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UNIVERSITY OF CALIFORNIA,
IRVINE

Cancer Risks in Shipyard Workers Exposed to Asbestos and Welding Fumes

DISSERTATION

submitted in partial satisfaction of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

in Epidemiology

by

Citadel Jungco Cabasag

Dissertation Committee:
Professor Hoda-Anton Culver, Chair
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2016

DEDICATION

To

All the women of color in science who came before me and paved the path for women like myself and the next generation of women.

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ABSTRACT OF THE DISSERTATION

Cancer Risk in Shipyard Workers Exposed to Asbestos and Welding Fumes

By

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Doctor of Philosophy in Epidemiology

University of California, Irvine, 2016

Professor Hoda Anton-Culver, Chair

The association between asbestos exposure and lung cancer, as well as between asbestos exposure and mesothelioma, had long since been established, while the relationship between asbestos exposure and other types of malignancies remains unclear. Aside from asbestos, numerous other potential exposures are present in the shipyard. Several occupations are exposed to substances such as welding fumes. The purpose of this dissertation is to examine the association between occupational agents in the Long Beach Naval shipyard and the health outcomes experienced by the workers employed in the shipyard. The study will assess the relationship between asbestos exposure and colorectal cancer by asbestos exposures levels, as well as, the incidence and mortality rates of lung cancer in relation to the exposure to welding fumes.

The leading causes of deaths and the incidence of cancers was evaluated in 13,924 shipyard workers employed in the Long Beach Naval shipyard employed between 1978 and 1985. Mortality data (1978-2013) was ascertained through the California Deaths Statistical Master files. The incidence of cancer (1988-2011) was ascertained through the California cancer

registry. Workers were classified into low, intermediate, and high asbestos exposure groups. Workers were also separated into exposed versus non-exposed to examine the effects of welding fumes exposure. Age-specific standardized mortality ratio and age-specific standardized incidence ratio for cancer were calculated using the general population of the state of California as the standard population. The Kaplan-Meier method was used to determine the time until occurrence of disease for colorectal cancer and lung cancer among workers exposed to asbestos and workers exposed to welding fumes.

The leading causes of deaths in the Long Beach Naval shipyard included diseases of the circulatory and neoplasms. There was excess mortality and incidence of cancer in the study cohort including excess mesothelioma, lung, and colorectal cancer. Excess incidence of mesothelioma were observed in all three asbestos exposure groups. The study found no statistical difference in the time to disease occurrence between exposure groups for colorectal and lung cancer outcomes. This study showed that employment in the Long Beach Naval shipyard increased workers' risk to a wide variety of cancers including asbestos-related malignancies.

CHAPTER 1

Introduction

In the past, the shipyard industry employed a large population of workers in the United States as well as internationally. In the U.S., the Naval Shipyard Complex (NSC) employed both military and civilian personnel. At its peak, the NSC consisted of over 353,000 workers coming from a wide variety of occupations.[1]

Prior to 1970s, asbestos materials were widely used in the shipyard industry, primarily as an insulating and fireproofing agent, exposing many shipyard workers who had either direct or indirect contact with these materials. Early studies on shipyard workers that emerged in the 1960s, such as one by Harries involving H.M. Dockyard in Devonport, Great Britain as well as one by Selikoff, et. al. in U.S. Naval shipyards, focused on hazards and diseases because of asbestos exposure.[2,3] Such studies helped ignite efforts to further examine the long-term adverse health effects due to asbestos exposure in shipyard workers.

There is a large collection of studies that showed excess incidence and mortality rates of lung cancer and mesothelioma in shipyard and non-shipyard workers who were exposed to asbestos.[3-8] Other types of cancer, such as colorectal cancer and other gastrointestinal cancers, have also been observed in workers exposed to this agent.[9-13] Although the association between asbestos exposure and lung cancer, as well as between asbestos exposure and mesothelioma, had long since been established, the relationship between asbestos exposure and other types of cancers continues to be debated in the current literature.

Aside from asbestos, numerous other potential exposures are present in the shipyard, specific to certain occupations. Several occupations are exposed to substances such as welding fumes and gases, solvents, and other agents. The overall objective of this dissertation is to

examine the association between occupational agents in the Long Beach Naval Shipyard (LBNS) and the health outcomes experienced by the workers employed in the shipyard between 1978 and 1985. This dissertation will investigate rates of cancer incidence among LBNS workers. Specifically, this dissertation will assess the relationship between asbestos exposure and colorectal cancer according to different occupations with varying levels of asbestos exposures using a historical occupational cohort. In addition, it will examine the incidence and mortality rates of lung cancer in relation to the exposure to welding fumes.

1.1. Occupational exposures in the shipyard industry

In general, shipyard workers are exposed to a wide variety of hazards (e.g. asbestos fibers, toxic chemicals, solvents, and welding fumes) and perilous working conditions (e.g. lack of ventilation, confined and enclosed spaces, heat, and poor lighting). The majority of the naval shipyard workers are civilians, and most are skilled journeymen or trained workers from 80 to 100 different occupations.[1] As a result, studies on the long-term effects of exposure to hazardous substances in shipyards could potentially impact a large population of individuals.

Overall, previous studies found excess incidence of asbestos-related diseases in shipyard workers. Often, insulators in the naval shipyard were directly exposed to high concentration of asbestos materials. Workers from other occupations may also have been exposed to some level of asbestos indirectly by working in spaces adjacent to where asbestos materials were handled.[5,14] Several studies observed an increased incidence of asbestos-related diseases in other shipyard workers, such as pipefitters, machinists, boilermakers, welders, electricians, and other occupations that did not have a direct contact with asbestos, suggesting that secondary exposure to asbestos occurred.[14-17] Poor ventilation, the lack of personal protective equipment, in addition

to working in confined spaces could potentially have contributed to the secondary exposure experienced by these workers.

Mesothelioma is often used to indicate a potential exposure to asbestos. Mortality from mesothelioma, lung cancer, and other non-malignant respiratory diseases are widely reported among shipyard workers [3,4,6,15,17-22] A study by Sanden, et. al. observed a high prevalence of asbestosis and pleural plaques among shipyard workers in Gothenburg, Sweden at least 20 years after the onset of asbestos exposure.[23] After years of cessation from asbestos exposure, the increased risk of lung cancer in the study population was no longer observed.[17,23] These observations coincided with a study by Selikoff, et. al. where a decline in death rates from lung cancer, peritoneal mesothelioma and asbestosis were observed among insulators in the United States and Canada after asbestos use was regulated.[24]

Although shipyard studies mostly focused on cancer, some studies also observed excess mortality in non-cancer diseases.[3,15,17,18,25-28] Most non-cancer related diseases observed in the shipyard are respiratory diseases, and were thought to be due to asbestos exposure. For instance, Krstev, et. al. observed increased mortality from emphysema in civilian workers from a U.S. Coast Guard shipyard cohort (1950-1964).[15] In the same cohort, mesothelioma was exclusively found in the group exposed to hazardous substances, indicating that the population was potentially exposed to asbestos. Decreases in deaths caused by cardiovascular disease and cirrhosis of the liver were also observed. The decrease in mortality from cardiovascular disease could be explained by the healthy worker effect: often, individuals who enter the workforce are healthier than the general population.

