly smoking. To date, this research is the only cohort investigation of workers in poultry slaughtering/processing plants. Evidence of potentially hazardous exposures in the poultry industry consistent with those found in the meat industry may strengthen the credibility of the previously-proposed occupational etiology (McLean & Pearce, 2004) of lung cancer. Policy formation as a result of epidemiological evaluation has been a critical tool used to ensure that workers are provided with a safe work environment (Hertz-Picciotto, 1995). The findings of this study, combined with evidence from other epidemiological studies that identify hazardous exposures in the poultry industry, may influence workplace regulatory controls that aid in protecting the health of this occupational group.

CHAPTER 2

REVIEW OF LITERATURE

Etiology/Basic Science

Lung cancer(non-small cell and small cell combined) is the second most frequently occurring cancer among men and women in the United States (US) and is the leading cause of cancer mortality for both. Annually lung cancer kills three times as many males than prostate cancer and almost twice as many females as breast cancer, the most commonly occurring cancers for each gender (Breath, 2006). Although the vast majority of lung cancer cases can be attributed to smoking, other etiologic factors may influence the risk of lung cancer independently or combined with smoking. These factors include genetics (Bromen, Pohlabeln, Jahn, Ahrens, & Jockel; Mayne, Buenconsejo, & Janerich, 1999; Tokuhata & Lilienfeld, 1963), environmental (Bennett et al., 1999; Boffetta & Nyberg, 2003), and occupational carcinogens (Alberg & Samet, 2003).

Early diagnosis of lung cancer typically does not occur because patients often do not exhibit symptoms until later stages of the disease. Common symptoms include a cough that gets worse or does not go away, swollen lymph nodes, trouble with breathing, constant chest pain, blood in sputum, a hoarse voice, recurrent lung infections, frequent fatigue, and unexplained weight loss (Pass, 2005). Depending upon the symptoms presented a chest x-ray, magnetic resonance imaging (MRI), or computed tomography (CT) scan is performed to examine if tumors are present. Diagnoses may be confirmed by a pathologist using a variety of tests such as: sputum cytology, thoracestesis, bronchoscopy, fine-needle aspiration, thoracoscopy, thoracotomy, or a mediastinoscopy in which cell samples are collected and then examined under a microscope to determine lung cancer type.

Lung cancer staging is threefold and it provides an estimate of tumor burden and extent spread and individualized prognostic information (Ginsberg, 2003). Staging is distinctly different for the two main types of lung cancer. Non-small cell lung cancer (NSCLC) has more complex staging categories and groupings than small cell lung cancer. First TMN classification of malignant tumors (TNM) staging system categorizes NSCLC spread prior to it being assigned to a stage group. T represents tumor size and spread within the lung and nearby tissues; N stands for affected lymph nodes; and M describes whether or not there is a spread to distant organs (ACS, 2007). Invasive non-small cell, the most commonly diagnosed type of lung cancer, has five stage groupings (Appendix A, Table I) while small cell lung cancer (SCLC) only has two stage groupings (Appendix A, Table II). The majority of lung cancer cases, 41%, are diagnosed at a distant stage after the cancer has already metastasized; 35% are diagnosed after it has spread to regional lymph nodes or directly beyond the primary site; 16% are diagnosed at a localized stage; and the remaining 8% of diagnoses have the an unknown or unreported stage (Ries, Melbert, & Krapcho, 2007).

Treatment options are based upon staging, personal choice of the patient and upon recommendation by the patient's physician. There are six standard treatments for NSCLC: surgery, radiation therapy, chemotherapy, laser therapy, photodynamic therapy and observation until symptoms appear. Treatment for SCLC is limited to chemotherapy, which is the main treatment, radiation, and surgery for a few number of localized cases (ACS, 2007). Chemotherapy may be combined with radiation as a usual treatment or used as an additional treatment following surgery. Lower-staged lung cancer tends to be localized and have a better prognosis than advanced stages of the disease because it is most treatable at those stages.

The overall prognosis for both types of lung cancer is relatively poor. The one year survival rate is 42%; the two year survival rate is 25%; and the five year survival rate is only 16%(ACS, 2007). Although very small in number, some people become cured from lung cancer and are long-term survivors. Improvements in treatments and combinations of surgical techniques has slightly increased the one-year survival rate from 38% in 1979 to 42% in 2002 (ACS, 2007); however, much work is still needed in the areas of lung cancer prevention and treatment research. The 5-year relative survival rates by stage are: 49.1% for localized; 15.2% for regional; 3.0% for distant; and 8.1% for unstaged (Ries, Melbert, & Krapcho, 2007). Newer, more effective techniques are also needed for early detection so that more treatments can be applied to prevent invasive lung cancer and reduce mortality among those diagnosed with the disease.

Epidemiology

An estimated 213,380 new cases and 160,390 deaths are predicted to occur in the US by the end of the year 2007 (ACS, 2007). The lifetime risk of lung cancer for men and women is 6.98% or 1 out of 14 based upon 2002-2004 rates (Ries, Melbert, & Krapcho, 2007). The average annual age-adjusted incidence rate per 100,000 (standardized to the 2000 US standard population) from 1999-2003 was 89.6 in males and 54.7 in females (ACS, 2007). The lung cancer epidemic in the US is reflected by patterns of cigarette smoking by birth cohorts and gender. While the incidence rate of lung cancer in men has declined significantly since the early 1980's, in women the incidence rate increased by an average of 4.1% per year between 1973-1990 prior to reaching a 0.2% average increase during the years of 1990-2000 (Pass, 2005). Lung cancer incidence and mortality rates pattern cigarette smoking and possibly reflect a deferring epidemic between women and men due differences in smoking initiation between the two sexes. The average annual age-adjusted mortality rate per 100,000 from 1999-2003 was 74.8 in males and 41.0 in females (ACS, 2007). Due to the often advanced stage of disease at the time of diagnosis, lung cancer mortality rates typically correspond with incidence rates.

Lung cancer is the most commonly diagnosed cancer in the world (Coleman, 1994). Developed countries in Eastern Europe, North America, Australia, and South America have the highest incidence and mortality rates while the lowest rates have been observed in southern Asia, India, and Pakistan. Geocultural variations in lung cancer incidence is influenced by the prevalence of smokers, type and amount of cigarettes smoked, age at initiation and duration of smoking exposure, and proportions of heavy smokers in the population (Schottenfeld & Searle, 2005). Geographic variations in lung cancer may also be attributed to environmental pollutants. In China and Singapore fossil fuel combustion products and pollutants from cooking oils used in the home attributed to elevated risks found among Chinese women (Ko et al.; MacLennan et al., 1977).

Lung cancer risk is one of many existing racial and ethnic health disparities. African Americans in the US experience lung cancer incidence rates that are among the highest worldwide (Alberg & Samet, 2003). The most profound difference is between African American and Caucasian men in the US. African American men have a 50% higher risk of developing lung cancer in comparison to Caucasian men, while age-adjusted lung cancer incidence in African American and Caucasian women are similar (Ries, Melbert, & Krapcho, 2007). According to Surveillance Epidemiology and End Results (SEER) data (Ries et al., 2007), African Americans had the highest mortality rate, 95.8 per 100,000 men, while Caucasians had the highest rates, 42.1 per 100,000, among women for deaths occurring in the US from 2000-2004. Targeted marketing campaigns by the major tobacco companies in the 20th century have vastly influenced tobacco usage in minority communities. Additionally, minorities are put at an increased risk of lung cancer if they are employed in occupational settings with known or suspected high risk industries for lung cancer (Zeka et al., 2006).

Risk Factors

Epidemiologic literature extensively discusses tobacco smoking as the leading etiologic agent for lung cancer (Peto, Lopez, Boreham, Thun, & Heath, 1994; Schottenfeld & Searle, 2005). Genetic factors also appear to play a role in the etiology of lung cancer (Brownson, Alavanja, Caporaso, Berger, & Chang; Spitz et al., 2007). It is difficult to assess the exact roles that other risk factors play in the etiology of lung cancer because of the enormous influence of cigarette smoking. However, there are additional risk factors independent of smoking, particularly those found in occupational settings, which increase the risk of lung cancer among nonsmokers and create synergistic effects on lung cancer risk among smokers. (Ahrens & Merletti, 1998)) developed a detailed list of occupations and industries known and suspected to present an excess risk of lung cancer among employed workers. The food industry, which included the profession of butcher, was listed as a suspected excess risk of lung cancer occupational risk factor.

Lung cancer is the most common cancer associated with occupational exposures (Doll & Peto, 1981). Clinical case studies of the early 1900's (Cooke, 1927; Lynch & Smith, 1939; Wedler, 1944; Wood & Gloyne, 1934) hypothesized the relationship between asbestos and lung cancer; however, it was not until Doll (Doll, 1955) observed a 10 fold increase in lung cancer risk among asbestos textile workers that epidemiological evidence established asbestos as an occupational carcinogen. Occupational exposures to radon are substantially higher than levels experienced by the general population. Occupational cohorts of miners have established the carcinogenicity of radon (Lubin, 1997; Lubin & National Institutes of, 1994; National Research, Agency, United, Committee on the Biological Effects of Ionizing, & Commission, 1988). Indoor air pollution as a result of exposure to asbestos and radon may present a risk for lung cancer but previous cohort (Dockery et al., 1993; Pope et al., 1995) and case-control studies (Barbone, Bovenzi, Cavallieri, & Stanta, 1995; Jedrychowski, Becher, Wahrendorf, & Basa-Cierpialek, 1990; Vena,1982) reported no to very modest elevated lung cancer risk. Metals including, arsenic (Lee & Fraumeni Jr, 1969; Ott, 1974; Pinto, Henderson, & Enterline, 1978), cadmium (Sorahan & Lancashire, 1997; Waalkes, 2000, 2003), chromium (Alderson, Rattan, & Bidstrup, 1981), and nickel (Sunderman Jr, 1976) have been associated with occupational lung cancer.

Hazardous Occupational Exposures in the Poultry Industry

Several studies have investigated the occurrence of lung cancer among workers in the meat industry, particularly among butchers (Coggon & Wield, 1995; Doerken & Rehpenning, 1982; Fox, et al.,1982; Griffith, 1982; Johnson, Dalmas, Noss, & Matanoski, 1995; Johnson & Fischman, 1982; Johnson, et al., 1986a; Lynge, Andersen, & Kristensen, 1983); however there are only a few studies published (Fritschi, et al., 2004; Johnson, et al.,1986b; Johnson, et al., 1997; Netto & Johnson, 2003) investigating lung cancer risk among poultry workers. Similar to meat industry workers, poultry workers experience many hazardous occupational exposures that may put them at an increased risk of lung cancer mortality (Johnson, 2005). Possible harmful exposures in the poultry industry include transmissible agents such as prions, viruses, bacteria, and protozoa that have been shown to cause cancer and other diseases in animals (Johnson, 2005). Retroviruses such as avian leukosis sarcoma viruses (ALSV), reticuloendotheliosis viruses (REV) and Marek's disease virus (MDV), a herpes virus, frequently infect chickens and turkeys and can naturally induce cancer in them (Payne, 1998); (Payne, 1985) It is currently unknown if these retroviruses are carcinogenic in humans, despite a review of previous virological studies (Johnson, 1994b) showing their ability to infect human cells *in vitro* and *in vivo*. Employees of poultry slaughtering and processing plants have one of the highest exposures to transmissible agents that cause cancer and other diseases in chickens and turkeys (Johnson, Shorter, Rider, & Jiles, 1997;

Netto & Johnson, 2003). Although poultry workers have a high risk of exposure to carcinogenic viruses there are only three epidemiological studies (Johnson, et al.,1997; Netto & Johnson, 2003; Fritschi, 2004) published that examine cancer mortality experienced by these workers.

Agents involved in the processing and preparation of meat or poultry that could have a carcinogenic potential in humans are nitrosamines (Jakszyn et al., 2004), used during the curing of meat; butylated hydroxyanisole and butylated hydroxtoluene, which are used as preservatives (Johnson, et al.,1986a); and plastic pyrolysis products that occur during meat wrapping (Vandervort & Brooks, 1977). Fumes emitted from the thermal decomposition of plastic films used to wrap meat include hydrogen chloride, hydrocarbons- primarily benzene and polycyclic aromatic hydrocarbons, plasticizers phthalates, adipates and their breakdown products (O'Mara, 1970; S. Halabi, Netto, Lucier, Bechtold, & Henderson, 1999; Vandervort & Brooks, 1977).

Exposure to airborne carcinogenic chemicals emitted from the fumes of thermal decomposition of plastic film used to wrap poultry may have an influence on the occurrence of lung cancer among these workers. Meat wrapping, an occupation traditionally dominated by females in the meat industry, may induce lung cancer due to high exposure to carcinogenic products released by melted plastic from the wrapping machine. Polyvinyl chloride (PVC) plastic films melted in hot wire or cold rod wrapping machines are widely used throughout the meat industry to wrap and label meat products (Johnson et al., 1999). Fumes emitted from these machines contain small amounts of benzene, polycyclic aromatic hydrocarbons (PAHs), and phthalates, which are all carcinogenic (Boettner & Ball, 1980; Kluwe et al., 1982; Monographs, 1987; Vandervort & Brooks, 1977; O'Mara, 1970). These fumes emitted from plastic wrap and the application of labels have been postulated in a number of studies as an exposure that could possibly cause tumors in exposed workers (Fritschi, et al., 2004; Johnson, et al.,1986a, 1986b; Johnson, et al., 1997; Metayer, Johnson, & Rice, 1998). Benzene has been found to induce lung tumors in animals (IARC, 1982) and PAHs are well known lung carcinogens in humans (IARC, 1973; World Health & Humans, 1985). Previous epidemiological studies in the meat industry (Johnson, 1991; Johnson, et al., 1986a; Kristensen & Lynge, 1993) have suggested that exposure to plastic pyrolysis products found in fumes emitted from the thermal decomposition of plastic during the wrapping process of meat may have an influence on the excess occurrence of lung cancer among workers exposed to those fumes. No studies have ever specifically investigated the long-term effects of exposure to these fumes and the occurrence of lung cancer in the meat industry.

