TITLE PAGE

A) FINAL PROGRESS REPORT FOR GRANT

Title: "Cancer and Non-cancer Mortality in Meat Workers"

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Principal Investigator: Eric S. Johnson, M.D., Ph.D., M.P.H., D.T.P.H.
University of North Texas Health Science Center
Department of Epidemiology, School of Public Health,
UNT Health Science Center
3500 Camp Bowie Blvd.
Fort Worth
TX 76107
Phone: 817 735 0327
E-mail: Eric.Johnson@UNTHSC.edu

Co-investigators:
Karan Singh, Ph.D. Statistician
Harrison Ndetan Dr.P.H., Computer Programmer, UNT Health Science Center
Martha Felini, PhD. Project Coordinator

TABLE OF CONTENTS

LIST OF TERMS & ABBREVIATIONS

Cohort
Mortality
Cancer
Non-malignant Disease
Transmissible Agents
Oncogenic Viruses
Polycyclic Aromatic Hydrocarbons
Nitrosamines
Benzene
Phthalates
Fat/Cooking Aerosols
Smoke
Wrapping Machine
Curing
Risk
Standardized Mortality Ratio
Proportional Mortality ratio
Follow-up
Tracing
Occupational
Workers
Exposure
Case-cohort
Cattle
Pigs
Sheep
Food Animals
Neurologic Diseases

ABSTRACT

This project investigates mortality in a cohort of workers in the meat industry identified from a meatcutters' union in Baltimore, because they were exposed at work to transmissible agents that are known to infect or cause cancer and other diseases in cattle, pigs and sheep, and were also occupationally exposed to known chemical carcinogens. The study is of importance as it adds to the growing evidence that meat workers are at increased risks of developing cancer and other diseases. Workers in the meat industry who handle cattle, pigs and sheep or their raw products are heavily exposed to a plethora of transmissible agents such as prions, viruses, bacteria, protozoa, etc., that are known to cause disease in these animals, including cancer and neurologic diseases. For example, bovine leukemia virus (BLV) commonly infects and causes lymphosarcoma in cattle and sheep, and the prevalence of infection in herds can be as high as over 40% (Burny and Mammerickx, 1987). Lung cancer in sheep is caused by the jaagsiekte sheep retrovirus (Palmarini & Fan, 2001). Prion agents cause the subacute severe neurologic disease known as bovine spongiform encephalopathy (BSE) or 'mad cow' disease in cattle, and scrapie in sheep. In an epidemic of BSE in the United Kingdom more than one-third of dairy herds were affected and over 200,000 animals died (Belkin, 2003). BSE prion is believed to be the cause of a variant of Creutzfeldt-Jakob disease (vCJD) in humans (Weihl & Roos, 1999). Losses in sheep from scrapie can vary from 15 to over 20% annually (Gravenoret al, 2004). There is historical and current evidence that some of these agents are transmissible to workers and subjects in the general population, and cause zoonotic acute infection and disease in them such as leptospirosis, Q-fever, brucellosis, vesicular stomatitis, etc., as reviewed in Johnson (1984). However, although the acute effects of exposure to some of these agents are well established, the long-term effects of the majority have received little attention. It is not known for example whether those microbial agents which cause cancer and other diseases in cattle, pigs and sheep also cause cancer in humans. The study thus has implications not only for the workers but also for the general population who are also exposed to these agents through contact with live animals and their raw products, and ingestion of raw or inadequately cooked meat products.

Cohort mortality studies have been the mainstay for evaluating cancer and other chronic disease risks in subjects resulting from exposures in the workplace. They have proven effective and reliable in detecting the carcinogenic effects of agents such as asbestos, benzene, aniline dyes, etc. in workers. They have also been the main sources of the epidemiologic evidence that these agents are carcinogenic in humans. They have led to regulatory actions that have resulted in the dramatic reduction of such harmful exposures in the workplace, hence succeeded in protecting workers' health. However, although a large number of these studies have been conducted in various occupational and industrial groups, much attention has not been paid in the United States to workers in the meat industry who are highly exposed to transmissible agents known to be potent causes of cancer, neurologic diseases such as 'mad cow' disease, and other severe infectious diseases in the animals they handle at work.