1.2. Exposure to asbestos in the shipyard

In the past, shipyard cohorts served a significant role in assessing the long-term health outcome of asbestos exposure. Similar finding from shipyard cohorts were observed in non-shipyard studies that assessed the health effects of asbestos exposure.[29-38] Asbestos is a naturally occurring fibrous mineral that gained popularity in the 1930s as an insulation material due to its high tensile strength, flexibility, resistance to thermal degradation, and electrical resistance. The U.S. Navy's requirement of the use of asbestos as the main insulation material in naval ships contributed to the increase in asbestos use from World War II through the Vietnam War to the mid-1970s.[39] Asbestos was also commonly used in residential and commercial building constructions, appliances, clutch/transmissions as well as brake components.[40]

Studies of the health hazards of asbestos exposure started in the 1900s, but it was not until the 1940s that the topic started to gain attention. During that time, research focusing on the health effects of asbestos exposure in the occupational setting gained popularity, and research identifying the tolerable levels of airborne asbestos concentrations in the workplace followed. Between 1960 and 1970, large population studies such as by Harries, et. al. and Selikoff, et. al., reported increased risks of lung cancer and mesothelioma in workers exposed to asbestos.[2,3,20,41-43] Numerous studies have found an increased incidence of cancer in occupations with prolonged exposure to this substance. [2-4, 6-13, 16, 23-26]

Most shipyard studies often use a dichotomous measure (expose vs unexposed) to indicate asbestos exposure. The study cohort I used in this dissertation has information on the level of asbestos exposure for each major shops and occupations in the LBNS. Consequently, each worker was assigned either low, intermediate or high asbestos exposure depending on the worker's shop number and occupational category.

1.3. The use of asbestos in the U.S.

Recently, health hazards due to asbestos exposure in the United States have been significantly reduced due to various regulations and standards implemented to protect workers. Around the early 1970s, the U.S. Navy terminated the use of asbestos-containing thermal insulation.[1,5,44] At the same time, the Occupational Safety and Health Administration (OSHA) developed and implemented occupational health standards to regulate the handling of asbestos.[14] After health standards were implemented in the workplace, workers' exposure to asbestos dramatically decreased. By 1976, asbestos use was not permitted in U.S. merchant marine vessels.[45] Nevertheless, potential asbestos exposure continued to exist during ship repair and maintenance.

In general, workers employed years after the implementation of asbestos regulations in the workplace were likely exposed to less concentrations of asbestos compared to the workers who were employed prior to the regulation of asbestos. Selikoff, et. al. suggested that health effects from asbestos exposure might be reversible. However, other studies, such as a one by Kolonel, et. al. continued to observe an increased risk of lung cancer 15 years and 30 years after asbestos exposure in shipyard workers.[6] Adjusting for the decrease of asbestos exposure after the mid-1970s would allow an opportunity to better examine the adverse health outcomes from other sources of exposures at the shipyard, such as welding fumes, which otherwise are masked by the varying levels of asbestos exposure.

Although asbestos exposure has dramatically reduced in recent years, retired workers previously exposed to asbestos are still potentially at risk for various cancers. The period between initial asbestos exposure and the onset of cancer related to the exposure is usually 20 to 30 years.[42,46,47] For example, among the engine workers aboard a Norwegian Navy vessels, the

mean latency time for cases of mesothelioma was 41 years.[4] Another study observed a 30 to 34 year period for the appearance of lung cancer after initial asbestos exposure.[48] Additionally, studies by Kolonel, et. al. suggested that longer time duration is required to completely evaluate the full extent of various cancers due to asbestos exposure.[6] Nicholson, et. al. projected an increase of mortality rate due to asbestos-related diseases in the U.S. until the year 2000, and although they predicted a decrease in mortality rate thereafter, they suggested that it would remain substantial for another three decades.[40] Due to the long latency period of cancer development, it is important to increase screening and prevention measures for high-risk asbestos-exposed individuals. The study cohort used in this dissertation has at least 28 years of follow-up, allowing sufficient time for the development of cancer.

1.4. Asbestos exposure: a global crisis

Investigations of the hazards of asbestos were not confined only in the United States. Similar studies were also performed in other countries, such as in Great Britain.[3,43] Although the production and use of asbestos in the United States has been reduced, its usage in other countries continues to rise; mostly in developing countries. According to a 2010 report published by the World Health Organization (WHO), the burden of asbestos-related diseases is increasing.[49] The WHO added that developing countries should prepare for an increase in asbestos-related diseases. Several recent studies using non-U.S. cohorts have already observed an increased in mortality rates of mesothelioma, lung cancer, and other asbestos-related diseases from asbestos exposure.[35,37,50-56] Although countries may have begun to regulate asbestos, compliance with standard protocols and the use of personal protective equipment are not always followed. Thus, identification of other adverse health outcomes, aside from lung cancer and mesothelioma,

associated to asbestos exposure continues to be important for identifying high-risk populations.

1.5. Colorectal cancer and asbestos exposure

Increases in other types of cancers have been linked to asbestos exposure, specifically colorectal cancer.[2,11-13,15,41] The relationship between asbestos and colorectal cancer is inconsistent. Several studies showed a strong association between asbestos exposure and colorectal cancer, but others found that asbestos exposure had no or negative association with the risk of colorectal cancer.[4,9-13,57-59] Thus, the relationship between colorectal cancer and asbestos exposure remains ambiguous, and further study of this relationship continuous to be relevant at the present.

Inhaled asbestos has been shown to result in the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS).[60] Inhalation of asbestos in rats showed asbestos-induced inflammation in the lungs.[61] Accumulation of asbestos fibers could result in chronic inflammation, and induced pro-inflammatory and anti-inflammatory responses, leading to the development of cancers. Although most studies of asbestos focused on lungs and mesothelioma, this could be applied to colorectal tissues. There have been multiple evidence showing asbestos bodies in the colon. For example, some asbestos bodies were found in the colon carcinoma from a patient who worked as an insulator in the past.[62] The mechanism behind migration of asbestos from the environment to the colon remains unclear. One suggested mechanism, aside from direct ingestion of asbestos fibers, is through the mucocialliary escalators. Mucocialliary excalators facilitate the migration of asbestos fibers from the lungs, by removing asbestos fibers in the airway.[63] These fibers are swallowed and excreted in the feces, potentially exposing the colon and rectal area to asbestos fibers and inflammation.

Studies have shown that chronic inflammation in the colon; such as that seen in inflammatory bowel disease (IBD), increases the risk of colorectal cancer.[62] The characteristics of the colorectal tumor in these individuals were different from sporadic colorectal cancer, suggesting a different mechanism. Due to this mechanistic difference, exposure to asbestos could potentially result in colorectal cancer with similar characteristics as in individuals suffering from IBD. In a case study, Goodfellow, et. al. reported a rare case of squamous cell carcinoma in an asbestos worker.[64] Goodfellow, et. al. speculated that asbestos exposure may have contributed to the development of this rare type of colorectal cancer, and that irritants such as asbestos may have lead an adenoma to change to squamous cell carcinoma.[65] To our knowledge, a study comparing tumor characteristics between shipyard workers exposed to asbestos and non-exposed shipyard workers has not yet been conducted.