Poultry workers involved in the commercial preservation and cooking of poultry products are potentially exposed to carcinogenic compounds formed during these processes. Workers in smokehouses are exposed to combustion products from meat smoking, especially PAHs (Colmsjö, Zebühr, & Östman, 1984). Exposure to PAHs from smoking of meat has been generally regarded as an occupational exposure possibly related to lung cancer risk (Gustavsson, Fellenius, & Hogstedt, 1987; Johnson, Dalmas, Noss, & Matanoski, 1995) confined to meatpacking plants (Johnson, et al.,1995; Nordholm, Espensen, Jensen, & Holst, 1986). A previous investigation of butchers and slaughterhouse workers found that exposure to smokehouse fumes was not associated with the excess lung cancer reported in this group (Gustavsson, et al., 1987). This study's negative results can not rule out lung cancer risk factor in the meat industry because the proportion of exposed workers was small and limited to an occupational subgroup of the meat industry that is traditionally not involved in the smoking of meat (Kristensen & Lynge, 1993). The frying of meat at high temperatures results in the formation of carcinogenic PAHs and heterocyclic amines(HAs) (Jakszyn et al., 2004; Wang, Chen, Yang, & Ueng, 2001). Lung cancer is the leading cause of cancer death among non-smoking women in China (Gao et al., 1987; Koo, 1990) and Taiwan (Ko et al., 1997); exposure to airborne emission particulate from frying meat and fish has been associated with an increased risk in these populations (Ko et al., 1997; Seow et al., 2000; Wang, et al., 2001). There is a need to research lung cancer among cooks in the poultry industry because workers that fry poultry may also be exposed to relatively high levels of carcinogenic compounds formed during the cooking process. Carcinogenic nitrosamines are generated from the interaction of nitrates with amines during the curing and storage of meat (Monographs, 1987). A few authors suggest that workers involved meat preservation may be exposed to carcinogenic nitrosamines by inhalation (Johnson, et al., 1995; Sen, Miles, Donaldson, Panalaks, & Iyengar, 1973), despite others that don't support this hypothesis (Coggon, et al.,1989; Gustavsson, et al.,1987; Kristensen & Lynge, 1993) because of a lack of empirical support. Other studies have hypothesized that the nitrosamines present in cured meat pose a possible carcinogenic effect on people who consume it (Jakszyn et al., 2004; Sen, Donaldson, Charbonneau, & Miles, 1974;

Sen, Miles, Donaldson, Panalaks, & Iyengar, 1973), although there is no conclusive evidence to support this dietary carcinogen. Research that controls for possible confounding factors is needed to further examine the role of curing meat in the etiology of lung cancer among exposed workers.

Lung Cancer Investigations in the Meat Industry

Evidence of an excess risk of lung cancer in among butchers was first reported in 1982 in a review of Danish occupational mortality data (Lynge, 1982), which was followed by a series of published short reports based on mortality among meat workers in Denmark (Fox, Lynge, & Malker, 1982; Lynge, 1982), England and Wales (Fox, et al.,1982; Griffith, 1982), and Sweden (Fox, et al.,1982) with comparable excesses. The first published studies of meat workers in the US also appeared in 1982. A proportional mortality study that reviewed death certificates from the state of Washington over a 30 year period did not observe an increased risk of lung cancer for meat workers inside or outside of slaughterhouses (Milham,1982); whereas, a proportional cancer mortality study of meat cutters belonging to a Baltimore union revealed an excess in all cancers examined including lung (Johnson & Fischman, 1982).In the aforementioned brief reports of 1982-1983, lung cancer risk for butchers employed in slaughterhouses was higher than butchers employed elsewhere.

A review of cancer in the meat industry (McLean & Pearce, 2004) noted these early studies reflected lung cancer risk differences in the exposure categories of slaughtering and contact with meat. In more recent studies, the excess risk of lung cancer among meat industry workers was also most strongly associated with occupational task exposure to recently-slaughtered meat (Boffetta et al., 2000; Coggon, et al.,1989; Guberan, Usel, Raymond, & Fioretta, 1993; Gustavsson, Fellenius, & Hogstedt, 1987; Johnson, 1991, 1994a; Johnson, et al.,1995; McLean, Cheng, t Mannetje, Woodward, & Pearce, 2004). These results suggest that disease causing biological agents may be involved in the etiology of lung cancer in among certain groups of meat workers. Meat industry workers are exposed to potentially harmful oncogenic agents that have proven to be carcinogenic in animals (Johnson, 1994b; Johnson, et al.,1986a; Johnson & Griswold, 1996) including Bovine Leukemia Virus (Burny, 1987), Bovine Papilloma Virus (Campo, 1987; Lancaster & Olson, 1982), and Jaagsiekte Sheep Retrovirus (Palmarini & Fan, 2001; Wootton, Halbert, & Miller, 2005).

The intimate nature of meat handling, which includes contact with internal organs, blood, and feces, places workers at risk of exposure to biological agents through the skin, inhalation, and ingestion. Cuts and abrasions are frequent among meat workers (McLean & Pearce, 2004), increasing the possibility of direct entry of the biological agents into the circulatory system (Johnson, 2005) via penetrating injuries. Power equipment used in slaughterhouses facilitates the airborne transmission of bioaerosols (Rahkio & Korkeala, 1997) because of the powerful force of the machines. Exposure through ingestion is possible among workers that drink the blood of the animals slaughtered, which has been known to occur among workers in the "kill floor" area in cattle abattoirs (Johnson, 2005) and possibly other areas of the meat industry.

Cohort studies of cancer in the meat industry in the United States (Johnson, 1994a; Johnson, et al.,1995; Johnson, et al., 1986a, 1986b), Switzerland (Guberan, Usel, Raymond, & Fioretta, 1993), Australia(Fritschi, Fenwick, & Bulsara, 2004), Sweeden (Boffetta et al., 2000), New Zealand (McLean, et al., 2004) and the United Kingdom (Coggon, et al., 1989) have all shown elevated risk for lung cancer among butchers who killed or were exposed to the meat shortly after it was killed. An early cohort study of butchers in Germany (Doerken & Rehpenning, 1982) found a 2.4 relative risk of lung cancer compared with bakers, however these results were reported as a chance finding (McLean & Pearce, 2004). As mentioned in a previous review (McLean & Pearce, 2004), despite the limitations of more recent studies including small lung cancer sample sizes (Fritschi, et al.,2004);(Johnson, 1989);(McLean, et al., 2004); possible selection bias by loss to follow-up (Coggon & Wield, 1995; McLean, et al., 2004); and possible information bias in exposure information obtained from proxies(Johnson, 1991), union records (Johnson & Fischman, 1982);(Johnson, et al.,1986a); (Johnson, et al., 1986b); (Johnson, 1989); (Johnson, 1994a; Johnson, et al.,1995); (Fritschi, et al., 2004), or census data (Boffetta et al., 2000); there is a general consensus that meat workers who handle cattle, pigs and sheep are exposed to an elevated risk of lung cancer. However, these results must be interpreted with caution because none of the aforementioned studies controlled for tobacco smoking with the exception of Johnson's nested case- control study (Johnson, 1991).

Two cohort studies (Besson, Banks, & Boffetta, 2006;Coggon, 1995) have contrasted the previous cohort observations of increased lung cancer mortality among meat workers. A possible explanation of the negative findings in both studies may be a result of misclassification of the occupational exposure. In the Coggon study (1995), all butchers were grouped together as opposed to being stratified by occupational task performed to assess the effects of butcher subgroups, for example those that killed, handled warm meat, or handled chilled meat. The Besson study (2006) was a retrospective cohort study of death certificates and there is a possibility of information bias due to inaccuracies in the reported usual occupation or cause of death.

The first study to control for smoking among meat workers did not find a risk of lung cancer; the odds ratio of 1.1 was reduced to 1.0 after adjustment (Vena, 1982b); this study was anecdotal and included only 21 lung cancer cases that were employed in the meat industry. In a series of case studies based on cancer registry data an excess in lung cancer was found among New Zealand meat workers; smoking in this study was indirectly controlled for using census data. There was a possibility of selection bias by using other cancers as the reference group if working in the meat industry is associated with multiple cancers, thereby reducing the estimate of relative risk (Reif, Pearce, & Fraser, 1989). Additionally, information bias may have been present because the last known occupation was reported by a cancer registry and this may not have reflected the usual lifetime occupation of the case. In Germany, a case-control study of occupational risk factors for lung cancer revealed a twofold excess of lung cancer after adjusting for smoking and asbestos exposure in the meat industry as a whole and also in the occupation of butcher (Jöckel, Ahrens, Jahn, Pohlabeln, & Bolm-Audorff, 2004). Two studies nested within cohorts have been published to date that adjusted for smoking status in meat workers. One, a nested case control study of lung cancer in the US meat industry (Johnson, 1991) which collected detailed information on occupational exposures and potential confounders found elevated risks of lung cancer in meat-packing plants after adjusting for smoking (OR=7.9, 95% CI 0.4, 163.7) and meat departments of supermarkets (OR= 2.4, 95% CI 0.3, 19.2) the results of this study indicated that there is a risk of lung cancer that exists after controlling for smoking; however, these results should be interpreted with caution because of its small sample size with 60 cases and 60 controls, and resultant wide confidence intervals. Prior to the US study, a Swedish nested case control study (Gustavsson, et al.,1987) in the meat industry failed to observe an excess of lung cancer in packaging workers(RR= 0.85, 95% CI 0.39 to 1.88). This negative finding may have been due to the authors comparison of the risk for working at a specific job to the risk of working all other jobs in the meat industry, thereby making it difficult to detect an underlying risk (Johnson, 1991). Additionally, it is possible that the negative findings may have been influenced by misclassification of the exposure which was dependant on next-of-kin responses.

Lung Cancer Investigations in the Poultry Industry

Only three cohort studies have been published examining cancer mortality among workers in the poultry industry and all found elevated risks for lung cancer. The earliest study was a follow-up of a sub-cohort of poultry slaughtering/processing plant workers that were members of a local meat-cutters' union in Baltimore, Maryland (Johnson, 1989; Johnson, et al.,1986a, 1986b). In the initial cohort study the only statistically significant result in poultry workers was among white women with a four-fold risk of lung cancer (Johnson, et al., 1986b), the standardized mortality ratio in the update was reduced to 1.8 with a relative risk of 1.5 (Johnson, Shorter, Rider, & Jiles, 1997). The authors postulated this decreased of lung cancer in women may be related to a reduction in exposure to fumes during the wrapping process that occurred in 1975 due to modifications of cutting and wrapping machines which provided a means to control sealing and cut-off wire temperature (Vandervort & Brooks, 1977). Meat wrapping is a task usually performed by women in the meat department of retail supermarkets (Johnson, et al.,1986b).

A Missouri based cohort study of unionized poultry workers revealed a reduced lung cancer risk among males and a slightly elevated risk for females (Netto & Johnson, 2003). There are similarities in the limitations of both the Baltimore and Missouri cohort studies. Possible influences of the negative findings are low statistical power, relatively young members with a short latency periods, and only 14% in Baltimore and 6% in Missouri were deceased at the end of follow-up. Additional follow-up of both cohorts is needed to assess their risk of lung cancer, which has been previously observed to occur in excess among exposed poultry workers (Johnson, et al.,1986b; Johnson, et al.,1997). In the most recent study (Fritschi, et al.,2004), only 19 lung cancer deaths occurred in the entire cohort and none of those were among poultry workers.

None of the three cohort studies had data on smoking habits of the cohorts. Tobacco smoking is possibly the strongest potential confounder in investigating the association between occupational exposures and the risk of lung cancer (McLean & Pearce, 2004). There is a need for case-cohort examinations of poultry workers that collect detailed information on lifestyle factors, particularly tobacco smoking, and specific occupational task exposures to supplement further follow-ups of these cohorts.

CHAPTER 3

METHODOLOGY

The current research uses a subset of data that were originally collected for a retrospective cohort mortality and case-cohort study that investigated cancer risk in workers exposed to oncogenic viruses. Theses studies were conducted in cooperation with the United Food and Commercial Workers International Union (UFCW). Occupational exposures thought to be associated with increased lung cancer risk were investigated in workers formerly employed in poultry slaughtering/processing plants.

Retrospective Cohort Mortality Study Methods

Purpose

The purpose of the retrospective cohort mortality study was to identify increased risk of death from specific causes, malignant and non-malignant, associated with working in poultry plants where exposure to oncogenic viruses occurs. The source population consisted of 47,400 individuals who were members of UFCW local unions at any time between July 1, 1949, and December 31, 1989. The start date of follow-up was from the start of union dues payment for each individual or 1949, which ever was earlier. These workers were identified from three sources:(1) Local 27, formerly known as the Amalgamated Meat-cutters' Union, in Baltimore, Maryland (Baltimore), the earliest date was 1949;(2) AFL/CIO Local 410 in Marshall, Missouri (Missouri), earliest date was 1969; and (3) the Pension Fund, earliest date 1975. Two of the three union cohorts

(Baltimore & Missouri) were studied previously(Johnson, 1989, 1994a; Johnson, Dalmas, Noss, & Matanoski, 1995; Johnson, Fischman, Matanoski, & Diamond, 1986a, 1986b; Johnson & Zhou, 2007) and the third union cohort, Chicago, was not yet studied.