To investigate if exposure to transmissible agents present in food animals at work is associated with excess occurrence of cancer and other diseases, we initially studied mortality (cancer and non-cancer) for the period 1949 to 1989 in an exposed cohort of 19,849 subjects who worked in abattoirs/slaughterhouses, beef and pork processing plants, and supermarkets, where exposure to these transmissible agents occurred, from handling cattle, pigs and sheep or their products, and an unexposed control group of 6,149 subjects without such exposures (Johnson 1994; Johnson et al, 1995; Johnson et al, 2007a; Johnson et al, 2007b). Exposed and unexposed subjects were identified from the rosters of a local meatcutters' union in Baltimore, Maryland. Compared to the United States general population, and the internal control group, excess risks of certain causes of death including cancers were observed in the exposed meat workers cohort. Because only 25% of the study population had died at the time, and there were not enough deaths to adequately investigate cancer and other less common chronic diseases in the initial study, for this current grant award, we updated mortality in the cohorts through the end of 2006, during which time a total of 12,931 deaths (50%) had occurred, and we examined mortality risk for a total of 185 individual causes of death as compared to 60 causes of death investigated in previous studies. "Infectious Diseases" is a NIOSH priority area. This new study confirmed that several cancers and other chronic diseases Including neurological diseases, were occurring in excess in the exposed cohort, as well as identifying new causes occurring in excess. The excesses included lung cancer, cancer of the buccal cavity & pharynx, colon cancer, cancer of the esophagus, as well as diseases such as

bacterial diseases, infections, diabetes and kidney diseases, including neurological diseases such as senile and pre-senile psychotic conditions (Alzheimer's disease). These results are very interesting, but it is not known from this type of study the specific exposure(s) responsible in each case, and confounding factors were not controlled for. Now that this large study has demonstrated clearly that these workers are dying at excessive rates from particular causes of death, it is now urgently required for proper, large-scale studies that are adequately designed to find out the specific exposure(s) responsible such as nested case-control studies to be carried out in future.

SECTION 1

HIGHLIGHTS/SIGNIFICANT FINDINGS

Statistically significant excess occurrences of deaths from several causes, including cancers, neurologic, cardiovascular and other diseases, were observed in the cohort as a whole and in all major subgroups of the industry. It is concluded that this large study has succeeded in establishing that workers in the meat industry have increased risk of dying from these diseases. Infectious or other transmissible agents present in the animals and their raw products that the workers are exposed to, are most likely the primary causes of these excesses. This has important public health implications, since subjects in the general population are also exposed to these transmissible agents. Thus it is possible also that some of the chronic diseases in the general population of unknown etiology may be caused by transmissible agents present in animals used for food such as cattle, pigs, sheep and goats. In the case of the excess cancer occurrence observed, apart from transmissible agents, other occupational carcinogenic chemicals some of the workers are also exposed to, may also be involved. There is urgent need for measures to be taken to reduce or eliminate exposure to these disease-causing agents in the workplace so that workers can be protected. Studies are now needed to identify the specific transmissible agents responsible.

TRANSLATION OF FINDINGS

1) Engineering and ventilation controls and best practices should be introduced to further minimize aerosol transmission of transmissible agents throughout the meat industry workplace, and to minimize airborne exposure to aerosols fumes and smoke from the wrapping machine and during smoking and frying of poultry.

2) The continued use of the “hot wire” and “cool rod” wrapping machine should be effectively terminated and these machines replaced with ones that do not involve thermal decomposition of the plastic film used to wrap meat, e.g., use of a mechanical blade to cut the film, as previously recommended.

3) Educate workers, employers and unions on the potential hazards associated with various tasks and exposures within the industry and measures to be taken to protect workers.

4) Provide workers with appropriate protective equipment and body wear such as special gloves that will protect them against injury from knives, mechanical saws, and sharp bone splinters, to minimize entry of microorganisms into the body.

5) Efforts should be made to eradicate, control or reduce infectious agents in cattle, pigs, sheep, and other food animals in general, in farms prior to slaughter.

6) The use of closed oven systems for smoking and frying meat that do not involve worker exposure to smoke should be universally adopted.

7) Contact with live animals, and slaughtering activities which are known to associated with the highest exposures to transmissible agents and the highest risks of some of the diseases observed to be occurring in excess should be particularly targeted for control measures.

OUTCOMES/RELEVANCE/IMPACT

This study has succeeded in definitively confirming that chronic diseases such as certain cancers, neurologic , cardiovascular, and other diseases are occurring in excess in meat workers. This was possible because every worker in the study was observed for at least between 28 – 58 years i.e., more than adequate time for an occupationally induced cancer or other chronic diseases to develop from the time of first exposure. Also virtually half of the cohort (49.7%) have died, thus the causes of deaths observed to be occurring in excess probably represent all the major causes associated with increased occupational risks. The findings of adverse outcomes (cancer & non-cancer) some of which are expected to be related to occupational exposure to transmissible agents in these workers have far-reaching implications beyond the occupational setting, since exposure to transmissible agents in food animals and animal food products is virtually universal in the general population. It is believed the study has contributed significantly in potentially identifying a major cause(s) of cancer and other diseases not only in the working population but also in the general population. There is need for studies that will carry out industrial hygiene measurements and carefully characterize the potential harmful exposures in this industry in detail, so that at-risk workers can be identified and appropriate measures taken to adequately protect them. It is to be pointed out that industrial hygiene assessments of exposure to infectious agents in the workplace in general, is poorly developed and needs to be improved. It should be realized that with respect to cancers there are other known carcinogenic exposures in the meat industry associated with jobs such as smoking, cooking, curing, and wrapping of meat. We could not assess the role these other exposures play, because typically for tasks such as smoking and curing of meat, only a few workers are involved, and much larger study sizes and different study designs than used here are necessary if the effects of these other exposures, if any, are to be adequately assessed. Epidemiologic and laboratory-based studies are urgently needed that will begin to attempt to identify which specific biological or chemical agent is the cause of the excess occurrence of these diseases. Thus the potential impact of this study is immense from both the occupational and public health perspectives.