1.6. Lung cancer and welding exposure

Asbestos is only one of the many agents found in a shipyard. Some workers could have also been exposed to high concentrations of other hazardous substances, which could contribute to other adverse health outcomes unrelated to asbestos exposure. For example, welders are exposed to welding fumes that could potentially contain chromium and nickel depending on the materials utilized. Generally, the majority of all welding uses mild carbon and low alloy steel, while less than 10% use stainless steel, aluminum, titanium, nickel, and other metals.[66] Stainless steel was thought to increase the welder's exposure to nickel and chromium compared to mild steel.[67] Welding fumes have been suggested to increase mortality from lung cancer, although findings are inconsistent.[15,68-76] Moulin, et. al. showed significantly increased mortality from lung cancer in mild steel welders, which was not observed in stainless steel welders.[68] Several

other studies have shown similar results.[77-79] In shipyard studies, the type of materials used is often unknown, and welders could potentially have had secondary exposure to asbestos. Various studies of lung cancer in shipyard welders are inconsistent, and often the levels of asbestos exposure were unknown.[80-82] Generally, due to inconsistencies in the literature, further investigations into the relationship between lung cancer and welding fumes is necessary.

1.7. Specific aims and hypotheses

Aim 1: Compare the cancer incidence and mortality rates of LBNS workers employed between 1978 and 1985 to the cancer incidence and mortality rates of the state of California's population. This will be done in different occupational subgroups (e.g. based on the varying levels of asbestos exposure).

Hypothesis 1: I hypothesize that the common causes of deaths found in the LBNS study cohort is similar to that of the general population of California. Similar to the mortality trends in California, cardiovascular diseases and cancer are hypothesized to be the most common cause-of-death in the study cohort. Nevertheless, an excess incidence of lung cancer, mesothelioma, and other asbestos-related cancers will be observed in subgroups of workers with high asbestos exposure, compared to the general population of California.

Aim 2: Assess the relationship between colorectal cancer risk (incidence and mortality rates) and varying levels of asbestos exposure (i.e. low, intermediate, high) in LBNS workers employed between 1978 and 1985.

Hypothesis 2: I hypothesize that there will be an increased risk of colorectal cancer in the high asbestos exposure group compared to the low asbestos exposure group. In addition, the length of

employment in the shipyard will impact the strength of association between colorectal cancer risk and asbestos exposure.

Aim 3: Compare colon and rectum tumor characteristics, such as histological types and stage at diagnosis, across low, intermediate and high asbestos exposure levels in LBNS workers diagnosed with colorectal cancer.

Hypothesis 3: Adenocarcinoma is the most common histology for colorectal cancer. As a result, I hypothesize that the majority of colorectal cancer across the three exposure groups will be adenocarcinoma. Nevertheless, uncommon types of colorectal cancer, such as squamous cell carcinoma, will more likely be observed in groups of workers exposed to high levels of asbestos and less likely to occur in workers with low asbestos exposure.

Aim 4: Measure the association between lung cancer risk (lung cancer incidence and mortality rates) and various levels of exposure to welding fumes (exposed vs unexposed) in the LBNS. The analysis will be further stratified by duration of employment in the shipyard.

Hypothesis 4: I hypothesize that after adjusting for asbestos exposure, LBNS shipyard workers with high exposure to welding are at a higher risk of lung cancer compared to workers unexposed to welding fumes.

1.8. Chapter outline

Chapter 2: General methodology

Chapter 3: A validation method to determine missing years of birth in a cohort study of shipyard workers using Social Security Number

Chapter 4: Causes of deaths, and incidence of cancers in the Long Beach Naval shipyard study cohort

Chapter 5: The risk of colorectal cancer between Long Beach Naval shipyard workers exposed to low, intermediate, and high asbestos exposure levels

Chapter 6: The risk of lung cancer between Long Beach Naval shipyard workers exposed to welding fumes and unexposed workers

Chapter 7: Conclusion

CHAPTER 2

Methods

2.1. Study population

The LBNS first opened on February 1943 and was permanently closed on September 1997. [83,84] It employed approximately 40,000 shipyard workers during its 50 years of operation. In this dissertation, the LBNS study cohort consists of 13,924 LBNS shipyard workers employed in the shipyard between 1978 and 1985 (**Figure 2.1**).

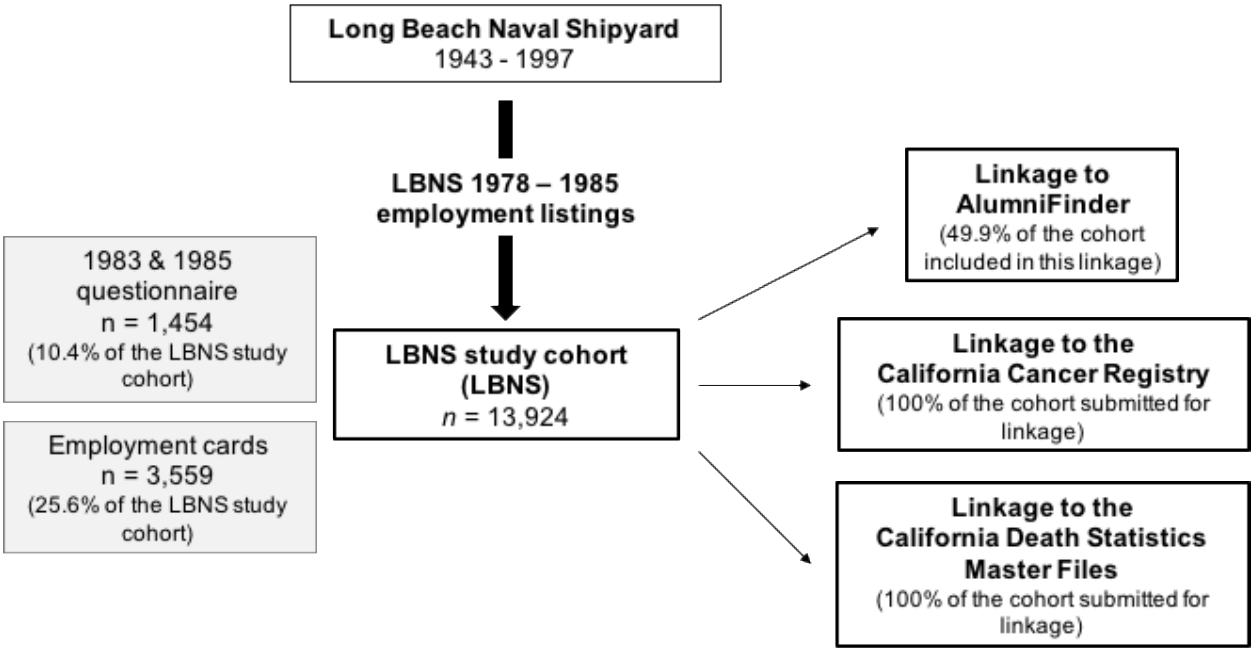


Figure 2.1. Flow chart of the study population

2.1.1. Employee rosters (listings)

The cohort was formed by compiling all available annual LBNS employee rosters (listings) between 1978 and 1985 (**Figure 2.1**). Each listing was scanned alphabetically by year. Each scanned page was manually verified (line-by-line) by an undergraduate student intern for

errors to ensure accuracy of the scanned data. The scanned data were also checked and corrected for any anomalies such as duplicate entries, insufficient digits in the social security number (SSN), and two or more participants sharing the same SSN. Workers who appeared in multiple listings were added in the database once, and the earliest listing year was used as the worker's year-of-entry to the study. Data from the listings included first initial, last name, SSN, address, employee number, and shop number. The LBNS study cohort has complete data on SSN, last name, and shop number.