Sample Description

The retrospective study updated mortality for the period of 1990-2003 in a cohort of all 2,580 poultry workers employed in six chicken slaughtering/processing plants who were members of the UFCW in Baltimore and 7,700 poultry workers from 5 plants in the state of Missouri. The Pension Fund cohort, which drew their membership from a geographically wide area of the United States, consisted of 20,712 poultry workers from 11 plants belonging to six UFCW local unions. These plants were located in six states distributed as follows: Louisiana three, Maine three, Arkansas two, and one each in Missouri, Arizona, and Texas. Mortality was also investigated in a group of 16, 408 non-poultry workers belonging to two of the union cohorts (6,052, Baltimore; 10,356 Pension Fund). This heterogeneous group of workers was employed in exclusively non-meat companies, such as soft-drink manufacturing, fisheries, egg, milk, canning, and fertilizer companies (Appendix B).

Data Collection

Deceased members of the cohort were identified by searches of:(1) current union records, (2) Social Security Administration Mortality Files, (3) state department of vital records, (4) motor vehicle registrations, (5) US Postal Service, (6) Credit Bureaus, (7) State Department of Vital Records, (8) direct contact by letter or telephone, (9) Pensions Benefit Information (PBI), and (10) the National Death Index (NDI).

Vital status was also determined matching the 47,400 union members with records in PBI and NDI. PBI is a private research company that provides death audit information from a combination of public and private data such as the Social Security Administration, Civil Service Commission, Retirement Boards, and state agencies ("Pension Benefit Information Participant Research Service", 2007). NDI, a branch of the National Center for Health Statistics, is a computerized index of death record information submitted by state vital statistics offices for all recorded deaths occurring in the US, beginning with 1979 deaths (2007). The method of matching in PBI relies predominantly on social security number as the matching criteria whereas NDI uses a twelve criteria algorithm. NDI matching is a modification of probabilistic approaches developed by Fellegi and Sunter (1969) that assume the matching algorithm is conservative and will result in limited false non-matches. There were 5,656 deaths identified by PBI and NDI from January 1, 1990, through December 31, 2003, cause of death was unknown for 399 of the deceased.

Based on the previous mortality findings of studies conducted within the Baltimore (Johnson, Fischman, Matanoski, & Diamond, 1986a) and Missouri cohorts (Netto & Johnson, 2003) a pilot case cohort study was conducted to acquire detailed information on individual exposures and possible confounding factors among deceased subjects with malignant causes of death that occurred at an abnormal frequency when compared to the US standard population. Cancers of the lung, esophagus, colon, rectum, liver, pancreas, kidney, bladder, bone, lymphoid & haemotopoietic, buccal cavity and pharynx occurred in excess in these cohorts.

Case-Cohort Study Methods

Data Collection

Each study subject was assigned a unique identification number that was entered into a computer file along with demographic information obtained from the subject's death certificate. The subject's next-of-kin, as listed on the death certificate, was then traced and asked to voluntarily participate in the study by answering questions pertaining to the deceased subject. The next-of-kin were traced and identified using a wide ranging system of tracing techniques including searches of: Union Medical & Pension Fund Records, State Departments of Motor Vehicles, Social Security Administration, Credit Card Bureaus, Telephone Directories, ProPhone & PhoneDisc, (computerized data bases of names, telephone numbers and address of telephone subscribers nation-wide) and Private Eye & Ancestory.com (web-based databases). If the next-of-kin listed on the death certificate did not want to participate or was untraceable, other relatives or acquaintances listed on the death certificate were traced and asked to participate.

The questionnaire was administered via a computer-assisted telephone software, Questionnaire Development System (NOVA Research Company, Bethesda, Maryland) containing over 600 comprehensive questions regarding the subject's work in the poultry industry, their history of exposures at work, medical history, and history of allergies, history of cancer, radiation, drug intake, diet history, and occupational history other than in the poultry industry was administered over the telephone to the next of kin. Oral consent was obtained prior to beginning the questionnaire. These data were imported into SAS (SAS Institute Inc, Cary, North Carolina) for data cleaning and analysis. The variables examined by this research included: occupational exposure histories and specific occupational tasks associated with exposures in the poultry industry in addition to demographic and selected lifestyle variables.

Sample Description

There were a total of 1,217 deaths (cases) from nine selected cancers of interest identified by PBI and NDI that occurred in the cohort from January 1, 1990 to December 31, 2003 (Appendix C). Death certificates for the cancer cases were retrieved from various state departments of vital records to confirm cancer as the cause of death and to ascertain next-of- kin information. A total of 552 cases had a diagnosis of lung cancer (*International Classification of Diseases*, Ninth Revision, code 162.2-162.9) or (*International Classification of Diseases*, Tenth Revision, codes C33-C34). Death certificates were not received for 95 (17%) of the lung cancer cases, 54 of theses cases died in states that did not provide approval for the usage of death certificates to identify and contact the next-of-kin (Appendix D). No record was found by the requested state department of vital records for the remaining 41 lung cancer cases because these deaths were identified by methods other than NDI for which the state of death was unknown.

The demographic variables: date of birth; date of death; gender; race; highest grade completed; martial status, and state of death were extracted from the death certificates. Age at time of death was a continuous variable that was categorized into age groupings. The education variable was grouped into less than high school for those that did not complete the 12th grade or receive a GED; high school for those that completed the 12th grade or received a GED; and some college for those that reported 13 years of greater for highest grade completed. Year of death was categorized into three groups. The state of death was categorized into regions according to the United States Census regions. Start and end dates of union membership and the name of the company employed by were taken from the union records. Duration of employment was calculated by subtracting the end date from the start date; survival time since employment was calculated by subtracting the date of death from the end date. The individual companies belonging to the union were categorized by type of product they manufactured. Smoking status was obtained by the study's questionnaire.

An internal comparison group (sub-cohort) was ascertained by drawing two simple random samples of 1000 individuals from the base population alive as of January 1, 1990. The sub-cohort consisted of live and dead subjects at the time of sampling. The union distribution of the sub-cohort was as follows:

Table 1

Distribution of Sub-cohort by Union

Pension Fund	Baltimore	Missouri
1409	283	308

From the two random samples 24 individuals were sampled twice. Interviews were completed with 163 living members of the sub-cohort. The demographic variables for the sub-cohort group were restricted to information included in the union record: date of birth, gender, start date, end date; and gathered during the interview, race and smoking status. Age was calculated by subtracting the end of the study period, December 31, 2003, from the date of birth. Survival since last employment was calculated by subtracting the end of study period from the end date of employment. All of the poultry worker comparison group members were alive at the time of interview which was after the end of the study period. No deceased lung cancer cases employed in the poultry industry were sampled in the sub-cohort, although they were eligible. Race and smoking status were ascertained at the time of interview for the comparison group.

Statistical analyses

Descriptive statistics (mean, frequency and percents) of the sample were calculated to describe the characteristics of the study participants and the proxy respondents. Bivariate and multivariate analyses were conducted to observe the relationship between occupational task exposure and lung cancer mortality with and without the presence of independent variables thought to influence lung cancer mortality. Assessment for effect measure modification and confounding was conducted for the following variables, smoking status, gender, race, age group, and start group. These variables are thought to be of importance because occupational exposures change over time and they are known to differ by gender and race (Johnson, 1991); (Johnson, Fischman, Matanoski, & Diamond, 1986a); (Johnson, Fischman, Matanoski, & Diamond, 1986b); (Johnson, 1989); (Johnson, 1994a). Because of its strong association with lung cancer mortality, smoking was controlled for in all exposure/disease relationships and was assessed as an effect-measure modifier for each occupational exposure. Variables that were determined as potential confounders and effect-measure modifiers were included in logistic regression models. Only independent variables found to be statistically significant predictors of lung cancer mortality or those of biological importance were retained in the final logistic regression models. The exploration of lung cancer mortality by poultry occupational groups was conducted by logistic regression analyses, which controlled for smoking and time employed.

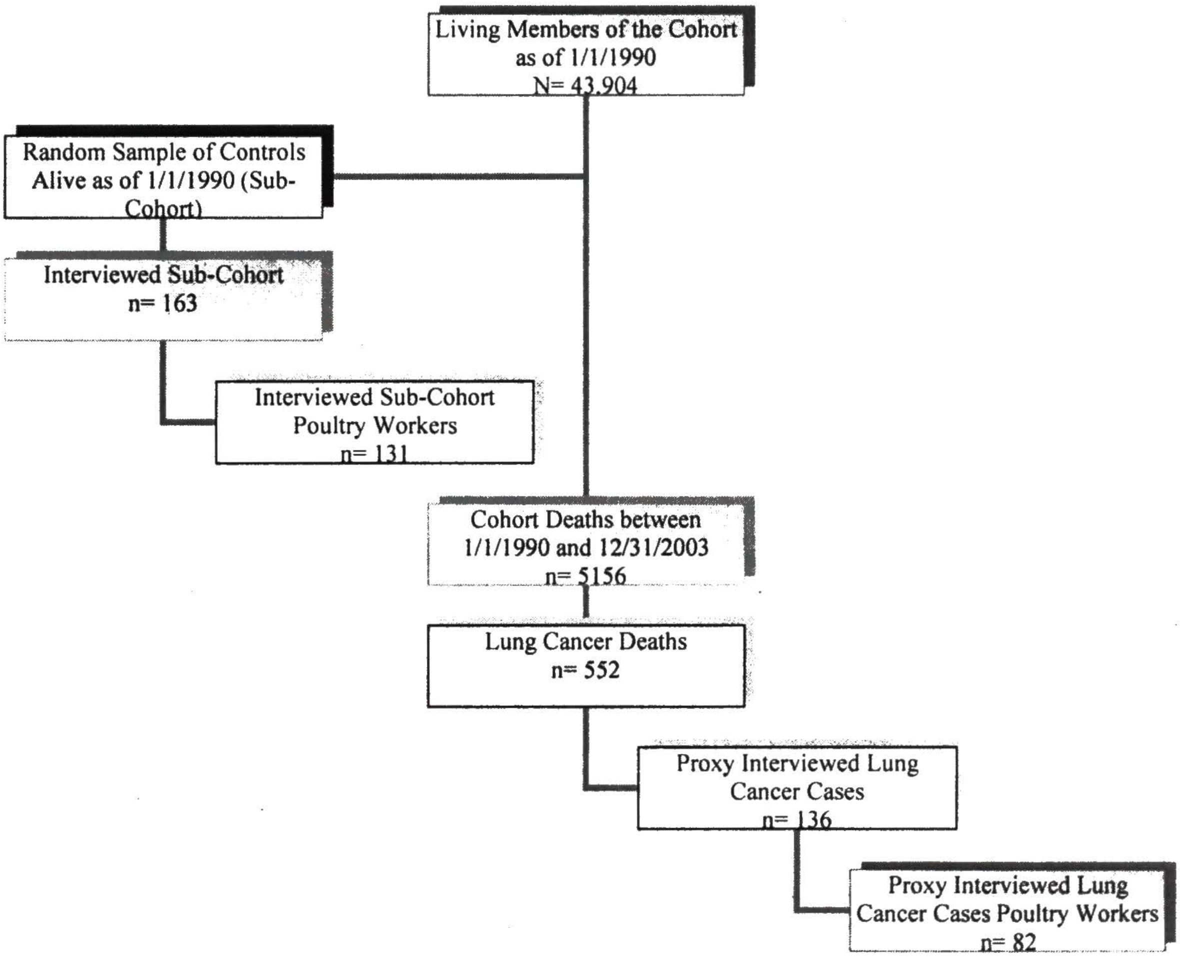
CHAPTER 4

RESULTS

Inclusion criteria for this study were restricted to a subset of poultry workers only. There were 265 death certificates received for workers employed in poultry plants. The overall interviewed rate was 31%, n=82 (Figure 1). This low response rate was largely attributed to not finding a next-of kin match for 64% of the cases. Because this was a pilot study exhaustive attempts were not made to trace individuals. We relied mainly on telephone directories, death certificate information, and web-based methods of tracing individuals. If a match was found, the next-of-kin non-participation rate in the study was 80%. A comparison of demographic, death, and employment variables was made between the interviewed and non-interviewed poultry workers who died of lung cancer to determine if there were demographic differences between those cases that were interviewed versus those that were not. Age at death, gender, education level, year of death and survival since last employment was not significantly different among the subjects interviewed and those not-interviewed. There were significant differences between proportion of Blacks, non-married, deceased in the south and employed less than a year subjects (Tables 2 & 3).

Figure 1

Study population description



Note. The study population consisted of 131 members of the sub-cohort and 82 lung cancer cases.

Table 2

Demographic characteristics of interviewed versus non-interviewed lung cancer cases among United Food and Commercial Workers poultry employees, deceased 1990-2003

	Interviewed n(%)	Non-interviewed n(%)	χ^2
Race			6.69*
White	74 (90.2)	141 (77.1)	
Black	8 (9.8)	40 (21.9)	
Other	0 (0)	2 (1.1)	
Marital status			4.43*
Married	50 (61.0)	86 (47.0)	
Not married	32 (39.02)	97 (53.0)	

*p < .05

Table 3

Death and employment characteristics of interviewed lung cancer cases among United Food and Commercial Workers poultry employees, deceased 1990-2003

	Interviewed n (%)	Non-interviewed n (%)	χ^2
Region of Death according to US Census Region			17.50**
Midwest	21 (25.6)	43 (23.5)	
Northeast	21 (25.6)	18 (9.8)	
South	37 (45.12)	121 (66.1)	
West	3 (3.7)	1 (0.55)	
Duration of Employment according to Union Record			9.8*
<1	12 (18.8)	44 (30.3)	
1-5	34 (53.1)	84 (57.9)	
6-10	12 (18.8)	10 (6.9)	
>10	6 (9.4)	7 (4.8)	

*p < .05
**p < .01

Of the next-of-kin proxies that responded to the questionnaire, the majority of responses were from females, Figure 2 and they were a first degree relative to the deceased case as seen in Figure 3 and Figure 4.