SECTION 2

SCIENTIFIC REPORT

Background

Evidence is accumulating from our studies and those outside the United States that workers who handle cattle, pigs and sheep in the meat industry are at increased risk of chronic diseases, including cancer and non-cancer. These workers have one of the highest human exposures to the oncogenic viruses and other transmissible agents of cattle, pigs, and sheep. Thus if these agents cause disease in humans, this group is an ideal group to carry out such an investigation. Our studies have been at the vanguard of this investigation. Many of the studies conducted thus far elsewhere have not had sufficient statistical power to adequately investigate risk. Our current study is the largest thus far.

Specific Aims

1. To update mortality in 4,996 slaughterhouse workers, 3,642 workers in beef processing plants, 510 workers in pork processing plants, and 10,701 workers in the meat department of supermarkets, who were exposed to the transmissible agents of cattle, pigs and sheep. Their mortality pattern will be compared to that of the United States general population, as well as separately to that of their fellow 6,149 unexposed non-meat workers in the same union. Mortality in these 25,998 workers was previously studied for the period 1949 to 1989, during which time only about 20% of the cohort had died (Johnson et al 1986a; Johnson et al 1986b; Johnson 1987; Johnson 1989; Johnson, 1994; Johnson et al 1995; Johnson 2007a; Johnson 2007b). In this proposal, follow-up will be extended from 1990 to the end of 2006 and mortality determined for the period 1949-2006, by which time it is estimated at least half of the cohort would have died, and the minimum interval between exposure and death for any individual in the cohort (latency) would be at least 28 years. Increased risk of death from specific causes will be identified through the estimation of standardized mortality ratios (SMR), proportional mortality ratios (PMR), using the United States general population as comparison as well as the unexposed control group from the same union.

2. At the end of the proposed study, we plan to do the following: 1) to apply for separate funding to conduct a case-cohort study of causes of death for which a statistically significant excess risk is observed, in which detailed information on exposures and potentially confounding factors will be obtained by means of a questionnaire administered to the workers directly, or to their next-of-kin; 2) to obtain paraffin tumor blocks of workers who died of cancer sites observed to be occurring in excess in this proposed study. These blocks will be used in laboratory-based molecular studies planned in the future to detect the presence of viruses integrated within the DNA of these samples. These laboratory studies will be used to confirm the epidemiologic findings and ultimately provide the definitive proof that these viruses cause cancer in workers.

Methods

Description of the Baltimore Meatcutters' Union

The cohort studied was derived from 28,900 subjects who were members of the local Baltimore Meatcutters' union (Local 27) at any time between July 1, 1949 and December 31, 1979, which is a chartered member of the United Food & Commercial Workers (UFCW) International Union. Ninety-four percent of the members lived in the State of Maryland (84% resided within the Baltimore metropolitan area), and the rest lived in the adjacent areas of the neighboring States of Delaware (2%), Pennsylvania, Virginia and West Virginia (1%), and 3% had unknown residence. Membership in the union was compulsory within 30 days of date of hire. The study population for the research reported here was defined as the 19,849 exposed subjects who throughout their membership in the union had worked exclusively in only one of four departments where exposure to the transmissible agents of cattle, pigs and sheep occurred and an unexposed control group of 6,149 subjects from non-meat companies in the union such as soft drinks manufacturing and oyster shocking, making a total of 25,998 study subjects altogether. The exposed group of 19,849 individuals was made up of, 1) workers in abattoirs/slaughterhouses (N=4.996); 2) workers in beef processing plants (N=3,642); 3) workers in pork processing plants (N=510); and 4) workers in the meat department of

supermarkets (N=10,701). Information available on cohort members include gender, social security number, dates of birth, section of the meat industry (departments), dates of membership in the union, place of residence (city/town, county, state), name and address of next-of-kin. The cohort was initially followed up on two previous occasions for the occurrence of cancer and other causes for the period 1949 to the end of 1989, by which time 20% of the cohort had died. For the current grant, follow-up was updated to the end of 2006, and at the end of the follow-up, over 49.7% of the cohort had died.

The cohort was followed up for the occurrence of death through the use of various tracing methods (union records, the National Death Index - Plus, the Pension Benefit Information Company, personal contact (telephone, mailing, post office, etc.), credit bureau, Maryland Department of Vital Records, Maryland Department of Motor Vehicles, and internet sources such as "Public Records Now" and "Ancestry.com". All study subjects not identified as deceased were assumed to be alive at the end of the study.