2.1.2. Employment records

In addition to the employee listings, 25.6% (n=3,559) of the LBNS study cohort workers had available personnel employment cards during their tenure at the LBNS, which included information such as shop number, job title, initial date of employment in the shipyard, and last date of employment in the shipyard. Job titles were also obtained for some workers using the LBNS medical recall program records from 1979 to 1980. Each of these records was entered in the database by a student intern, and each data entry was checked by a different intern for accuracy.

2.1.3. Pilot study of the LBNS

In 1983 and 1985, screening questionnaires were sent by mail to the addresses of LBNS workers. A detailed description of the study was reported by Jacoby, et. al. and Gagnon, et. al.[85,86] The pilot cohort is composed of workers who returned the questionnaire by mail or in person. Aside from demographic information, personal medical history, and occupational history, the questionnaire also provides information about each participant's exposure to 20

different occupational agents. There was a total of 1,734 workers who completed and returned the questionnaire. From the 1,734 workers in the pilot cohort, 83.9% (n = 1,454) were also members of the LBNS study cohort.

2.2. Linkage to the California cancer registry and the death statistics master file

Linkage of the LBNS study cohort to the California Department of Public Health cancer registry (CCR) was performed to obtain information on cancer diagnosis. In this study, the CCR captured any cancers that were diagnosed in the State of California starting in 1988 to 2011. CCR uses the International Classification of Diseases for Oncology 3rd revision (ICD-O-3) Surveillance, Epidemiology, and End Result (SEER) site recode to define each cancer type. The LBNS study cohort was matched in the CCR database using the following information: SSN, last name, first initial, and middle initial (if available). The linkage of the cohort to the CCR was performed by a CCR personnel, and the result of the linkage was made available through the CCR Secure File Transfer Protocol.

Mortality and causes of death were ascertained using the California Department of Public Health Death Statistical Master Files (DSMF). Similar to CCR, the death data captured any deaths that occurred in the State of California between 1970 and 2013. The causes of death were coded using the International Statistical Classification of Diseases and Related Problems (ICD) coding. Since ICD coding was updated three times between 1970 and 2011 (8th, 9th and 10th revisions), both ICD-8 and ICD-9 were converted to ICD-10 coding prior to data analyses. SSN and last name were used to identify individuals from the LBNS study cohort in the DMSF database.

2.3. Years of birth in the study cohort

The observed years of birth in LBNS study cohort were acquired from the LBNS employment records (if available) and questionnaires (if available) from each individual, followed by the CCR and/or the DMSF, and lastly through AlumniFinder. The method developed by Block, et. al. published in 1983 was utilized to predict the years of birth for individuals with the missing information. Individuals whose birth year was not predicted by Block's method were excluded for further analyses. A validation study (*described in Chapter 3*) using a subset of the LBNS study cohort population was performed prior to using Block's method to predict the missing years of birth.

2.3.1. Linkage to the AlumniFinder for workers with missing years of birth

A linkage to the AlumniFinder (www.alumnifinder.com) was performed on individuals in the LBNS study cohort where age and/or the years of birth data were not found in the LBNS employment record, the questionnaire, the CCR or the DMSF. AlumniFinder is a private vendor of residential information that utilizes LexisNexis Accurint, an online database services that provides access to many databases, including public records. Individuals were matched in the database using the individual's SSN and last name. Information obtained from the AlumniFinder included full name, date of birth, date of death, previous addresses and current address. The use of AlumniFinder is further discussed in *Chapter 3*.

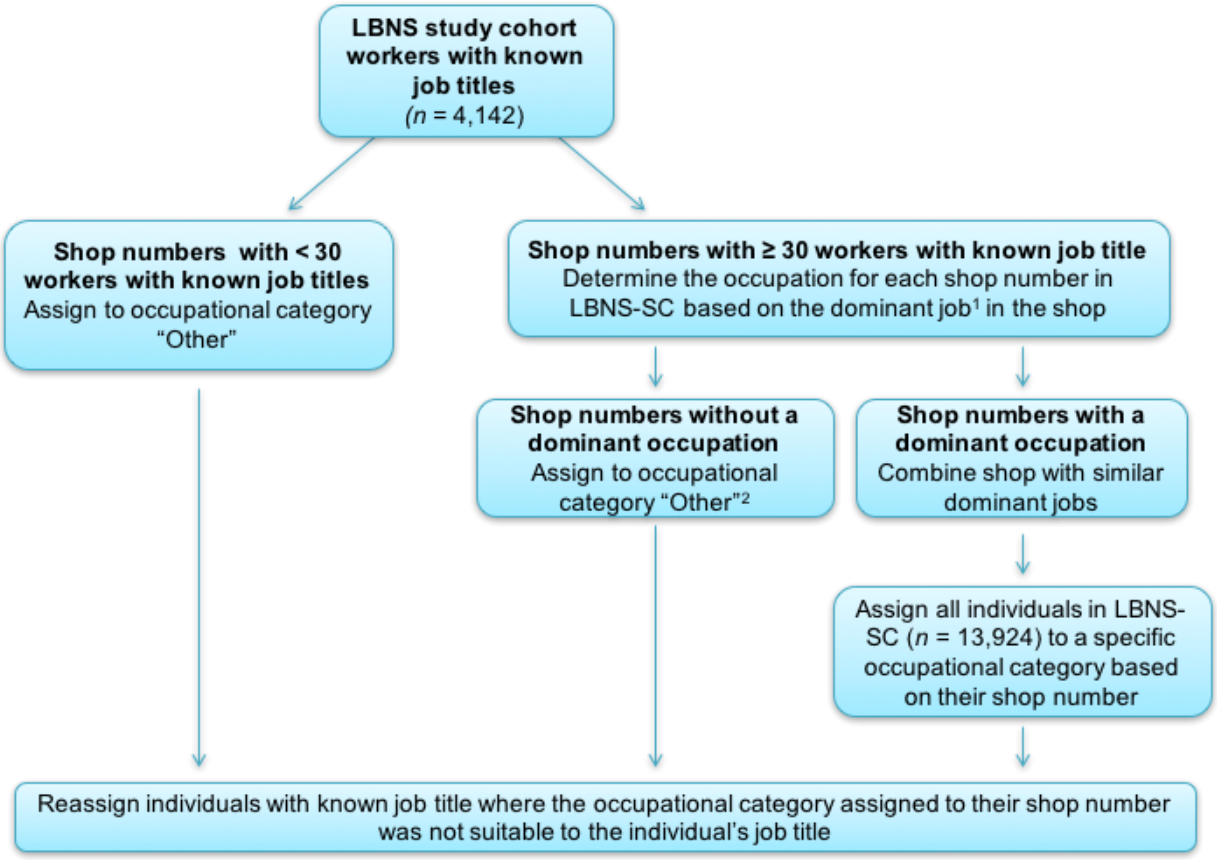
2.4. Occupations in the LBNS

Job titles of workers were obtained from employment cards or from the pilot study questionnaire, when available. In cases where the employment cards and questionnaire had the