Figure 2

Lung cancer case proxy respondent gender

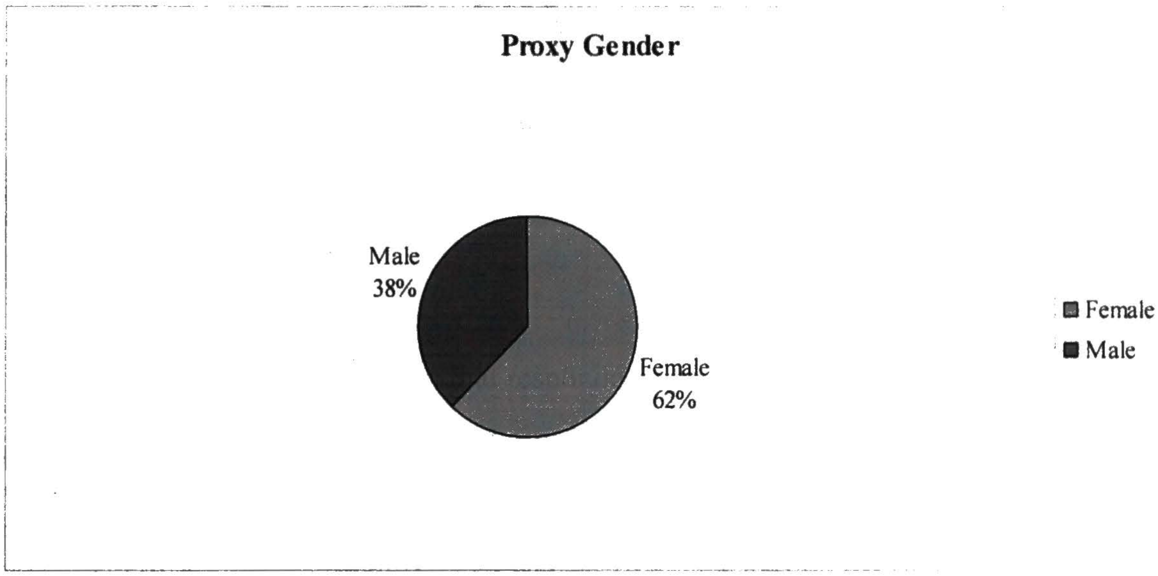


Figure 3

Female proxy respondent relationship to lung cancer case

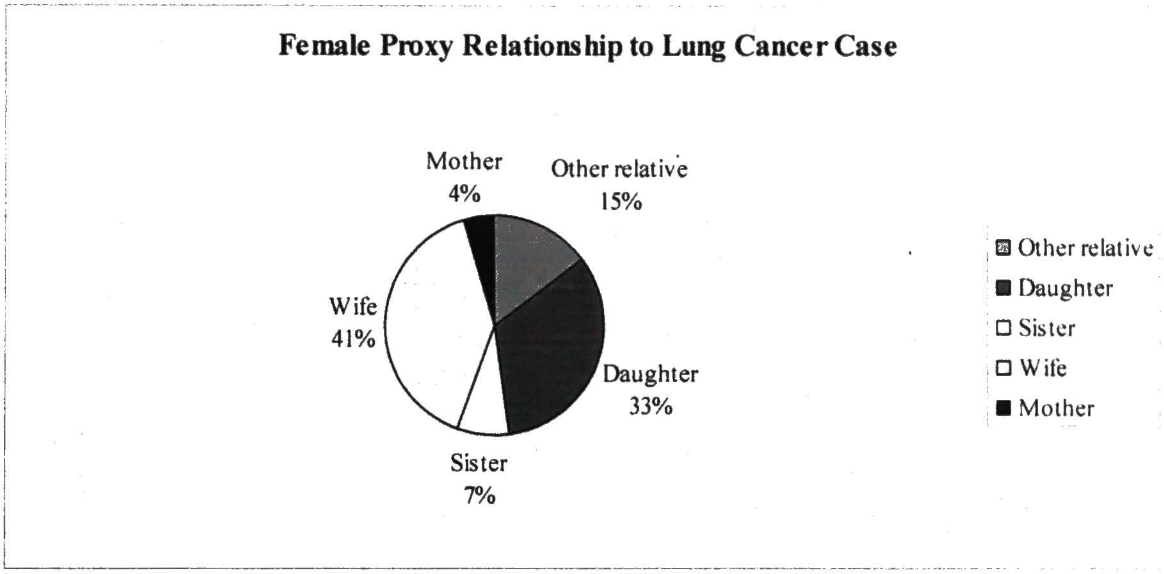
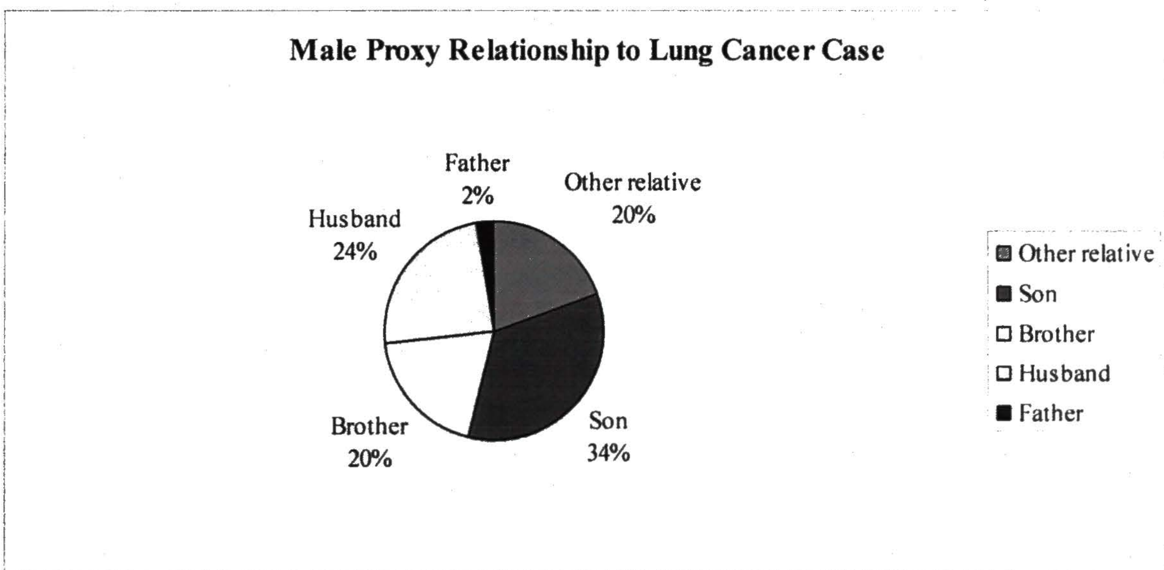


Figure 4

Male proxy respondent relationship to lung cancer case



Descriptive Analyses

Cases Demographics

Tables 4, 5, and 6 displays the frequency and proportion for selected characteristics describing the final sample of 82 interviewed lung cancer cases eligible for analysis. The average age of death was 63, ranging from 38-84 years old at the time of death. Interviews were received for mainly male cases (65%), likely because of there were more males in the base population. Majority of the cases were White, 90% and 10% were Black. Fifty-eight percent were high school graduates and almost ten percent of them had some level of college education. The average length of employment in the poultry industry was 4 years with over half working for 1-5 years; the range was 0-17 years. The average length of survival since last employment in the poultry industry was 18 years, ranging from 3 to 39 years. Majority of the deceased lung cancer cases smoked tobacco products, 93%, while only 7% never smoked.

Table 4

Demographic characteristics of interviewed lung cancer cases among United Food and Commercial Workers poultry employees, deceased 1990-2003

Characteristic	n	%
Age at time of death		
30-40	3	3.7
41-50	7	8.5
51-60	26	31.7
61-70	25	30.5
71+	21	25.6
Gender		
Male	50	61%
Female	32	39%
Race		
White	74	90.2
Black	8	9.8
Education		
< High School	32	42.7
HS Graduate	36	48
Some College	7	9.3
Marital status		
Married	50	61.0
Widowed	17	20.7
Divorced	12	14.6
Never married	3	3.7
Smoking status		
Smoked Tobacco	74	92.5
Never Smoked Tobacco	6	7.5

Table 5

Employment characteristics of interviewed lung cancer cases among United Food and Commercial Workers poultry employees, deceased 1990-2003

Characteristic	n	%
Survival since last employment in poultry industry		
10-20	33	45.2
21-30	33	45.2
31-40	7	9.6
Duration of employment according to union record		
<1	12	18.8
1-5	34	53.1
6-10	12	18.8
>10	6	9.4

Table 6

Death characteristics of interviewed lung cancer cases among United Food and Commercial Workers poultry employees, deceased 1990-2003

Year of death		
1990-1994	23	28.1
1995-1999	26	31.7
2000-2003	33	40.2
Region of death according to US Census Region		
Midwest	21	25.6
Northeast	21	25.6
South	37	45.1
West	3	3.7

Control Demographics

In the sub-cohort there were a total of 131 poultry workers interviewed and included in the analysis as a comparison group to the poultry worker lung cancer cases. The average age at the time of interview was 56, ranging from 37-87 years old. The respondents were primarily female, 63%. The highest response was from Whites, 79 %, 10% were Black and one Native American responded; seven percent were Hispanic. The average length of employment in the poultry industry was 4 years, the same as the cases. Almost 63% of them worked for at least 1-5 years and the length of employment ranged from 0-23 years. The average amount of years since last employment in the poultry industry was 22, ranging 13-33 years. Sixty percent of the controls smoked tobacco products and 40% never smoked. Table 7 presents the descriptive characteristics of the sub-cohort.

Table 7

Demographic characteristics of interviewed randomly sampled sub-cohort United Food and Commercial Worker poultry employees

Characteristic	n	%
Age [a]		
30-40	10	8.2
41-50	42	34.4
51-60	26	21.3
61-70	29	23.8
71+	15	12.3
Gender		
Male	47	37%
Female	81	63%
Characteristic	n	%
Race		
White	97	79.5
Black	24	19.7
Native American	1	.82
Ethnicity		
Hispanic	9	7.3
Non-Hispanic	113	92.7
Smoking Status		
Smoked Tobacco	77	60.2
Never Smoked Tobacco	51	39.8

a. Calculated by the years between date of birth- end of study, December 31, 2003

Table 8

Employment characteristics of interviewed randomly sampled sub-cohort United Food and Commercial Worker poultry employees

Characteristic	n	%
Duration of employment according to union record		
<1	21	21.9
1-5	60	62.5
6-10	10	10.4
>10	5	5.2
Years since last employment [b.]		
10-20	35	36.5
21-30	60	62.5
31-40	1	1

a. Years between date of last employment and end of study, December 31, 2003

Cases versus Controls Characteristics

Cases were compared to controls using chi-square tests on demographic, employment and smoking characteristics. Significant differences were observed in all demographic categories examined and in smoking status, as shown in Table 7. Responses from Blacks participating in the study came mostly from controls (75%, χ^2= 3.6, p = 0.05), although Blacks represent only 20% of the controls interviewed. The controls tended to be younger than the cases with 84% of the cases being age 50 or younger(χ^2= 21.1, p = <0.0001). The responses from the controls tended to come from females, 64%, and 72% of all female study participants were controls (χ^2= 12.2, p < 0.01). Responses from male controls were similar to the gender of the cases, 48% and 52% respectively. There were profound differences in the smoking status of the cases and controls. Only less than 8% of cases were never smoker while majority, 90%, of the never smokers were controls (χ^2= 25.9, p <0.0001). There were no significant differences in the duration of employment or the years since last employment in the poultry industry. Majority of the cases (53%) and controls (63%) were employed in the poultry industry between 1-5 years.

Table 9

Characteristics of Case vs. Controls

	Cases n(%)	Controls n(%)	χ^2	*p*-value
		Demographic		
	Race		3.6	0.054
White	74(43)	98(57)		
Black	8(25)	24(75)		
	Age[a]		21.1	<0.0001
≤50	10(16)	52(84)		
51+	72(50)	71(50)		
	Gender		12.2	0.0005
Female	32(28)	82(72)		
Male	50(52)	47(48)		
	Smoking Status		25.9	<0.0001
Ever Smoke	74(43)	77(49)		
Never Smoke	6(10)	51(90)		
		Employment		
Duration of Employment[b]			4.1	0.25
<1	15(36)	27(64)		
1-5	44(38)	71(62)		
6-10	16(53)	14(47)		
>10	6(27)	16(73)		
Years Since Last Employment[c]			3.5	0.17
10-20	42(43)	56(57)		
21-30	28(30)	65(70)		
30-40	3(30)	7(70)		

a. Cases (age at death); Control (age at time of interview)
b. Years according to union record
c. Years between date of last employment and end of study, December 31, 2003 or time of death, which ever came first

Objective 1

To examine the influence of occupational task related exposures on the risk of lung cancer mortality among poultry workers.

Crude Analyses (Unadjusted Risk Ratios)

Occupational task related exposures were investigated to examine the risk of lung cancer mortality in a cohort of poultry workers. Bivariate analyses were conducted to determine the effect of four occupational tasks exposures on lung cancer mortality in the poultry industry, previously found to be associated with an excess risk of lung cancer in the meat industry (Johnson, 1991); (McLean & Pearce, 2004); (Kristensen & Lynge, 1993). Table 10 reports the unadjusted risk ratios (RR) according to specific occupational task exposures.