Using a computer program (OCMAP Plus) for analyzing occupational cohort studies developed by the University of Pittsburgh, risk of death was primarily measured by estimation of Standardized Mortality Ratios (SMR) and Proportional Mortality Ratios (PMR), with the United States general population as the comparison group, and simultaneously controlling for race, sex, age, and calendar time. The SMR and PMR analyses were conducted separately for 1) workers in abattoirs or slaughterhouses where cattle, pigs or sheep were slaughtered or slaughtered and processed; 2) workers in beef processing plants where mainly cattle carcasses were processed (no killing performed); 3) workers in pork processing plants where pig carcasses were processed (no killing performed); 4) workers in the meat department of supermarkets where raw meat products from cattle, pigs, sheep, poultry, etc., were handled; and 5) for a control group of non-meat workers who worked in jobs such as oyster shucking, soft drinks manufacturing, soup canning, etc.

For this report, we present only separate results for all workers combined who worked in each of these four sections of the meat industry. The results for detailed subgroup analyses by race and gender are summarized only briefly as they will be presented in publications at a later date, since both gender and race are usually associated with specific exposures in the industry (e.g. wrappers in supermarkets were predominantly females, meatcutters in supermarkets were nearly all males and nearly all white**).**

Results

A. Cancer Results

The results for cancers and non-cancers are given in the Tables 1 & 2 below:

1) Cattle, Pig, & Sheep Abattoirs/Slaughterhouses

The main findings are that mortality from all causes of death was significantly elevated. The only elevated SMR that was statistically significant was observed for cancer of the trachea, bronchus and lung. Similarly, significantly depressed SMRs were observed only for cancers of the thymus, heart & mediastinum; and breast.

2) Beef Processing Plants

Both all-causes mortality and all-cancer mortality were significantly elevated in this group of workers. In addition, statistically significant SMRS that were elevated were observed for cancer of the base of the tongue; and cancer of the trachea, bronchus & lung.

3) Pork Processing Plants

All-causes mortality was significantly elevated in this group of workers as well. In addition, the SMRs for cancer of the trachea, bronchus & lung and cancer of the colon were significantly elevated.

4) Meat department of Supermarkets

All-causes mortality was significantly elevated in workers. Cancers of the tonsil and oropharynx; trachea, bronchus & lung; and benign neoplasms of the thyroid and other endocrine glands were significantly elevated also. Significantly depressed SMRs were recorded for cancers of the stomach; thymus, heart, & mediastinum; breast; and other specified and unspecified types of leukemia.

5) Non-Meat control Group

None of the cancers that were significantly elevated in any of the exposed groups (1-4) was significantly elevated in the control group.

The results provide strong evidence that lung cancer occurrence is in excess in meat workers throughout the industry, as the excess was evident in al workers combined in each of the four major exposed groups, but not in the control group. On the other hand, excess of cancer of the base of the tongue seems confined to workers in beef processing plants, while cancer of the colon is restricted to workers in pork processing plants, and cancer of the tonsils & oropharynx is confined to workers in the meat department of supermarkets. These results appear specific for these locations, and none of these sites was significantly in excess in the control group.

In addition although not shown in the Tables, significant excess occurrence of certain cancers were observed that were restricted to only certain race/sex subgroups: 1) in abattoirs, cancer of the bladder in white males and cancer of the esophagus in white females were significantly in excess; 2) in beef processing plants, cancer of the esophagus was in excess in non-white males; 3) in supermarkets, cancer of the gall bladder was significantly in excess in white males.

These results on the whole may be reflective of particular jobs that were specific for these race/sex subgroups and plants. It is well known that exposures vary by race and sex in the meat industry in the United States. Occupational exposures especially oncogenic viruses are most likely responsible for the excess occurrence of some of these cancer types, and other candidate carcinogenic exposures that occur in the workplace such as polycyclic aromatic hydrocarbons (PAH) during the smoking and frying of meat products, heterocyclic amines during the frying of meat products, nitrosamines during the curing of meat, and benzene, PAH and phthalates emitted from the wrapping machine, may also be contributory (Boettner & Ball, 1980; IARC, 1973; IARC 1985; IARC 1987; Jakszyn et al, 2004; Johnson et al 1986a; Johnson et al 1986b; Johnson et al 1999; Johnson et al,2007c; Nordholm et al, 1986; Sen et al 1973; Vainotolo et al, 1993; Vandervort & Brooks, 1977) However, this study was a retrospective cohort mortality study, and this design does not normally lend itself to cause-and-effect inferences, since it was not possible to control for occupational and non-occupational confounding factors. However, the study is important. It is the largest study of these workers to date, and it clearly demonstrates excess occurrence of several cancers in meat workers, and the findings for some of the diseases like lung cancer have been reported in other similar studies internationally (Coggon et al 1989; Guberan et al, 1993; McClean et al 2004). Moreover, pilot nested case-control studies of lung cancer we have previously conducted in this cohort (Johnson, 1991), and in a combined poultry cohort (Felini et al, 2010 - manuscript re-submitted in response to reviewers' comments) in which we were able to adjust for tobacco smoking, have shown that the excess of lung cancer in the meat and poultry industries is not due to tobacco smoking. Rather, jobs associated with high exposure to oncogenic viruses, such as working in the stockyard and killing and dressing animals had the highest risks of the disease. Thus what is needed now are large nested case-control or case-cohort studies of the cancers observed to be occurring in excess in this cohort study, that have sufficient statistical power. These studies will have the capacity to adequately investigate the more rare occupational exposures such as smoking and curing of meat on which information was lacking from the pilot studies, while at the same time adequately controlling for occupational and non-occupational confounding factors. Such studies are urgently needed so that the right decisions can be made to adequately protect workers. These studies will also have profound public health effect for the general population if the oncogenic viruses of cattle, poultry, pigs and sheep are found to cause cancer in humans also.