job title recorded, the employment card was preferred over the questionnaire. Out of the 13,924 workers in LBNS study cohort, approximately 30% (n = 4,142) of workers had known job titles. The 1983 Guideline for Standard Occupational Classification (SOC) was utilized to identify job titles that could be collapsed into an occupation category. Furthermore, job titles that were very specific were simplified to a more generalized form. For example, the job titles of account maintenance clerk, clerk supervisor, clerk typist, and clerk assistant were collapsed into a simplified version of these jobs – clerk.

Figure 2.2 summarizes the procedure used to assign everyone in the study cohort to an occupational category. First, the dominant job for each shop in the LBNS study cohort was determined based on the information from the 4,142 workers with known job titles. A shop number may contain a variety of job titles. A job is considered dominant in a specific shop number if 50% or more of the workers (with known job titles) in the shop held similar jobs. Shop numbers consisting of similar dominant jobs were combined into one occupational category. The shops with less than or equal to 30 workers were assigned to the category, 'Other'. An exception was made for shop #72, which consisted of 170 workers with known job titles that had 29.4% equipment cleaners and 47.7% riggers. These two were grouped together into the category 'Riggers and Equipment Cleaners'. Other shops without a dominant job were assigned to "Other." **Table 2.1** lists the occupational categories in LBNS study cohort and the corresponding shops for each category. Once each of the shop numbers in the LBNS study cohort belonged to an occupational category, all workers in the LBNS study cohort (workers with and without job titles) were assigned to a specific occupational category based on their shop number. Workers with job titles better suited to a different occupational category than the one assigned to their shop number were reallocated to the category that closely reflected their job title.

Figure 2.2. Method in defining occupational categories in the LBNS study cohort



[1] If 50% or more of the workers (with known job titles) in the shop hold similar jobs.
[2] Excludes shop #72, which was assigned to the occupational category "Riggers and Equipment Cleaners."

Table 2.1. The distribution of LBNS study cohort workers with known job titles by occupational categories and shop number

Occupational categories[1]	Shop numbers	Total number of workers with the dominant job	%	Total number of workers in the shop
Architects, Engineers	319	38	69.1	55
	324	216	88.5	244
Boilermakers	41	136	87.2	156
Electricians	51	241	90.3	267
	99	44	62.9	70
Electronics and equipment mechanics	36	57	53.3	107
	67	187	93.5	200
Insulators	57	95	94.1	101
Machinists	31	190	88.8	214
	38	126	84.6	149
Office workers/Administrative personnel	> 99 (except 319, 324)	487	73.0	667
Painters	71	56	69.1	81
Pipefitters	56	225	85.6	263
Riggers, Equipment cleaners	72	135	79.4	170
Sheet metal workers	17	192	97.0	198
Structural workers	11	211	81.2	260
	64	52	65.0	80
Transportation and mobile vehicle operators	2	82	73.9	111
Warehousemen	50	69	89.6	77
Welders	26	292	97.3	300
Total[2]				**3,770**

[1] Only includes shops with ≥30 workers and with the dominant job encompassing ≥50% of the shops' population, except Riggers, Equipment cleaners which separately contains <50% of the shop's population. Shops with <30 workers or shops without dominant jobs were assigned "Other."
[2] Excludes occupational category "Other."

2.5. Occupational exposures in the Long Beach Naval Shipyard study cohort

Table 2.2 lists some of the occupational agents present in LBNS that were included in the 1983 and 1985 survey questionnaire. This dissertation focuses on two of the occupational agents in LBNS: asbestos and welding fumes.

Table 2.2. List of occupational agents in the 1983 & 1985 Long Beach Naval Shipyard questionnaire survey

I. Dusts
Asbestos
Fiberglass
Wood dust
II. Chemical compounds
Alcohol
Benzene
Carbon disulfide
Carbon tetrachloride
Chromate
Chromic acid
Fluoride
Isocyanate
Solvent/degreaser
Trichloroethylene
Vinyl chloride
III. Metals and Metalloids
Beryllium
Cadmium
Lead
IV. Other exposures
Metal priming
Spray painting
Welding/soldering

2.5.1. Exposure to asbestos

Appendix A contains the detailed asbestos exposure status for each job title organized by shop number. The list was developed with the aid of an industrial hygienist. Each shop number contains different job titles with corresponding asbestos exposure levels. A job title may appear in more than one shop number. Workers that both had known shop number and job titles with corresponding asbestos exposure were assigned one of the three asbestos exposure levels: low, intermediate, and high.

For workers who either did not have job titles or with job titles that were not in the list provided by the industrial hygienist, their asbestos exposure levels were derived from a pooled data. These pooled data (n = 2,922) consisted of workers whose job titles and shop numbers were found in **Appendix A**. The workers in the pooled data were clustered by their occupational category (excluding those in occupational category 'Other'). Due to the wide range of job types in the occupational category 'Other', asbestos exposure level cannot be assigned in this group. The distribution of workers in the pooled data was examined and utilized to assign the asbestos exposure level for each of the occupational category (**Appendix B**). The

asbestos level assigned to each occupational category depended on the proportion of workers from the pooled data with information on their asbestos exposure level. The most common asbestos exposure level (≥80%) in each of the occupational category, will be the level assigned to all workers in that occupational category. The ≥80% cut-off was decided prior to the exposure assignment.

The occupational category 'Transportation and motor vehicle operator' was the only group where none of the asbestos exposure levels contained at least 80% of its members. Thus, these workers did not have an assigned asbestos exposure level, except for individuals that were in the pooled data, who already had an assigned asbestos exposure. Furthermore, workers in occupational categories with two or more shops that have >30 members, and each shop had a different exposure level, were assigned exposure levels according to their shop numbers. In these occupational categories the reallocated workers, who were initially in a different occupational category, were not assigned to any of the three asbestos exposure groups. After each category was assigned an asbestos exposure level, all workers in the shipyard with missing job titles were assigned to one of the three asbestos exposure groups according to the occuaptinal category and shop number. **Table 2.3** lists the three asbestos exposure levels and the corresponding occupational categories associated with each of the levels.