Table 10

Crude Analyses of Occupational Task Exposures and Lung Cancer Mortality for Cases versus Controls

Exposure	n*	Risk Ratio	95% Confidence Limits (lower, upper)
Meat Curing Compounds	77	0.83	(.15, 4.66)
Transmissible Agents			
Kill Poultry	75	3.13	(1.09, 8.99)
Contact with Blood	70	2.06	(1.13, 3.73)
Contact with Raw Poultry	74	0.77	(0.43, 1.39)
Cut Raw Poultry	76	0.54	(0.30, 0.96)

Smoked Poultry	78	1.66	(0.10, 26.96)
		Wrapping Fumes	
Use Wrapping Machine	68	1.09	(0.51, 2.32)
Wrap Raw Poultry	68	0.67	(0.35, 1.29)
Complain of Fumes or Smoke	74	0.47	(0.20, 1.08)

* Number of deceased lung cancer cases

The crude analyses found an increased risk of lung cancer mortality among those that killed poultry (RR= 3.13, CI: 1.09, 8.99); had contact with blood (RR= 2.06, CI: 1.13, 3.73); smoked poultry (RR= 1.66, CI: 0.10, 26.96); and those that used a wrapping machine (RR= 1.09, CI: 0.51, 2.32). An additional analysis of all poultry-related exposures in the questionnaire and the risk of lung cancer mortality was conducted (data not shown) and an increased risk of lung cancer mortality was also observed in poultry workers that: caught live chickens (RR= 1.89, CI: 0.84 - 4.27); sprayed chemicals at a poultry farm (RR= 1.72, CI: 0.54 - 5.53); transported live poultry (RR= 1.43, CI: 0.46 - 4.27); and those who were exposed to feathers of poultry while at work (RR= 1.31, CI: 0.69 - 2.51).

Stratified analyses were conducted to explore stratum-specific risks and to determine if the crude risks were confounded and/or modified by covariates thought to be of importance in the relationship between occupational task exposures and lung cancer mortality.

*Stratified Analyses (*Mantel-*Haenszel Adjusted Risk Ratio)*

Due to the small number of subjects in each occupational task exposure many of strata were small and produced empty cells once stratified by the potential confounders. Sparse data within the stratum-specific categories made it impossible to calculate risk estimates when there were zero cell counts. Controlling for multiple confounders resulted in the additional loss of precision in some of the analyses, however the adjusted estimates were considered to be valid because they controlled for important factors that may have otherwise distorted the true estimate.

Although there were many instances when stratum-specific risk ratios (RR) were not computed, an adjusted risk ratio estimator was calculated through Mantel Haensezel stratified analyses. The Mantel-Haenszel risk ratio (RR_{MH}) measure is based on weights provided by the study population and remains valid in sparse data (Rothman, 1998) when the risk ratios are constant across the strata (Hosmer & Lemeshow, 2000). RR_{MH} was the most appropriate estimator to use because of its ability to provide an adjusted estimate despite zero cell counts. The covariate adjusted RR_{MH} used a correction of 0.5 for cells that contained zero subjects. A strata specific estimate was not calculated for data that contained a zero row or column; however an adjusted risk ratio was still computed because of the correction estimator feature.

Each occupational task exposure was stratified by the covariates thought to be of importance in the influence of lung cancer mortality: tobacco smoking, age, race, gender, and year of start of employment in the poultry industry. Tobacco smoking is a well established risk factor of lung cancer and meat workers are usually heavy smokers

(Coggon, et al.,1989). As with any chronic condition the risk of mortality increases with age, therefore age was a variable of interest in this investigation, particularly deaths occurring among those less than the age of 50 which is rare for lung cancer mortality. Consideration of race and sex was important because both are considered determinants of specific jobs within the poultry industry (Johnson, et al., 1995; Johnson & Fischman, 1982; Johnson, et al., 1986a, 1986b; Johnson, 1994a). Year of start of employment was important because occupational exposures are known to change over time because of improvements in technology and identification of hazardous exposures that can be prevented.

Multiple stratified analyses were conducted with varying grouping levels of covariates. Because of sparse data many covariate categories were collapsed or deleted. In general the covariates were dichotomized in order to obtain stratum-specific estimates; year of start of employment, however, was grouped into three categories to adjust for changes in occupational exposures due to time. Tobacco smoking was categorized as ever use or never use, age groups as age 50 and younger or age 51 and older, race as White or Black, gender as male or female, and year of start as 1956-1976, 1977-1980, and 1981-1988 based upon the distribution of subjects. For exposures pertaining to wrapping, the covariate year of start of employment was dichotomized into beginning employment prior to 1976 or after because of an industry wide change in wrapping machinery.

Transmissible agents. The strata-specific risks of lung cancer mortality among workers that killed poultry was highest among older respondents aged 51 and older that were nonsmokers RR= 6.50 (CI: 0.33, 126.06), smokers that started work between 1956 and 1976 RR= 5.42 (CI: 0.61, 47.83), White smokers RR= 4.75 (CI: 0.98, 23.03), and male smokers RR= 2.42 (CI: 0.45, 12.88). The Breslow-Day test of homogeneity of the risk ratio found no significant differences between the strata. Table 11 displays the tobacco smoking adjusted risk ratios for the suspected confounders.

Table 11

Mantel- Haenszel adjusted risk ratios of killing poultry and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	2.44	0.81 – 7.35
Race[a]	3.17	0.96 – 10.54
Age Group[b]	2.82	0.85 – 9.4
Start of Employment[c]	2.21	0.75 – 6.59

Note. All risk estimates were adjusted by tobacco smoking status.
a. White, Black, Other.
b. 50 or less years of age and 51 or more years of age.
c. 1956-1976, 1977-1980, 1981-1989.

There was no increased risk for cutting raw poultry was observed in the stratum-specific and adjusted estimates. Although the risk ratios tended to be depressed, with the exception of the stratum estimate for White smokers which was RR= 1.29, but not statistically significant, CI: 0.16 – 10.45. Each tobacco smoking adjusted estimate was close to the crude estimate of RR= 0.54 for all of the suspected confounding variables as shown in Table 12.

Table 12

Mantel- Haenszel adjusted risk ratios of cutting raw poultry and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	0.51*	0.27 – 0.96
Race[a]	0.44*	0.23 – 0.84
Age Group[b]	0.49*	0.25 – 0.94
Start of Employment[c]	0.42*	0.22 – 0.80

Note. All risk estimates were adjusted by tobacco smoking status.
* Statistically significant, $p < .05$.
a. White, Black, Other.
b. 50 or less years of age and 51 or more years of age.
c. 1956-1976, 1977-1980, 1981-1989.

Those that started work between 1956 and 1976 who were nonsmoker, RR = 1.5, CI: 0.17, 12.94 that had contact with raw poultry were the only strata to have elevated risks of lung cancer mortality, although it was not significant. The remaining stratum-specific risk ratios for were depressed. None of suspected confounders were effect measure modifiers according to the homogeneity tests. The tobacco smoking adjusted risk ratio estimates for the covariates ranged between 0.52 and 0.59. This suggested the possibility of confounding by some covariates when they were compared to the crude estimate of 0.77 for contact with raw poultry.

Table 13

Mantel- Haenszel adjusted risk ratios of contact with raw poultry and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	0.59	0.30 – 1.16
Race[a]	0.52	0.26 – 1.03
Age Group[b]	0.57	0.28 – 1.16
Start of Employment[c]	0.56	0.28 – 1.10

Note. All risk estimates were adjusted by tobacco smoking status.
a. White, Black, Other.
b. 50 or less years of age and 51 or more years of age.
c. 1956-1976, 1977-1980, 1981-1989.

Statistically significant increased risks of lung cancer mortality was seen in the strata of those that started employment between 1956 and 1976 who were smokers, RR= 4.14 (CI: 1.42, 12.09) and smokers aged 51 or older, RR= 2.58 (CI: 1.13, 5.90) that had contact with poultry blood. The covariate tobacco smoking adjusted estimates ranged for gender, race, and age group were statistically significant.

Table 14

Mantel- Haenszel adjusted risk ratios of contact with poultry blood and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	1.96*	1.02 – 3.77
Race[a]	2.06*	1.06 – 4.00
Age Group[b]	2.19*	1.09 – 4.42
Start of Employment[c]	1.75	0.92 – 3.33

Note. All risk estimates were adjusted by tobacco smoking status.
a. White, Black, Other.
b. 50 or less years of age and 51 or more years of age.
c. 1956-1976, 1977-1980, 1981-1989.

Wrapped poultry. There was no association between those that wrapped raw poultry and lung cancer mortality for any of the strata estimates. The tobacco smoking adjusted estimates for each of the potential confounders also did not show an association between wrapping raw poultry and lung cancer mortality as shown below in Table 15.

Table 15

Mantel- Haenszel adjusted risk ratios of wrapped raw poultry and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	0.70	0.34 – 1.45
Race[a]	0.58	0.28 – 1.17
Age Group[b]	0.56	0.26 – 1.18
Start of Employment[c]	0.57	0.28 – 1.16

Note. All risk estimates were adjusted by tobacco smoking status.
a. White, Black, Other.
b. 50 or less years of age and 51 or more years of age.
c. Prior to 1976 and After 1976

The use of wrapping machines showed a depressed risk for lung cancer mortality in Whites that smoked tobacco and a 2.7 times elevated risk in Blacks that smoked tobacco, not statistically significant. Respondents aged 50 and less that smoked had a slightly elevated risk 1.57 of lung cancer mortality if they used a wrapping machine, however it was not significant (CI: 0.23, 10.49). Controlling for tobacco smoking status and age, women who used the wrapping machine were 4.28 (CI: 1.14, 16.06) times more likely to die of lung cancer whereas, men who used a wrapping machine had no association with lung cancer mortality. Women who used the wrapping machine prior to 1976 after controlling for smoking had a 6.0 times increased risk of lung cancer mortality which was border line statistically significant (CI: 1.0 – 36.70) whereas those who reported using the machine after 1976 showed no association with lung cancer mortality.

Table 16

Mantel- Haenszel adjusted risk ratios of used wrapping machine and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	1.17	0.51 - 2.72
Race[a]	0.98	0.42 - 2.29
Age Group[b]	1.08	0.44 - 2.68
Start of Employment[c]	0.98	0.42 - 2.29

Note. All risk estimates were adjusted by tobacco smoking status.
a. White, Black, Other.
b. 50 or less years of age and 51 or more years of age.
c. Prior to 1976 and After 1976

A depressed risk of lung cancer mortality was observed across all stratum-specific odds ratios and adjusted odds ratios for workers that complained of fumes and smoke at work.

Table 17

Mantel- Haenszel adjusted risk ratios of those that complained of fumes and smoke and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	0.45	0.18 - 1.13
Race[a]	0.41	0.17 - 1.03
Age Group[b]	0.52	0.20 - 1.37
Start of Employment[c]	0.42	0.17 - 1.03

Note. All risk estimates were adjusted by tobacco smoking status.
a. White, Black, Other.
b. 50 or less years of age and 51 or more years of age.
c. Prior to 1976 and After 1976

Smoked poultry. The tobacco smoking adjusted Mantel-Haenszel risk ratio for smoked poultry were all slightly elevated, however none were statistically significant.

Table 18

Mantel- Haenszel adjusted risk ratios of those that smoked poultry and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	1.54	0.16 - 14.39
Race[a]	1.73	0.18 - 16.47
Age Group[b]	1.41	0.14 - 13.91
Start of Employment[c]	1.49	0.15 - 15.23

Note. All risk estimates were adjusted by tobacco smoking status.
a. White, Black, Other.
b. 50 or less years of age and 51 or more years of age.
c. 1956-1976, 1977-1980, 1981-1989.

Meat curing. Strata-specific results revealed that no women or individuals of races other than White cured meat. Additionally, risk ratios were not calculated for the strata's aged 50 and less, non-smokers, and those that started employment from 1981-1988. None of the covariates appeared to significantly modify the relationship between curing meat and lung cancer mortality according to the Breslow-Day tests for homogeneity of the risk ratios. Comparison of stratum-specific estimates and evaluation of the crude versus Mantel- Haenszel adjusted RRs for each of the covariates did not reveal confounding, however there were differences in the 95% confidence intervals.

Table 19

Mantel- Haenszel adjusted risk ratios of those that cured poultry and lung cancer mortality

Covariate	Risk Ratio	95% Confidence Limits
Gender	0.42	0.07 – 2.65
Race[a]	0.55	0.09 – 3.35
Age Group[b]	0.66	0.09 – 4.88
Start of Employment[c]	0.64	0.11 – 3.81

Note. All risk estimates were adjusted by tobacco smoking status.

a. White, Black, Other.

b. 50 or less years of age and 51 or more years of age.

c. 1956-1976, 1977-1980, 1981-1989.

Logistic Regression Analyses

The selection of the covariates included in the multivariable logistic regression models were based on prior knowledge of their influence on occupational task exposures in the poultry industry. The results of the stratified analyses provided insight on the occupational task exposure effect within the strata of the covariates with respect to the risk of lung cancer mortality. However, because of the lack of many stratum-specific estimates, and it's an inability to simultaneously control for multiple covariates, model fitting was conducted to adjust for confounding. All measured covariates thought to confound or modify the occupational task exposure and lung cancer mortality relationship: smoking status, gender, race, age group, and start group, were included in the full models and assessed for significance. A check of the collinearity diagnostics, tolerance and VIF, among the independent variables did not reveal any problems with multicollinearity. Variables to found to be important predictors of lung cancer mortality risk and those of biological importance remained in the final logistic regression models as shown below in Table 20.