B. Non-cancer Results

1) Cattle, Pig, & Sheep Abattoirs/Slaughterhouses

Significantly elevated SMRs were observed for other bacterial diseases; other diseases of the kidney & ureter; and diabetes. Significantly depressed SMRs were observed for functional diseases of the heart; occlusion/stenosis of the pre-cerebral and cerebral arteries; and accidents (including accidental poisoning and suicide).

2) Beef Processing Plants

Increased SMRs that were statistically significant were observed for other bacterial diseases; intracranial & intraspinal abcess; and acute rheumatic fever. Significantly depressed SMRs were recorded for occlusion/stenosis of the pre-cerebral and cerebral arteries; and accidents (including accidental poisoning and suicide).

3) Pork Processing Plants

Elevated SMRs that were significant were recorded for senile & pre-senile psychotic condition; acute rheumatic fever; and pneumonia. Significantly depressed SMRs were observed for occlusion/stenosis of the pre-cerebral and cerebral arteries; and transport accidents.

4) Meat department of Supermarkets

Statistically significantly elevated SMRs were observed for other bacterial diseases; intracranial & intraspinal abcesses; ischemic heart disease; and peritonitis, while the SMRs for functional diseases of the heart and accidents (including accidental poisoning and suicide), were significantly depressed.

5) Non-Meat control Group

The SMRs for certain zoonotic bacterial diseases; and other bacterial diseases; were significantly elevated, while those for senile &pre-senile psychotic conditions; occlusion/stenosis of the pre-cerebral and cerebral arteries; and accidents (including accidental poisoning and suicide) were significantly depressed.

Deaths from other bacterial diseases were the only cause of death which was significantly elevated in any of the exposed groups and also significantly elevated in the control group.

Discussion

The results provide strong evidence that infections and infectious diseases as expected were clearly occurring in excess in meat workers (other bacterial diseases; intracranial & intraspinal abcesses; acute rheumatic fever, pneumonia; and peritonitis. The excess of other bacterial diseases was observed in all exposed groups, and apart from sample size considerations for pork processing plants, this was also true for intracranial & intraspinal abcesses, and possibly acute rheumatic fever also. This lends support to the notion that infectious agents may be involved in the excess occurrence of both cancer and non-cancer deaths observed in the exposed cohorts. Infections could play a role also in the excess occurrence of other diseases of the kidney and ureter. Interesting findings for which an infectious etiology is not previously established were the excess occurrences of diabetes, senile and pre-senile psychotic conditions, and ischemic hear disease. The cohort appears to have low risk of dying from various accidents. As mentioned above under cancers, what are needed now are large nested case-control studies or case-cohort studies of sufficient statistical power to investigate these observed associations here in greater detail while adequately controlling for occupational and non-occupational confounding factors. As for cancers, the public health implications for the general population are profound if exposure to transmissible agents found in food animals are later found to be implicated in chronic human diseases. The ultimate proof that transmissible agents are involved in some of these diseases will be forthcoming in the laboratory-based molecular and serologic studies, and we plan to apply for funding to conduct these types of studies in the near future. It will be possible in these types of studies to identify the specific agent responsible for causing a specific disease(s).