Table 2.3. Occupational categories in each asbestos exposure level in the Long Beach Naval shipyard study cohort

Asbestos exposure level	Main occupational groups
Low (*n*= 3,586)	Architects, Engineers Electronics and equipment mechanics† Transportation and motor vehicle operators† Office workers/Administrative personnel Painters Riggers, Equipment cleaners† Others†
Intermediate (*n* = 2,550)	Electronics and equipment mechanics *(shop # 36)* Electricians Machinist (*shop # 31)* Transportation and motor vehicle operators† Warehousemen Others†
High (*n*= 5,848)	Electronics and equipment mechanics *(shop # 67)* Insulators, Pipecoverers Machinists *(shop # 38)* Transportation and motor vehicle operators† Pipefitters Riggers, Equipment cleaners Sheet metal workers Structural workers Welders Others†
No exposure level assigned (*n* = 1,728)	Electronics and equipment mechanics Machinists† Transportation and motor vehicle operators Others†

† Consists of workers with shop number and job titles found in **Appendix A**

2.6. Person-years in California

Individuals in LBNS study cohort were censored if death occurred or when they move-out of California. Workers in the LBNS-VC (sub-cohort used for the validation study) were assumed to be in California throughout the study and the follow-up period in accordance to the CCR records. Workers who were not in this sub-group were followed-up through the AlumniFinder. The AlumniFinder had multiple recorded addresses for each individual as well as the year of death. Only the state of residence portion of the address was examined. All non-California addresses that was used by the worker for ≥5 years were included in determining the person-years.

All workers in the LBNS study cohort are assumed to be a California resident during the years they were employed in the LBNS until 1985, regardless of the address history in AlumniFinder. Individuals are censored on the first period they moved out of California based on the AlumniFinder. In the years that California addresses overlapped with non-California addresses, the residence status, whether the person was in California or not, could not be clearly determined (**Appendix C**). As a result, it was assumed that the worker was in California during these years if the prior address was in California.

2.7. Duration of employment

The duration of employment in the LBNS is defined as the total years of employment in the LBNS starting from the year of hire to the last year of employment or 1985, whichever came first. There were 3,478 LBNS workers in the study that had information about their date of hire from the employment cards. This information was used to determine the worker's duration of employment in the LBNS. The last available employee listing where the worker was included

served as the last year of employment for all the workers in the LBNS. For all workers in the study, the last year of employment was between 1979 and 1985. There were 4,846 LBNS workers in the study hired after 1978 (between 1979 and 1985), and for these workers the year of hire was the year they were included in the LBNS annual employee listings (1979-1985).

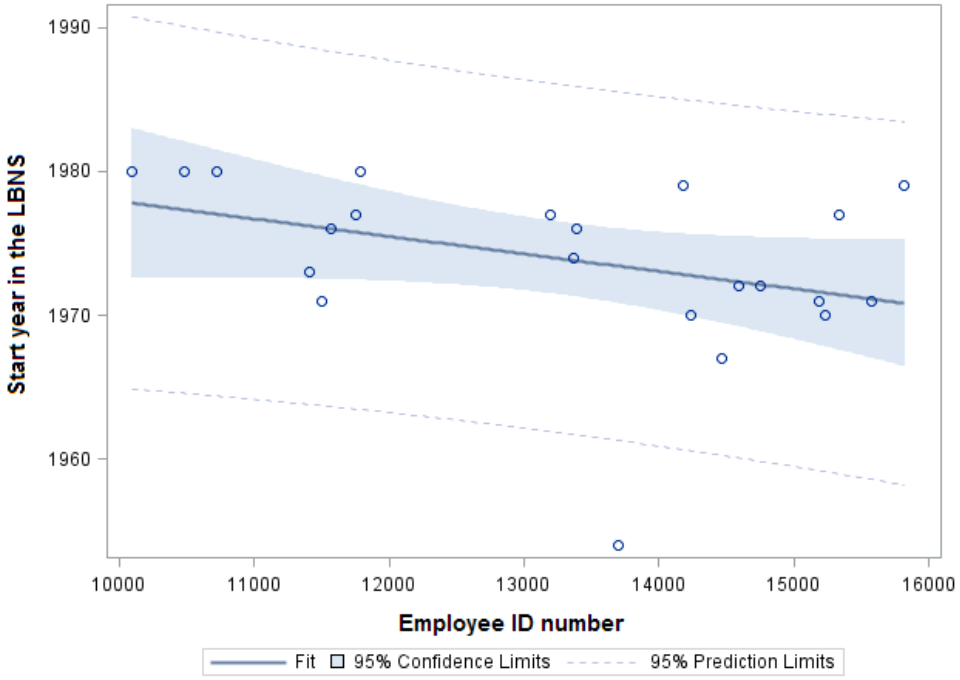
There were 5,600 workers who were in the 1978 employee listing, where the year of hire could not be determined. LBNS annual employee listings prior to 1978 were not available, and thus workers who were newly hired in 1978 and current workers that were hired in previous years could not be separated. For these workers, the duration of employment in the shipyard was estimated using information derived from a simple linear regression of the employee ID number and the year of hire in workers with employment cards. **Figure 2.3A** illustrates the regression between employee ID number and the year of hire for 3,478 LBNS workers. These workers were further separated into two groups; workers with employee ID number greater than 20000 (n = 3,456), and workers with employee ID number less than or equal to 20000 (n = 22). The predicted year of hire for workers in the 1978 employee listing was calculated using the equation in derived from **Figure 2.3B & C**, which is dependent on worker's employee ID number.

Figure 2.3. Scatter plots of employee ID numbers and year-of-hire of Long Beach Naval shipyard workers between 1978 and 1985 (n = 3,478)

A. Includes all workers with employment records and information on year of hire in the LBNS (n = 3,478)

C. Includes workers with employee ID number >20000 (n = 3,478)

C. Workers with employee ID number ≤20000 (n = 22)



2.8. Summary of statistical analyses

Workers that were 64 years or older during the first year of the study or were employed in the LBNS at the age of 64 years or older between 1978 and 1985 were excluded in the study (*see Chapter 3*). Workers younger than 16 years old were also excluded from the analyses. A total of 201 workers were excluded in this study due to the age-at-entry exclusion. Furthermore, deaths that occurred before 1978 or deaths that occurred between 1978 and 1985 where the worker continued to appear in the employee listing the year after their death were excluded in the study (n = 11).

The occupational category 'Office workers and Administrative personnel' were excluded in the majority of the analyses, except for the SMR analysis. This specific category had a large proportion of women. However, the majority of the occupational categories in the shipyard were predominantly populated by males (**Appendix D**). In this study, we restricted our analysis to males only.

The age-adjusted standardized mortality ratio (SMR) for white males was also calculated to compare the most common causes of death experienced in the LBNS study cohort to the causes of death experienced by the general population of California. Deaths found through AlumniFinder did not have cause-of-death information. As a result, it was assumed that the distribution of the cause-of-death for this group was similar to the deaths derived through the DSMF, which has information on the cause-of-death. The proportion for each underlying cause-of-death category derived from the DSMF mortality data was applied to the AlumniFinder deaths to estimate the number of deaths that occurred for each of the cause-of-death category in the group with no information on the causes of deaths. The sum of the deaths from DSMF data and the estimated number of deaths calculated for the AlumniFinder was used to calculate the

adjusted SMR for each underlying cause-of-death category. Moreover, to evaluate cancer incidence in the LBNS study cohort, the age-adjusted standardized incidence ratio (SIR) for white males was calculated comparing LBNS study cohort to the general population of California. The 95% confidence intervals were determined for both SIR and SMR, where a 95% confidence interval that excluded 1.0 indicates significant.