Table 20

Final logistic regression models of lung cancer mortality for occupational task exposures in the poultry industry

Exposure	Risk Ratio	95% Confidence Limits (lower, upper)
Kill Poultry	2.72	0.79 - 9.34
Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status[a]	7.10	2.51 - 20.07
Age[b]	8.57	3.32 - 22.15
Gender[c]	2.82	1.37 - 5.78
Exposure	Risk Ratio	95% Confidence Limits (lower, upper)
Contact with Blood	2.44*	1.17- 5.09
Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status[a]	7.16	(2.48 – 20.65)
Age[b]	9.03	(3.44 – 23.75)
Gender[c]	2.98	(1.42 – 6.26)
Exposure	Risk Ratio	95% Confidence Limits (lower, upper)
Contact with Raw Poultry	0.69	0.33- 1.45

Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status[a]	7.54	2.65 - 21.49
Age[b]	8.75	3.37 – 22.73
Gender[c]	2.90	1.38 – 6.18
Exposure	Risk Ratio	95% Confidence Limits (lower, upper)
Cut Raw Poultry	0.60	0.30 – 1.20
Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status[a]	6.46	2.46 - 17.02
Age[b]	6.31	2.62 - 15.20
Gender[c]	2.80	1.36 - 5.73
Exposure	Risk Ratio	95% Confidence Limits (lower, upper)
Use Wrapping Machine	1.48	0.57 - 3.86
Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status	10.48	2.92 - 37.63
Tobacco Smoking Status[a]	11.48	4.09 - 32.27
Age[b]	4.33	1.99 - 9.43
Gender[c]	Risk Ratio	95% Confidence Limits (lower, upper)
Wrap Raw Poultry	0.71	0.32 – 1.58

Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status	7.73	2.49 - 23.96
Tobacco Smoking Status[a]	10.53	3.78 - 29.32
Age[b]	3.80	1.76 - 8.22
Gender[c]	Risk Ratio	95% Confidence Limits (lower, upper)
Complain of Fumes or Smoke	0.68	0.25 – 1.82
Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status	6.77	2.42 - 18.99
Tobacco Smoking Status[a]	7.44	2.96 - 18.70
Age[b]	3.26	1.58 - 6.72
Gender[c]	Risk Ratio	95% Confidence Limits (lower, upper)
Smoked Poultry	1.69	0.04 - 68.62
Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status[a]	7.39	2.63 - 20.72
Age[b]	8.04	3.25 - 19.85
Gender[c]	3.10	1.52 - 6.30
Exposure	Risk Ratio	95% Confidence Limits (lower, upper)
Meat Curing Compounds	0.64	0.09 - 4.56

Predictors	Risk Ratio	95% Confidence Limits (lower, upper)
Tobacco Smoking Status[a]	9.35	3.05 - 28.67
Age[b]	8.55	3.39 - 21.55
Gender[c]	3.50	1.67 - 7.32

* Statistically significant, $p < .05$.
a. Referent group is never tobacco smokers.
b. Referent group is 50 or less years of age.
c. Referent group is female.

Transmissible agents. The final model for killing poultry found a 2.7 times increased risk of lung cancer mortality ($\chi^2_{HL} = 3.34$ p= 0.77). The final logistic regression model for the exposure ever cut raw poultry was not significant, whereas in the full model containing the covariates tobacco smoking, age, gender, race and start of employment, the exposure of cutting raw poultry was associated with a decreased risk of lung cancer mortality. The predictors remaining in the fitted model, tobacco smoking status, age, and gender, revealed no association among individuals who cut raw poultry and lung cancer mortality after controlling for tobacco smoking, age, and gender. Smoking status, age group and gender remained significant predictors in a final fitting of the model contact with raw poultry and lung cancer mortality, respondents that did not have contact with raw poultry were 40% more likely to die of lung cancer than those that did. Following adjustment for smoking status, age group, and gender a significant, greater than twofold risk of lung cancer mortality remained for those that had contact with blood (RR= 2.44, CI: 1.17, 5.09).

Wrapping. For the logistic regression models of wrapping exposures a new start of employment group variable was created (prior to 1976 and post 1976) and included in the model because of a change in wrapping equipment in 1975 (Vandervort & Brooks, 1977) which reduced the amount of fumes emitted from the machine, which contained carcinogenic agents. The best fitting model of wrapping raw meat and the risk of lung cancer mortality controlled for smoking status, age group, and gender, all significant predictors of lung cancer mortality, RR= 0.71, there was no statistical advantage to include race or start of employment in the model. Those that used a wrapping machine to wrap raw meat had a slightly elevated risk of lung cancer mortality, RR= 1.48, although it was not significant, CI: 0.57- 3.86.

The final logistic regression model that controlled for tobacco smoking, age, and gender was chosen as the best fitting model for the exposure, those who complained of fumes and smoke. Race and start of employment were not significant predictors in the model,

Smoked poultry. Tobacco smoking status, age group and gender were significantly associated with smoking meat and lung cancer mortality; there were no significant interaction terms. The final logistic regression model included tobacco smoking status, age group and gender as significant predictors. The risk of lung cancer mortality was 1.7 among those that smoked poultry in comparison to those that did not controlling for smoking status, age group and gender, there were no significant differences between the observed and predicted values in the final model ($\chi^2_{HL} = 7.64$ $p = 0.18$).

Meat curing. In the saturated model containing all five of the covariates of interest and the exposure variable only two variables, smoking status and age group, showed evidence predicting of lung cancer mortality risk based upon inspection of the 95% Wald confidence interval estimates that did not contain the null value of 1. In the final logistic regression model it was found that individuals that cured meat were 69% less likely to die of lung cancer, though not statistically significant (RR = 0.31, CI: 0.04, 2.39), controlling for tobacco smoking status, gender, and age group. The Hosmer and Lemeshow's goodness-of-fit (χ^2_{HL}) statistic supports the fit of the reduced model containing smoking status and age group by indicating that the observed data do not differ significantly(χ^2_{HL} = 0.57 p= 0.90) from the expected values predicted by the model.

Objective 2

To investigate the occurrence of lung cancer mortality according to places of work that handled poultry.

Crude Analyses

The risk of lung cancer mortality was calculated using logistic regression models by the occupational activity of the employees' place of work. An unadjusted increased risk of lung cancer mortality was observed for the employees that ever worked in a deli department, place that smoked poultry, and on a commercial poultry farm, as shown in Table 21. The highest and only significantly elevated risks were observed for those that ever worked in a stockyard (RR= 13.75, CI: 2.92 – 64.69) and those that ever worked in the meat department of a supermarket (RR= 5.48, CI: 1.07 – 28.04). Working in the deli department of a supermarket was associated with greater than a twofold risk of lung cancer mortality and working in a place that smoked poultry or on a commercial poultry farm showed moderately elevated risks. Poultry slaughtering and processing plants were associated with decreased risks.

Table 21

Logistic regression models of lung cancer mortality and places of work in the poultry industry

Exposure	n*	RR 1	95% CI	RR 2	95% CI	RR 3	95% CI
Ever work in a stockyard	52	13.75	2.92-64.69	17.62	2.97-104.51	18.84	3.17-111.95
Ever work in a meat department of a supermarket	64	5.48	1.07-28.04	2.89	0.54-15.50	2.74	0.50-15.14
Ever work in a deli department of a supermarket	64	2.33	0.51-10.78	1.89	0.39-9.98	1.59	0.29-8.66
Ever work in a place that smoked poultry	54	1.32	0.21-8.15	1.76	0.23-13.47	1.25	0.16-9.78
Ever work on a commercial poultry farm	55	1.12	0.48-2.63	1.04	0.42-2.59	0.97	0.39-2.45
Ever work in a plant that slaughtered poultry	54	0.78	0.38-1.60	0.75	0.35-1.63	0.71	0.32-1.58
Ever work in a plant that processed poultry	59	0.55	0.28-1.09	0.46	0.21-1.0	0.47	0.21-1.04

* Number of lung cancer deaths
Referent group lacked the exposure of interest
RR 1 Crude risk ratio
RR 2 Risk ratio adjusted for smoking
RR 3 Risk ratio adjusted for smoking and years of employment (< 5 years and ≥5 years)

Adjusted Analyses

Following adjustment for tobacco smoking there was an increase in the risk of lung cancer mortality among one place of work, the stockyard. The risk of lung cancer mortality increased from 13.75 (CI: 2.92 - 64.69) to 17.62 (CI: 2.97 - 104.51) for those who reported ever working in a stockyard. The crude risk ratio was biased toward the null and smoking appears to be a confounder that masks the association of working in a stockyard and risk of lung cancer mortality. The remaining workplaces results in decreased risk after controlling for smoking. There was almost a threefold reduction in the risk of ever working in a meat department and lung cancer mortality after controlling for smoking from 5.48 (CI: 1.07 - 28.04) to 2.89 (CI: 0.54 – 15.50).

A similar pattern was seen in the increased risk of lung cancer mortality after adjusting for years of employment in addition to tobacco smoking for those who ever worked in a stockyard. The risk was further reduced for working in a meat department of a supermarket, deli department of a supermarket, and place that ever smoked poultry. For those that ever worked in a plant that slaughtered poultry there was reduction in the risk of lung cancer mortality. An inversion in the direction of association occurred in the risk estimate of ever work on a commercial poultry farm controlling for tobacco smoking and years of employment from a slightly increase risk in the crude and smoking adjusted estimates to a decreased risk when adjusting for smoking and years of employment simultaneously (RR= 0.97).

CHAPTER 5

DISCUSSION

This pilot study was conducted to examine the occupational risk of lung cancer mortality among a group of poultry workers exposed to hazardous agents. The study was analyzed as a case-control study of poultry workers, with a random sample of controls taken from the entire cohort and all deceased lung cancer cases were eligible for participation in the study. Due to the case-based sampling design the odds ratios calculated are unbiased estimates of risk ratios (Greenland & Thomas, 2003; Miettinen, 1976).

In the current study the highest occupational task risk factors of lung cancer mortality were found among those that killed poultry, had contact with poultry blood, smoked poultry, and those that used wrapping machines, after controlling for confounding factors. Although, having contact with blood was the only risk factor that was significantly elevated. An excess risk of lung cancer mortality was observed in places of employment among workers in stockyards, meat departments of supermarkets, deli departments, and places of work that smoked poultry, following adjustment for tobacco smoking and years of employment. The results of this study support those of earlier cohort follow ups of the Baltimore and Missouri cohorts, which also found elevated risks of lung cancer mortality in the same places of employment (Johnson, et al., 1986a, 1986b) (Johnson, 1989); (Johnson, 1991); (Johnson, 1994a; Johnson, et al., 1995);

(Johnson, et al., 1997; Netto & Johnson, 2003). Working in the stockyard was the only risk factor that was significantly associated with lung cancer mortality.

Contact with recently-slaughtered meat and an increased risk of lung cancer has been consistently observed in several studies (Boffetta et al., 2000; Coggon, et al., 1989; Guberan, et al., 1993; Gustavsson, et al., 1987; Johnson, 1994a; Johnson, et al., 1995; McLean, et al., 2004). However, none of these studies were able to control for smoking. Following adjustment for smoking and other confounders the current study found close to a threefold excess risk of lung cancer mortality among workers that killed poultry, which is higher than the findings of aforementioned studies in the meat industry. Meat workers, including poultry workers, come into contact with several hundreds or even thousands of animals that are slaughtered daily (Johnson, 2005). Their contact is very intimate and they are vulnerable to transmissible agents present in their work environment via multiple routes of exposure including inhalation, ingestion, and the skin. Exposure to animal blood increases the risk of infection with an oncogenic agent (Johnson, et al., 1997), which may possibly induce tumors in humans as well. The current results combined with evidence from other studies showing increased risk of lung cancer among recently-slaughtered meat are suggestive of an etiological role for biological agents. Further research is needed to investigate the specific biological agents that may be responsible for the excess risk of lung cancer among workers contacting recently killed animals. Contact with poultry blood was found to have a significant twofold risk of lung cancer mortality, following adjustment for smoking and other confounders. Although this risk is not as high as for those that killed poultry, it warrants attention for the possible role the exposures of biological agents may have in lung cancer occurrence. Avian leucosis sarcoma viruses and reticuloendothelisis cause cancer in poultry, and antibodies to these viruses have been detected in humans. However the there is a lack of epidemiological evidence that evaluates whether or not these viruses are oncogenic for humans (Johnson, 1994b). Additional research is needed to investigate theses viruses and other transmissible agents that may be involved in cancer risk among humans that are exposed to these agents. In the current study all workers were exposed to transmissible agents, thus an increased risk will be found only when compared to a truly unexposed group.

Chemical exposures in meat-processing industries such as those resulting from the curing or smoking of meat should not be excluded as a risk factor of lung cancer based upon the results of one study, as McLean and Pearce (2004) did in their review of cancer among meat industry workers. These authors did not mention in their review evidence from several studies that have found exposure to chemicals emitted from smoking of meat as an occupational risk factor of lung cancer in the meat industry (Colmsjö, Zebühr, & Östman, 1984); (Johnson, et al., 1995; Nordholm, Espensen, Jensen, & Holst, 1986) or studies that explored the frying of meat in formation of carcinogenic chemicals such as PAHs and heterocyclic amines(HAs) (Jakszyn et al., 2004; Wang, et al., 2001). Gustavsson et al.(1987) the authors of the study reviewed by McLean and Pearce (2004), cautioned readers in the interpretation of their results against smokehouse exposure and lung cancer risk because the study was limited to the tasks completed by butchers and slaughterhouse workers. The current study ascertained specific occupational task activities for all poultry workers regardless of their job classification. The occupational task of smoking poultry was found to have 1.7 times increased risk of lung cancer mortality, and meat wrapping, which has also been associated with increased lung cancer risk in the meat industry (Johnson, et al., 1986b), had an increased risk of 1.3 after adjustment for smoking and other confounders. These results were almost identical to the smoking and employment duration adjusted risk estimate for working in a place that smoked poultry, RR= 1.25.