In spite of its design, this cohort mortality study gives important clues as to specific causes of the excess risks observed. For example, an increase of risk due to transmissible agents will be most evident and highest among workers in slaughterhouses where exposure to these agents is highest. Thus risk for a particular cause of death that is highest in slaughterhouse workers would be most likely due to transmissible agents. Increased risk due to exposures associated with smoking of meat (PAH) and curing of meat (nitrosamines) will be most evident in pig processing plants where these exposures typically occur. Increased risk due to fumes from the wrapping machine will be most evident in women in supermarkets since this is the only activity they perform all day long. More detailed and more accurate assessment of risk due to specific exposures will be possible when a separate case-cohort study or nested case-control studies that will also control for occupation and non-occupational confounding factors are conducted within the cohort at a later date. Also, investigation of dose-response relations by duration of exposure which was

not possible in this cohort study, will be possible in these nested case-control types of study in which detailed personal exposure histories will be obtained for each individual. Surrogate dose-response analyses of a sort are still possible in this cohort mortality study. For example, for exposure to transmissible agents we will carry out analyses in which the relative risk for a given disease obtained by comparing the most highly exposed group of slaughterhouse workers with the non-meat control group is compared with that obtained for comparing the next highly exposed group of workers in meat processing plants with the control group, and with that obtained for comparing the least exposed group of supermarket workers with the control group thus allowing for a type of dose-response analysis.

Advantages & Limitations

One unique feature of the cohort is that it was completely defined. All subjects who had ever been a member of the union since its inception in 1939 and were alive in 1949 (the start of observation for the study) were included even if they were members for less than a week. This is possible because the union had a policy not to discard any records. If clerks made an error in completing a union application form or registration form and had to complete a new one, the old one is voided but retained. The principal investigator was able to verify the completeness of this cohort through cross-checking across various types of records and thoroughly examining their record, archives. Thus selection bias arising from an incompletely defined study population is unlikely in this study. The cohort study itself has tremendous power as we have shown above. It is the largest ever in this industry with an observation period spanning the period 1949-2006, with at least over 14,000 deaths occurring in all, and the minimum latency period for any subject in the study of 28 years and can be as large as 56 years, hence adequate for detecting any occupationally induced chronic diseases. None of the other published cohorts in the industry come close in size to it, hence this study has the best chance of investigating cancer and other causes of death in this industry. Furthermore the proposed examination of risk of death from 185 cancer and non-cancer causes is unique in occupational cohort mortality studies. As mentioned above, in the previous follow-up only 25% of the cohort had died, while in this proposed update considerable ageing of the cohort is expected to have taken place since, about half of the cohort (49.7%) are now deceased. Such benefits that would be derived from this study far outweigh any deficiencies that would be present. It is worthwhile noting that this is the only study of mortality from cancers and non-cancers in workers in the industry in the United States to date. All attempts by us over the past 20 years to define an occupational cohort for study from company records have been unsuccessful, as the industry has repeatedly refused access to their workers for this type of investigation. This could partly explain why no one else has studied this industry in the United States. Thus the proposed cohort with its limitations is the only source of information on long-term health effects of exposures in this industry, and is the largest and most informative cohort available to date world-wide. Limitations include lack of controlling for confounding factors, inadequate sample size for some deaths or some subgroups, no dose response analysis possible, and lack of exposure information.

The completed update of this cohort will enable us to retrieve more recent biological samples (paraffin tumor blocks of biopsy and autopsy tissues) that are needed for the molecular laboratory investigation to detect these agents in the DNA of tumor tissue from subjects dying from diseases observed to be occurring in excess in the cohort. The availability of recent samples in which the DNA has not deteriorated will be crucial in this investigation.

Conclusion

This study found that meat workers employed in cattle, pigs and sheep slaughtering and processing plants and in the meat department of supermarkets are at increased risk of dying from several cancers and non-cancers, including neurologic, metabolic and cardiovascular diseases. It is not known which specific workplace exposures are responsible, or whether non-occupational factors could be contributory. However, evidence available from the literature clearly indicates that transmissible agents are the predominant important exposure for consideration to explain at least some of the excesses. This has both profound occupational and public health implications, since the general population is also exposed to these agents. Studies are needed to adequately characterize industrial hygiene assessment of the various exposures in the industry. Methods to assess exposure to infectious agents need to be developed. Nested case-control studies of adequate statistical power are needed. Similarly, case-control or case-cohort studies nested within very large meat workers cohorts are urgently needed that could adequately investigate risks within the industry while controlling for confounding factors. Laboratory-based molecular and serological

studies in humans are urgently needed to provide the critical evidence needed to implicate specific organisms in the etiology of the diseases observed to be occurring in excess in this cohort of meat workers. There is now sufficient evidence available for the meat industry and the United Food & Commercial Workers union to start taking measures to protect workers from potentially harmful exposures in the industry.