The time to disease occurrence survival curve for the outcomes colorectal cancer and lung cancer were determined using the Kaplan-Meier (KM) method. The association between colorectal cancer and exposure asbestos was determined using the Cox's proportional hazard regression model adjusted for duration of employment in the shipyard. Workers were censored for deaths or due to loss to follow-up. A 95% confidence interval that excluded 1.0 was considered significant. All data analyses in this study were generated using SAS software, version 9.3 (SAS Institute, Inc., Cary, North Carolina). Each statistical method used for each specific aim will be further discussed in subsequent chapters: *Chapter 4, 5 & 6*.

Chapter 3

A Validation Method to Determine Missing Years of Birth in a Cohort Study of Shipyard Workers Using Social Security Number

Occupational cohorts are especially useful for etiologic studies when employment records, union records, and work-related exposure records are available. The objective of this study is to examine the relationship between occupational exposures and disease outcomes associated with employment in a shipyard cohort. Employment records used to construct historical occupational cohorts are not always compiled for the purpose of utilizing these data in epidemiological studies. A study to assess the effect of completeness of data may thus be necessary. Methods used to address the problems associated with incomplete data in historical occupational cohorts includes linkage with public records and databases, such as motor vehicle records, phone records, cancer registries, and state death files.[87] Methodological issues to compare the effect of the missing observations to the nonmissing observations of a given variable have been previously studied including methods to impute missing data.[88-90] In this paper, we present findings on a large historical occupational cohort of naval shipyard workers wherein we imputed dates of birth and evaluated a method to predict missing birth year and age variable based on SSN.[91]

Starting in 1936, workers in most occupations were required to have SSNs when entering the workforce.[92] The method developed by Block, et. al. predicts the year of birth of workers using information from these SSNs. Multiple studies have applied this prediction method to estimate missing age.[93-98] The method has also been utilized to help impute nativity and year of immigration to the United States when this information is unknown.[99-119] Block, et.

al. assessed the application of the method using the Florida phosphate workers employed between 1950 and 1979. Johnson, et. al. also performed a validation study with 1,000 meat-cutter union members prior to applying Block's method to members with missing age in their cohort.[97,98] Although Block's method has been used in several study populations, a validation study using a large retrospective cohort has not yet been performed.

We applied the method developed by Block, et. al. to predict the years of birth of workers in the LBNS cohort to evaluate the feasibility and external validity of this prediction method. To our knowledge, this is the first study to examine the generalizability of Block's method for predicting the years of birth using a large occupational retrospective cohort. Following our examination of the external validity (validation study), we modified Block's method to improve the accuracy of the predicted data.

METHODS

Study population

Our study included a sample of a large LBNS cohort, which was previously studied by Anton-Culver, et. al.[119,120] The LBNS employed over 41,000 workers at the shipyard between 1942 and 1997. In the current study, all available employment listings (rosters) were utilized, which contained 13,924 shipyard workers employed between 1978 and 1985. The 13,924 workers were included in the current study because of the availability of their data in the shipyard records and we were granted access to their specific jobs and shops through the LBNS employment rosters. We will refer to this group of LBNS workers as the LBNS-Validation Cohort (LBNS-VC). The data of the LBNS-VC included last name, first name/initial, SSN, shop number and job title, as well as other occupational data. The information on the cohort was

derived from both the LBNS annual employment roster and the LBNS employment cards. Linkage to both the California cancer registry and death statistics master files up to 2013 were carried out on the LBNS-VC to obtain additional information such as year of cancer diagnosis, type of cancer, year of death, and cause of death.

Of the 13,924 workers in the LBNS-VC, 6,980 (50.1%) had known years of birth through the original shipyard personnel data, and from the results of the linkage to the California cancer registry and death files. Meanwhile, 6,944 workers did not have data on age or year of birth but had data on their SSN. In order to study the health effects associated with occupational exposures at the shipyard, it was necessary to obtain, as complete as possible, either the age or the date of birth of the workers. In LBNS workers with missing age, before applying Block's prediction method, we used the data from the LBNS-VC with known years of birth to validate Block's method. Block's method was modified to improve the accuracy before the method was used to impute the birth years of LBNS workers with missing age and unknown year of birth.

Block's prediction method to impute years of birth

The method described by Block, et. al. uses the SSN to predict the year of birth, which is structured into three different segments: geographic area number (first three-digits), group number (middle two-digits), and serial number (last four-digits).[91,121,122] For each worker, the SSN year of issue was determined using information derived from the Social Security Administration. Block, et. al. combined data from the Social Security Administration and extrapolated data to construct a matrix for SSN years of issue from 1937 to 1978. The matrix contains the geographic area number, the group number, and the corresponding SSN years-of-issue. A simple calculation of the difference between the SSN year-of-issue and the age when

SSN was issued produced the predicted year of birth.

Validation using the 6,980 workers with known years of birth from the LBNS-VC

We used the 6,980 group of workers from the LBNS-VC with known years of birth to evaluate the external validity of Block's method. Of the 6,980 workers, we excluded 248 who were either more than 64 years old during the first year of the study or were hired at the age of more than 64 years between 1978 and 1985. The data on the remaining 6,732 workers were used for the validation analysis.

We applied the method and used the SSN year-of-issue matrix [included in the publication by Block, et. al.] to the 6,732 workers, and imputed the SSN year of issue for 4,909 workers. Workers whose SSN year-of-issue were not found using the matrix (n = 1,823) were not included in the subsequent calculations for the prediction of the year of birth. The true year of birth was known for the 4,909 workers in this validation study. We calculated the predicted year of birth using the same distribution of the median age at SSN used by Block, et. al. (**Table 1**) and the estimated SSN year-of-issue for each of the LBNS worker. We also performed additional analysis using the distribution of the median age of SSN issuance based on the LBNS-VC population (**Table 1**). Pearson's correlation coefficient (percent agreement) was calculated to assess the linear relationship between the predicted years of birth and the observed years of birth. A two-tailed *P* less than 0.05 is considered as a statistically significant correlation between the predicted and the observed birth years.

The predicted years of birth of the 4,909 workers calculated using Block's method with the median age distribution originally used by Block, et. al. had an 88.8% agreement ($P < 0.0001$, $R^2=0.789$) with the workers' observed years of birth, while the percent agreement

between the predicted and the observed years of birth using Block's method with the median age distribution from the LBNS-VC was 89.2% ($P < 0.0001$, R^2=0.796) (**Table 2**). In the original article, Block et al reported an agreement of 91.0% ($P < 0.00001$, $R^2 = 0.820$).

Table 1. Distribution of the Social Secuirty Number Median Age of Issue

Year obtained SSN	Median age used by Block et al. (1983)*	Median age from LBNS-VC
1937	26	18
1938	20	19
1939-1950	17	17
1951-1959	16	16
1960-1962	15	16
1963-1974	14	16
1975-1978	13	16

LBNS-VC, Long Beach Naval Shipyard validation cohort; SSN, Social Security Number.