Lung cancer mortality was not increased among those involved in meat curing. This decreased association may be due to the small number of poultry workers involved in this process, n=6, or because there is no true lung cancer risk due to nitrosamine exposure in the poultry industry. Meat curing occurs in the poultry industry, however, majority of the plants in this study were not involved in the curing process. There are no published studies that explored the occupational risk of nitrosamines formed during meat smoking and lung cancer mortality, although some authors have suggested carcinogenic effects on people who consume nitrite-treated meat products (Jakszyn et al., 2004; Sen, et al.,1974; Sen, Miles, Donaldson, Panalaks, & Iyengar, 1973). Future studies of nitrosamine exposure and lung cancer risk may best be explored in the pork packing plants where exposure to nitrosamines occur almost exclusively (Johnson, et al., 1995). The hypothesis of chemical exposures in the meat industry should be further examined, particularly among those at highest risk of exposure such as meat smokers.

In contrast to the current study's findings of increased lung cancer mortality risk among workers that killed and came in contact with blood, contact with raw poultry was not found to have a risk of lung cancer mortality for the exposures of cutting raw poultry and contact with raw poultry. It is possible that the decreased risks are due to the dissimilarity of the temperatures of the meat. Freshly-slaughtered meat is warm whereas meat that has already been butchered is likely to be chilled before it is further processed. Contact with raw poultry that has been chilled or was not freshly slaughtered was associated with a lesser risk of lung cancer than warm meat (Coggon, et al., 1989) in a previous investigation. Additionally, the reduced risk in the current study may be due to the small sample size, or there may have been misclassification of the exposure by the proxies.

Using a wrapping machine was associated with a threefold increased risk of lung cancer mortality among females in this study; although there were decreased risks for related occupational exposures of wrapping raw poultry and complaining of fumes or smoke. Polyvinyl chloride films are used to wrap meat in the poultry industry is usually conducted by rolling the film over a hot wire or cool rod machine (Johnson et al., 1999). If a person wrapped poultry using one of the above mentioned wrapping machines they were likely exposed to fumes when the plastic was heated prior to cutting. Therefore, it was expected that the findings of using a wrapping machine would be similar to those who complained of fumes and smoke at work; however that was not the case in this investigation.

Meat wrapping often occurs in the meat department of supermarkets. Lung cancer mortality was associated with a 3.18 times increased risk among females working in the meat department after controlling for smoking which was almost identical to the task exposure of using a wrapping machine for females. These data support the hypothesis that fumes emitted form the thermal decomposition of plastic increases the risk of lung cancer death as found by Fritschi et al. (2004). The relationship appears to be stronger in women, who are more likely to have this occupational exposure. In the initial Baltimore cohort study female poultry workers had a four-fold risk of lung cancer mortality (Johnson, et al.,1986b). This risk was reduced to RR= 1.5 for women overall in the update prior to this one, which followed up the cohort until 1989 (Johnson, et al., 1997). It is possible that these reductions in lung cancer mortality risk are a result of changes in exposure due to the replacement of wrapping machines in the mid 1970's. A previous investigation of meat workers (Johnson, et al.,1986b) showed an excess risk in lung cancer mortality ranging between 8.0 and 52.9 for employees under age 50 that work in meat packing and chicken plants that was not similar to lung cancer deaths observed in the general population (Johnson, et al.,1986b). Strata-specific estimates for workers age 50 and less in the meat department was not computed in the current investigation because of sparse data. The association of wrapping raw meat and the risk of lung cancer mortality warrants further investigation in other studies. Particular attention in these investigations should be directed toward women and those aged less than 50.

The lack of association of lung cancer mortality with the exposures of wrapping meat and complaining of fumes and smoke at work may be the result of chance or response bias if the proxies did not correctly recall the exposures, which in turn may have lead to differential misclassification of the occupational task exposure in the case group. It is possible that the non-association may have been due to workers that wrapped poultry using mechanical cutting as opposed to hot wire or cool rod machines. Alternatively, if we were to assume that the exposure of using a wrapping machine, which revealed an increased risk of lung cancer mortality, was not true, it is possible that this exposure was misclassified because the cases thought that use of the machine was influential in their deceased relative's lung cancer status and lead to an spurious estimation. However, the findings of the wrapping machine exposure are likely real due to their consistency with the results found in the current investigation for working in the meat department, external studies that have found comparable results (Johnson, 1994a; Johnson, et al., 1986b) and because of evidence of the carcinogens released during the use of the machines (IARC, 1973; O'Mara, 1970; Vandervort & Brooks, 1977). A disadvantage to the current study is the group unexposed to fumes was exposed to other harmful exposures like viruses that have a high risk of lung cancer. Using a referent group outside the poultry industry would have provided a group of truly unexposed individuals.

The inverse associations of the exposures ever wrapping poultry and complaining of fumes or smoke association with lung cancer mortality cannot be fully explained by the current data and is debatable. The proxies may not have understood or known about these particular questions, which could explain why their responses differed from the responses attained from the question about use of the wrapping machine. The results of the decreased risk of working in a plant that slaughtered or processed poultry are also questionable and are likely due to misclassification of the exposure by the proxies because they do not coincide with the observed increased risks from the occupational tasks that occur in these industries such as killing poultry and having contact with blood

Working in the stockyard provides exposure to live poultry, and the excess risk of lung cancer mortality in this group corroborates the elevated risks found in occupational task exposures associated with live poultry such as killing and contact with blood. Additionally, the current study's findings are quite similar to meat industry studies of cattle, pigs, and sheep that specifically examined live animal exposure (Coggon, et al., 1989; Durusoy et al., 2005; Fox, et al., 1982; Johnson, 1991). All of the aforementioned studies found the strongest associations for lung cancer mortality were among workers involved with killing or handling live animals. The apparent protective effect of smoking on lung cancer mortality risk in slaughterhouse workers is paradoxical. Tobacco smoking is the strongest, most established risk factor for lung cancer mortality. The change in risk estimate increased from the crude value of 13.8 to 17.6 following control for tobacco smoking. The results of this particular association should be interpreted with caution because tobacco smoking appeared to be a negative confounder. Upon investigation of the stratum-specific estimates of tobacco smoking and the relationship between working in stockyard and the risk of lung cancer mortality, this increase in the risk estimate was likely due to very sparse data in the strata.

Limitations

A main limitation of the current study was its small sample size, which was attributed to the low response rate for both the cases and controls. This was a pilot study and exhaustive attempts were not made to trace the subjects. A large proportion of the next of kin proxies and controls were not traceable due to changes in addresses and telephone numbers from moving, no current telephone or because of disconnected numbers. Because of the inability to find matches during the initial tracing process, a second random sample was drawn in an attempt to successfully find more matches. It is unlikely that participation in this investigation was a result of selection bias. There did not appear to be a differential motivation to participate between the case proxies and the controls; the underlying issue for lack of participation was positively identifying a match. Identifying a match was also limited by the completeness of union records. If the name, date of birth, social security number or other identifying information listed in the union record was incorrect, it was difficult to locate the actual individual. This was particularly a problem in identifying female members of the cohort by name because of changes in surname since union membership due to marriages and divorces. If a match was located, the individual generally agreed to participate in the study. The response rate after a match was found was 80%. The major reason for non-participation of the matches was they did not want to commit to the length of time that it would take to complete the questionnaire, which was approximately 45 minutes to an hour. Alternative methods of tracing individuals are currently being explored to ascertain a higher proportion of matches.

The data were limited by the accuracy of self-reports and proxy-reported information. Incomplete reporting by the proxies on exposure history of the cases or misclassification of the exposure as non-exposed may have negatively biased the study results toward the null. Alternatively, the recall of exposures that the proxies perceived to have influenced lung cancer mortality may have resulted in an overestimation of the risk for some occupational task exposures biasing the risk estimates away from the null. There may have been differential recall between the responses given by the next of kin proxies and live controls. The live controls may have given more detailed information on the exposure; therefore, the current investigation did not include the variables related to time and duration of exposure collected from the respondents, although they were included in the questionnaire. Lack of consideration of time involved with a specific occupational task is a weakness of the current study. Duration of union membership was used as a measurement of overall time of employment however; the period of union membership may not be an accurate surrogate for the duration of employment (Johnson, et al., 1986b). It is possible that the workers did not join the union at the start of their employment or they may have become inactive with the union but continued to work in the industry. Also, active union membership for the Baltimore cohort was not updated after 1979 and it is possible that some of these workers continued to work up until 1989.

It was expected that because the controls were the actual poultry employees their responses would be more accurate than the proxies with respect to specific occupational task specific measures such as how long they worked doing a task and the specific activities involved with the tasks. The issue of occupational task misclassification could have been addressed with the cooperation of the former employer to allow us to review company records to confirm or refute the self-reported responses. On the other hand the self-reported information may be more accurate depending on the thoroughness of record keeping by the company. The questions pertaining to occupational history in the questionnaire were designed to ascertain general task exposure and should not have been too difficult for the next-of-kin proxy to respond. Job title recall has been proven to be highly valid in retrospective case referent studies (Ahrens & Merletti, 1998). Recall is more difficult as time increases. This investigation restricted the lung cancer deaths to only those occurring in the past 18 years in an attempt to reduce this information bias.

The occupational task exposures are not mutually exclusive and some of these employees had multiple jobs, and therefore multiple exposures, within this industry, in this case the risk ratios may have been incorrectly estimated because of overlaps of exposures. By using poultry workers as the control group it is possible that the risk estimates presented in the current study are underestimates of the true occupational risk in this population. Despite participation in specific occupational tasks, all poultry workers are exposed to oncogenic agents present in poultry slaughtering and processing plants, just at different levels of exposure. An additional investigation is currently underway in this population using members of the same cohort who are "truly unexposed" which includes workers in fish, bottling, and soft drink manufacturing companies as a comparison group. By using these less exposed members of the cohort as a referent group, a possible dose-response relation between occupational exposure and lung cancer mortality will be examined.

Strengths

The current study was the first examination of lung cancer mortality among poultry workers. Despite its limitations, there were considerable strengths. Majority of the previous investigations of lung cancer mortality in the meat industry were cohort studies that did not allow for the control of any level of tobacco smoking. The results of the present investigation confirm the previous findings of the meat industry, which show an excess risk of lung cancer not due to confounding by tobacco smoking. The risk of developing lung cancer sharply increases when smokers are exposed in a occupation with a known risk of lung cancer (Yoder, 2003). Cigar and pipe smoking are both established causes of lung cancer (Boffetta et al., 1999) however, they are less than the risks associated with cigarette smoking because of differences in smoking frequency and depth of inhalation (Alberg & Samet, 2003). In the current study, tobacco smoking status was measured by ever versus never smoke tobacco products. This measurement was chosen for the analyses as opposed to other smoking-related variables that were measured in the questionnaire because it did not restrict the assessment of tobacco smoking to a particular type of tobacco product. The similarities of the estimated effect of occupational tasks exposure from studies using different methodologies in both the meat and poultry industries over the past 25 years involving different populations of workers enhance the causal inference of certain occupational risks.

The ascertainment of detailed demographic and employment variables in the current study supported its ability to control for variables thought to be confounders, in addition to smoking. Assessment of exposures based on individual job-specific tasks was limited in previous investigations of lung cancer mortality in the meat industry and typically grouped into broad categories. While earlier cohort investigations have directed attention toward the excess risk of lung cancer mortality in the meat industry, the data are limited on knowledge of possible etiologic agents that contribute to the increased risks observed. The current study brings attention to specific activities that may be involved with exposure to causative agents. The efficiency of this study design as a case-cohort versus the previous cohort studies allowed for a collection of individual data on the lung cancer cases in the cohort and the random sample of the entire cohort. The design of this study as a case-cohort also allowed for a direct estimation of the risk ratio in the base population without having to employ a full cohort investigation, thereby conserving resources and time.

Recommendations

The general population is commonly exposed to some of the same potentially harmful agents that poultry workers are exposed to through contact with poultry and poultry products, although it is likely that the highest human exposure to poultry oncogenic viruses and other carcinogenic transmissible agents occurs in poultry slaughtering/processing plants. It is of public health importance to investigate the potential carcinogenicity of poultry agents. Poultry workers are well suited to investigate the effect of human exposure to possible cancer causing agents because of their elevated exposure. There is a need for additional investigations of the causal role of occupational task exposures and cancer risk in this occupational group. Although the results of the current study should be interpreted with caution of the small sample size, there are numerous consistencies of the results with other studies that have also observed strong associations (risk estimates greater than 2) between risk of lung cancer mortality and occupational exposures in the meat industry. These substantial associations, which remain after adjustment for confounders, are likely not due to chance. Overall this is a young cohort with a relatively few deaths in comparison to the size of the cohort. Future follow-up is needed and should focus on the potential risks by classification of plant-specific operations, time and duration of occupational task exposure, and tobacco usage duration and quantity of to gain a more in-depth assessment of lung cancer risk to poultry related occupational exposures.