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Table 1. Standardized Mortality Ratios for Selected Tumors for the Period 1950 to 2006 – BALTIMORE WORKERS

Cause of death [Malignant and non-malignant tumors]	Abattoir N = 4,996	Beef Processing Plants N = 3,642	Pork Processing Plants N = 510	Meat Department of Supermarkets N = 10,701	Nonmeat N = 6,149
	Obs. SMR (95% CI)	Obs. SMR (95% CI)	Obs. SMR (95% CI)	Obs. SMR (95% CI)	Obs. SMR (95% CI)
All malignant tumors ICD 140-208	773 1.07 (0.99 - 1.14)	575 1.12 (1.03 – 1.22)	48 1.14 (0.84 – 1.51)	1082 1.04 (0.98 – 1.10)	651 0.97 (0.90 – 1.05)
Tongue: base; other and unspec ICD 14X	2 0.55 (0.07 – 2.00)	8 3.13 (1.35 – 6.17)	0 - (0.00 – 15.22)	5 1.06 (0.34 – 2.46)	2 0.62 (0.08 – 2.23)
Tonsil. oropharynx ICD 14X	0 - (0.00 – 1.64)	2 1.21 (0.15 – 4.37)	0 - (0.00 – 19.48)	8 2.71 (1.17 – 5.34)	6 2.64 (0.97 – 5.74)
Stomach ICD 151	31 1.25 (0.85 – 1.78)	16 0.92 (0.52 – 1.49)	1 0.64 (0.02 – 3.56)	17 0.60 (0.35 – 0.97)	27 1.12 (0.74 – 1.63)
Colon ICD 153	63 1.02 (0.78 – 1.30)	47 1.08 (0.80 – 1.44)	9 2.67 (1.22 – 5.07)	89 1.03 (0.83 – 1.27)	57 0.98 (0.75 – 1.27)
Trachea, bronchus, lung ICD 162	279 1.26 (1.11 - 1.41)	233 1.52 (1.33 – 1.72)	21 1.76 (1.09 – 2.68)	415 1.32(1.20 – 1.45)	205 1.13 (0.98 – 1.30)
Thymus, heart, mediastinum, pleura, etc. ICD 163-165	2 0.22 (0.03 – 0.80)	2 0.36 (0.04 – 1.31)	0 - (0.00 – 16.04)	3 0.33 (0.07 – 0.96)	2 0.41 (0.05 – 1.48)
Breast	16 0.61 (0.35 – 0.996)	25 0.98 (0.63 – 1.44)	2 0.59 (0.07 – 2.13)	52 0.73 (0.55 – 0.96)	45 0.88 (0.64 – 1.17)
Other specified type/ unspec type of leukemia	4 0.59 (0.16 – 1.50)	2 0.43 (0.05 – 1.56)	0 - (0.00 – 12.18)	3 0.31 (0.07 – 0.92)	4 0.72 (0.20 – 1.85)
Non-malignant tumors					
Benign neoplasm of thyroid, other unspec. Endocrine ICD 226-227	2 7.51 (0.91 – 27.11)	0 - (0.00 – 18.30)	0 - (0.00 – 155.26)	4 11.12 (3.03 – 28.46)	0 - (0.00 – 1121)
All causes	3,045 1.08 (1.04 – 1.12)	2,314 1.17 (1.13 – 1.22)	231 1.38 (1.21 – 1.57)	4,270 1.13 (1.10 – 1.17)	3,071 1.15 (1.11 – 1.19)

* Figures in parentheses are confidence intervals

Table 2. Standardized Mortality Ratios for Non-malignant Diseases for the Period 1950 to 2006 – BALTIMORE WORKERS

Cause of death [Malignant and non-malignant tumors]	Abattoir N = 4,996	Beef Processing Plants N = 3,642	Pork Processing Plants N = 510	Meat Department of Supermarkets N = 10,701	Nonmeat N = 6,149
	Obs. SMR (95% CI)	Obs. SMR (95% CI)	Obs. SMR (95% CI)	Obs. SMR (95% CI)	Obs. SMR (95% CI)
Intestinal Infectious Diseases ICD	3 1.93 (0.40 – 5.64)	3 2.76 0.57 – 8.06)	0 - (0.00 – 46.39)	2 0.90 (0.11 – 3.24)	1 0.69 (0.02 – 3.83)
Certain Zoonotic Bacterial Diseases ICD	0 - (0.00 – 39.47)	0 - (0.00 – 55.68)	0 - (0.00 - 553.07)	1 7.78 (0.19 – 43.32)	2 21.64 (2.62 – 78.18)
Other Bacterial Diseases ICD	43 1.80 (1.31 – 2.43)	30 1.69 (1.14 – 2.41)	4 2.04 (0.56 – 5.24)	50 1.55 (1.14 – 2.04)	46 1.56 (1.14 – 2.08)
Diabetes ICD 250	83 1.30 (1.04 – 1.61)	53 1.11 (0.84 – 1.46)	5 0.91 (0.30 – 2.12)	110 1.19 (0.98 – 1.43)	76 0.92 (0.73 – 1.15)
Schizophrenic Disorders ICD 295	1 3.10 (0.08 – 17.27)	1 4.20 (0.11 – 23.42)	0 - (0.0 – 160.11)	1 2.02 0.05 – 77.00)	0 - (0.00 – 10.38)
Senile & Pre-senile Psychotic Conditions ICD	22 0.90 (0.56 – 1.36)	15 0.87 (0.50 – 1.44)	4 5.11 (1.39 – 13.07)	37 1.26 (0.89 – 1.73)	12 0.55 (0.29 – 0.97)
Intracranial & Intraspinal Abcess ICD	1 2.55 (0.06 – 14.18)	3 10.20 (2.11 – 29.82)	0 - (0.00 – 98.56)	4 7.17 1.95 – 18.36)	0 - (0.00 – 8.20)
Acute Rheumatic Fever ICD	0 - (0.0 – 16.23)	2 12.02 (1.46 – 43.43)	1 66.23 (1.66 – 369.01)	1 3.36 0.08 – 18.70)	0 - (0.00 – 16.67)
Ischemic Heart Disease ICD	759 1.04 (0.97 – 1.12)	505 1.04 (0.96 – 1.14)	35 1.15 (0.80 – 1.60)	984 1.11 (1.04 – 1.18)	588 1.02 (0.94 – 1.11)
Functional Diseases of Heart ICD	34 0.60 (0.42 – 0.84)	37 0.91 (0.64 – 1.25)	1 0.27 (0.01 – 1.53)	38 0.50 (0.36 – 0.69)	51 0.85 (0.63 – 1.11)
Intracerebral Hemorrhage etc ICD					37 0.81 (0.57 – 1.11)
Occlusion/stenosis pre-cerebral and cerebral arteries ICD	32 0.38 (0.26 – 0.54)	20 0.34 0.21 – 0.52)	0 - (0.00 – 0.77)	69 0.64 (0.50 – 18.38)	53 0.60 (0.45 – 0.78)
Pneumonia ICD	60 0.80 (0.61 – 1.03)	49 0.92 (0.0.10 – 2.93)	10 2.61 (1.25 – 4.800	93 1.09 (0.88 – 1.34)	66 0.97 (0.75 – 1.23)
Peritonitis ICD	1 0.57 (0.01 – 3.19)	1 0.78 (0.02 – 4.33)	0 - (0.00 – 26.58)	9 3.66 (1.67 – 6.95)	3 1.53 (0.32 – 4.48)
Other Diseases of Kidney & Ureter ICD	12 3.02 (1.56 – 5.27)	4 1.30 (0.36 – 3.34)	0 - (0.00 – 8.63)	8 1.78 (0.77 – 3.51)	11 1.96 (0.98 – 3.51)
Transport accidents ICD	4 0.08 (0.02 – 0.21)	1 0.03 (0.00 – 0.17)	0 - (0.00 – 0.89)	9 0.10 (0.05 – 0.19)	2 0.04 (0.01 – 0.14)
Accidental Poisoning by Solid, Liquid, Gas, Vapor	0 - (0.00 – 0.59)	1 0.23 0.01 – 1.25)	0 - (0.00 – 3.85)	0 - (0.00 – 0.26)	0 - (0.00 – 0.38)
Accidental Falls ICD	5 0.28 (0.09 – 0.66)	1 0.08 0.00 – 0.45)	0 - (0.00 – 3.96)	3 0.13 (0.03 – 0.38)	2 0.13 (0.02 – 0.48)
Other Accidents ICD	2 0.07 (0.01 – 0.27)	2 0.09 0.01 – 0.37)	0 - (0.00 – 1.72)	7 0.17 (0.07 – 1.14)	4 0.14 (0.04 – 0.36)
Suicide & Self-inflicted Injury ICD	2 0.06 0.01 – 0.20)	0 - (0.000.16)	0 - (0.00 – 1.92)	4 0.06 0.02 – 0.15)	0 - (0.00 – 0.12)
All causes	3,045 1.08 (1.04 – 1.12)	2,314 1.17 (1.13 – 1.22)	231 1.38 (1.21 – 1.57)	4,270 1.13 (1.10 – 1.17)	3,071 1.15 (1.11 – 1.19)

* Figures in parentheses are confidence intervals

Publications
Manuscripts are being prepared for publication. Cancer and non-cancer findings may be published separately for each of the four major exposed groups, thus 6- 8 publications are expected. These will constitute the main findings. In addition, we have already submitted two manuscripts that are currently under journal review of subcohorts in the fish and soup manufacturing industries that were derived from the unexposed comparison group in this study.

Inclusion of Gender & Minority Study Subjects
The study population is estimated from death certificates to be 57.0% white men; 18.6% black men; 19.4% white women; and 5% black women, with date of birth ranging from 1874 to 1960. This probably reflects the true make-up of the union. Over 90% of the workers in the industry in the study area are members of the union.

Inclusion of Children
This is an occupational study, and all subjects are between the ages of 45 and 121 years.

Materials Available for Other Investigators
All findings will be published in peer-reviewed journals, and copies of publications are routinely sent to the local union involved in the study (Local 27, Baltimore), and the International United Food & Commercial Workers Union in Washington D.C.

Final FSR
Sent separately

Final Invention Statement
There are no inventions arising from this project