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APPENDIX A

STAGES OF LUNG CANCER

APPENDIX A

Table A1

Non-Small Cell Lung Cancer

Stage	Description
Stage I a/b	Tumor of any size is found only in the lung
Stage II a/b	Tumor has spread to lymph nodes associated with the lung
Stage III a	Tumor has spread to the lymph nodes in the tracheal area, including chest wall and diaphragm
Stage III b	Tumor has spread to the lymph nodes on the opposite lung or in the neck
Stage IV	Tumor has spread beyond the chest

Table A2

Small Cell Lung Cancer

Stage	Description
Limited	Tumor is found in one lung and in nearby lymph nodes
Extensive	Tumor has spread beyond one lung or to other organs

Tables A1 and A2 modified from Cancer*Care*. Lung Cancer 101.

http://www.lungcancer.org/patients/lc_101/lc_101_staging.htm

APPENDIX B

EMPLOYER DESCRIPTION

APPENDIX B

EMPLOYER DESCRIPTION

Sub-Cohort	Employer	Plant Activity
Baltimore	Cross & Blackwell	Soups, oysters, chunks of meat
Baltimore	Essday Cordova Poultry	Poultry/ Meat Processing, Slaughtering
Baltimore	Lord Mott & Co.	Canning pork, meat, beans, soup
Baltimore	Mcgee	Oyster
Baltimore	McGrath Cannery	Soup, small meat, canning
Baltimore	Pacific Hawaiian Punch	soft drink manufacturing
Baltimore	RAC	Turkey boning
Baltimore	Suburban Club	soft drink manufacturing
Baltimore	Caplan	Chicken packing
Baltimore	Coca Cola Bottling Co	soft drink manufacturing
Baltimore	Dover Poultry	Poultry manufacturing, slaughtering, processing
Baltimore	J.H. Filbert's Inc.	Margarine, mayonnaise
Baltimore	Manor Hill Salad Co.	Salad
Baltimore	Royal Crown	soft drink manufacturing
Baltimore	Southern States Coop	Fertilizer, seed
Baltimore	Wilchrome	Chrome furniture manufacturing
Pension Fund	Bluewater Seafood	Fishery
Pension Fund	Burhops Inc.	Fishery
Pension Fund	Clearfield Cheese	Cheese
Pension Fund	Container Corp of Am	Fishery
Pension Fund	Country Pride	Poultry slaughter and processing
Pension Fund	Crown Cork & Seal	Corks and seal
Pension Fund	El Charitto	Fishery
Pension Fund	Empire Fishery Co	Fishery

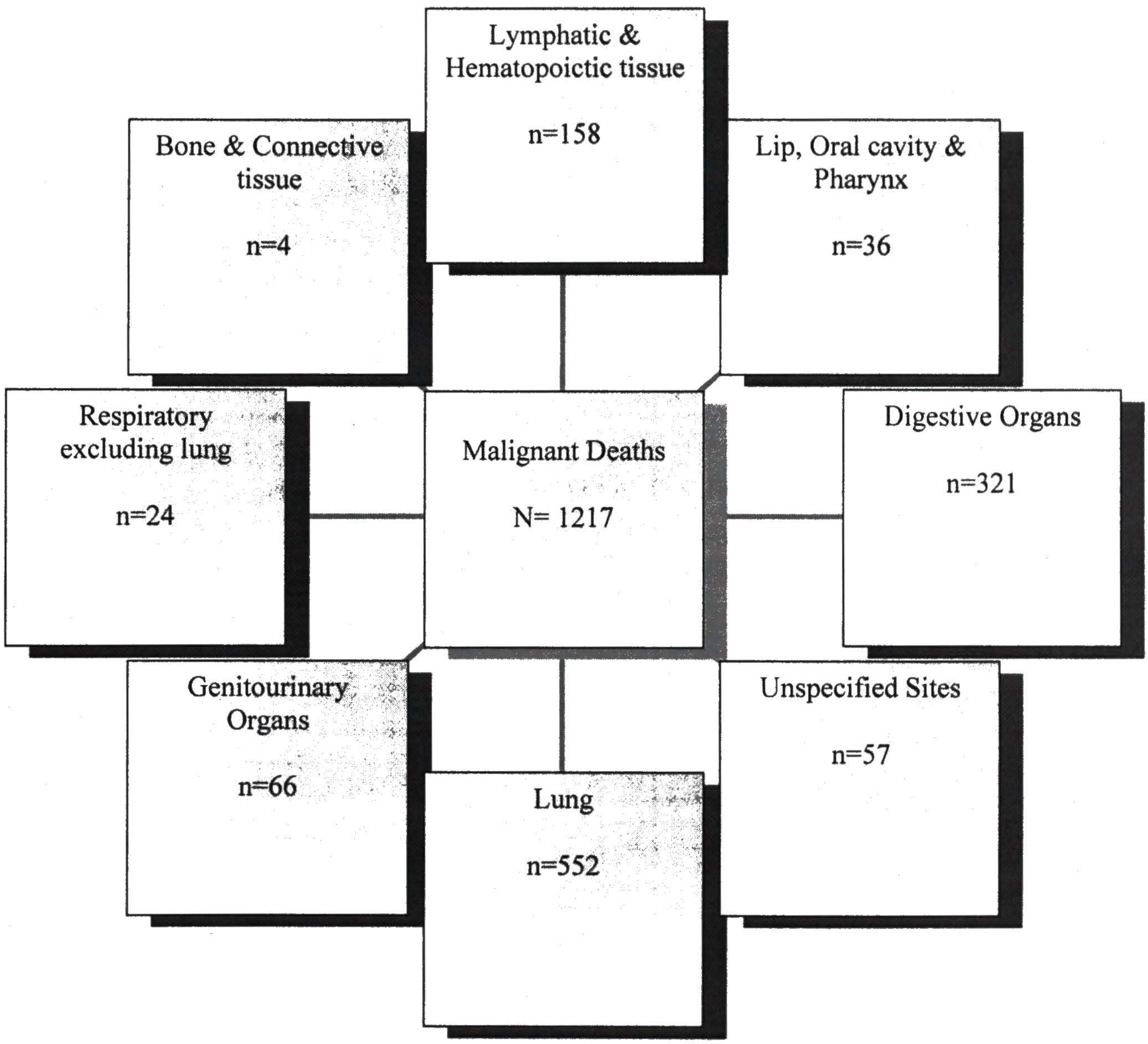
Sub-Cohort	Employer	Plant Activity
Pension Fund	Gorton Shrimp Products	Fishery
Pension Fund	Goya Foods	Fishery
Pension Fund	Handover Brands	Fishery
Pension Fund	Hillcrest Food	Poultry/ meats/ food service distribution
Pension Fund	J & M Inc.	Poultry/ meat packaging, processing
Pension Fund	Kroger Egg	Egg plant
Pension Fund	La Choy Food Product	Fishery
Pension Fund	Maplewood Packing	Poultry Packing
Pension Fund	O'Donnell Usen	Fishery
Pension Fund	Penobscot Poultry	Poultry broiler/ processing plant
Pension Fund	Pluss Tex Poultry	Poultry processing, distribution, preparation, packaging
Pension Fund	Ryan Milk	Milk
Pension Fund	Val-Mac Ind.	Poultry slaughter and processing
Missouri	Carrollton	Poultry processing, packaging, distribution
Missouri	Macon	Poultry/ meat packaging, processing
Missouri	Marshall	Poultry processing, packaging, distribution
Missouri	Milan	Poultry processing, packaging, distribution
Missouri	Moberly	Poultry/ meat packaging, processing, slaughtering

APPENDIX C

MALIGNANT MORTALITY 1990-2003

APPENDIX C

MALIGANT MORTALITY 1990-2003

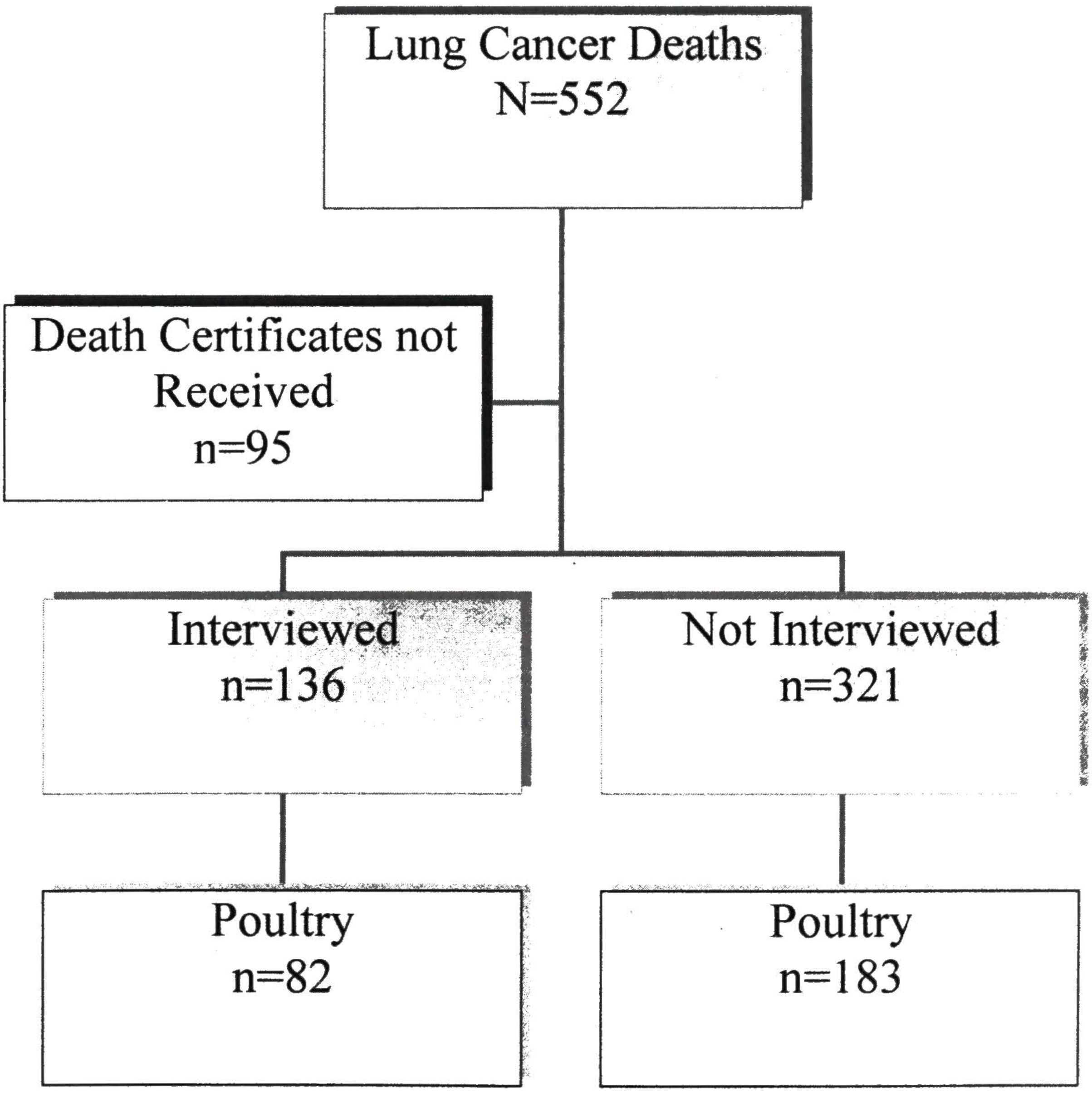


APPENDIX D

MALIGNANT LUNG MORTALITY 1990-2003

APPENDIX D

MALIGANT LUNG MORTALITY 1990-2003



APPENDIX E

INSTITUTIONAL REVIEW BOARD APPROVAL

UNIVERSITY *of* NORTH TEXAS HEALTH SCIENCE CENTER *at Fort Worth*
TEXAS COLLEGE OF OSTEOPATHIC MEDICINE
INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS

BOARD ACTION

IRB PROJECT #: 2007-127 DATE SUBMITTED: April 22, 2008

PRINCIPAL INVESTIGATOR: Eric Johnson, MD, PhD (with doctoral student Nykiconia Preacely)

PROJECT TITLE: Lung Cancer Risk Among Workers in Poultry Slaughtering and Processing Plants: A Pilot Study

PROTOCOL #: ____

DEPARTMENT: Epidemiology / SPH TELEPHONE EXTENSION: ____

In accordance with UNT Health Science Center policy on the protection of human subjects, the following action has been taken on the above referenced project:

Approval, when given, is **only** for the project as submitted. **No changes** may be implemented without first receiving IRB review and approval.

____ Project has received approval through ____.

____ Informed Consent approved as submitted on ____. You **MUST** use this version (attached) rather than previously approved versions. In addition, only consent documents which bear the official UNTHSC IRB approval stamp can be used with subjects.

____ Study Protocol dated ____ approved as submitted.

____ Protocol Synopsis approved as submitted on ____.

____ Amendment ____ to the protocol approved as submitted.

____ Based upon the recently completed Continuing Review (IRB Form 4), project has received continued approval through ____.

____ Project has been reviewed. In order to receive approval, you must incorporate the attached modifications. You must submit one "highlighted" copy and one "clean" copy of the revised protocol synopsis, informed consent and advertisements to the IRB for review. YOU MAY NOT BEGIN YOUR PROJECT UNTIL NOTIFIED BY THE IRB.

____ Consideration of the project has been tabled pending resolution of the issue(s) outlined below.

____ Project is disapproved for the reason(s) outlined below.

____ Completion of project is acknowledged and all required paperwork has been received.

✓ Special Findings:

Revised protocol title from "Malignant and Non-Malignant Mortality among United States Poultry Workers" to new title (noted above) "Lung Cancer Risk Among Workers in Poultry Slaughtering and Processing Plants: A Pilot Study" approved as submitted.

Chairman, Institutional Review Board

April 23, 2008
Date

IRB Form 2 revised 12-03 MA 04-1487