*Reproduced from Block G, Matanoski GM, Seltser RS. A method for estimating year of birth using social security number. *Am J Epidemiol* 1983;118(3):377-95.

Modification of Block's prediction method

In order to improve Block's method, we performed modifications on the original method. For our study, we use the median age of SSN distribution derived from the LBNS-VC. For the first modification (Modification I), we separated the 4,909 workers into three different groups based on each worker's predicted year of birth: less than 1920, 1920 to 1930, more than 1930. An additional four years were added to the birth year of workers with predicted years of birth less than 1920, while two years were added to the group with predicted years of birth from 1920 to 1930. These two values are the median difference (years) between the predicted and the observed years of birth for the corresponding groups of the LBNS-VC. No adjustments were

added to the more than 1930 group.

In the second modification (Modification II), the sample was not separated; instead, we excluded 208 workers who had SSN issued in U.S. territories (SSNs with area number 580 to 586), such as Guam, Virgin Islands, Philippines, American Samoa and Puerto Rico (**Table 3**). For this modified version of Block's method, the predicted year of birth was in 93.1% agreement ($P < 0.0001$, $R^2 = 0.867$) with the observed year of birth (**Table 2**). To assess whether excluding workers with SSN in U.S. territories will improve the correlations in Modification I, we combined Modification I and Modification II. Both modifications combined produced a very similar result when using Modification II alone (Pearson's $r = 93.2\%$, $P < 0.0001$, $R^2 = 0.869$). Overall, Modification II produced one of the highest percent agreements between the predicted and the observed years of birth.

Table 2. Comparison of Modifications of Block's Prediction Method Using the Long Beach Naval Shipyard Cohort (1978-1985)

Sample	Modifications	*N*	Pearson's *r* [a] (*% agreement*)	R^2	*P* [b]
LBNS-VC					
	Unmodified	4909	89.2	0.796	< 0.0001
	I	4909	89.1	0.793	< 0.0001
	II	4701	93.1	0.867	< 0.0001
LBNS-Alumni					
	Unmodified	3327	89.1	0.794	< 0.0001
	II	3094	92.6	0.857	< 0.0001

LBNS, Long Beach Naval Shipyard; LBNS-VC, Long Beach Naval Shipyard validation cohort; *N*, frequency.

[a] Pearson's correlation coefficient, expressed in %.

[b] Statistically significant if $P < 0.05$ for correlation between predicted years of birth and observed years of birth.

Applying the modified Block's method to the 6,944 workers with missing years of birth

In the confirmation study for Modification II, we used the LBNS-Alumni subcohort which contained the 6,944 shipyard workers who initially had unknown years of birth and who were later followed-up using the AlumniFinder (Accudata Integrated Marketing, Fort Myers, Florida) (**Figure 1**). Of the 6,944 workers, 1,850 were not found using the AlumniFinder, while 5094 workers were identified and information regarding their age and year of birth were subsequently obtained. These 5,094 workers were used to confirm our results from the validation study of Block's method with Modification II in the LBNS-VC.

Workers who were more than 64 years old during the first year of the study or workers hired at the age of more than 64 years between 1978 and 1985 were excluded from the sample (n = 5,052). Out of these 5,052 workers, there were 1,725 whose SSN year-of-issue could not be determined using the matrix provided by Block, et. al. As specified from Modification II, workers in the sample were separated according to the geographic location where the SSN was issued. This yielded 3,094 workers who had U.S. state-issued SSNs and 233 workers who had U.S. territories-issued SSNs (**Table 3**). To assess Block's method with Modification II, the predicted years of birth were calculated in workers who had both estimated SSN years-of-issue and SSNs that were issued from U.S. states (n = 3,094). All data analyses in this study were generated using SAS software, version 9.3 (SAS Institute, Inc., Cary, North Carolina).

Data Safeguards

This study was approved by the Institutional Review Board of the University of California, Irvine (HS # 2013-9428). The data are stored in protected file servers managed by the

Security Team of the University of California, Irvine Health Affairs Information Services. All data analyses were performed using secure and protected workstations within the Department of Epidemiology facility and managed by the University of California, Irvine Health Affairs Information Systems. Access to the data is restricted to study personnel only.

TABLE 3. U.S. Territories- and States-issued Social Security Number in the Long Beach Naval Shipyard Cohorts, 1978-1985

Sample	Location of SSN issuance	Frequency
LBNS-VC		
	U.S. territories	208
	U.S. states	4701
	Total	4909
LBNS-Alumni		
	U.S. territories	233
	U.S. states	3094
	Total	3327

LBNS, Long Beach Naval Shipyard; LBNS-VC, Long Beach Naval Shipyard validation cohort; SSN, Social Security Number.

RESULTS

Validation analysis of Block's method with modifications using LBNS-VC

Results from the modifications applied to Block's method are shown in **Table 2**. The percent agreement between the predicted years of birth and the workers' observed years of birth in the LBNS-VC for Modification I was similar to the result using Block's method without modifications (Pearson's r = 89.2%, $P < 0.0001$, $R^2 = 0.793$ vs. Pearson's r = 89.1%, $P < 0.0001$, $R^2 = 0.796$). The percent agreement in Modification II (Pearson's r = 93.1%, $P < 0.0001$, $R^2 = 0.867$) was higher than the percent agreement using the unmodified Block's method. As consistently observed in both plots (**Figure 2A and B**), the prediction method is highly variable in workers born prior to 1940, whereas the variability around the prediction line becomes smaller

in workers born after 1940. We also observed a cluster of outliers above the prediction line (**Figure 2A**), which was not present in the plot for Modification II (**Figure 2B**). In addition, the relationship between the predicted and observed years of birth contained empty spaces in the x-axis during the early 1920s and 1930s. This result indicates that the method was unable to predict the birth years of individuals born in those years.[91] The cross-tabulation of the SSN year-of-issue and the median year of birth is not a smooth continuous line, which causes the observed pattern.[91]

We examined the accuracy of Block's method with Modification II by analyzing the difference in the number of years between the predicted and observed years of birth grouped by the years of SSN issuance based on the type of Social Security Administration documentation/form utilized for the SSN year-of-issue (**Table 4**). The method accurately predicted the birth years for 916 (19.0%) workers. More than half of the workers (n = 2,415) had 1 to 2 years difference between the predicted and observed years of birth. The majority of the workers in both groups had their SSN issued after 1950. An opposite trend from the previous groups was observed in workers with 3 to 5 years difference between the predicted and observed years of birth. The majority of the workers in this group had SSN issued prior to 1948. Lastly, there were 460 (9.80%) workers out of 4,701 with more than 5 years difference between the predicted and observed years of birth.

Analysis to confirm modification of Block's method in a second subset of LBNS workers

In the LBNS-Alumni sub-cohort, the predicted years of birth using Block's method with Modification II was in 92.6% agreement ($P < 0.0001$, $R^2 = 0.857$) with the workers' observed

years of birth (**Table 2**). Block's method with the modification had a higher percent agreement compared to the unmodified method (Pearson's r =89.1%, $P < 0.0001$, $R^2 = 0.794$).

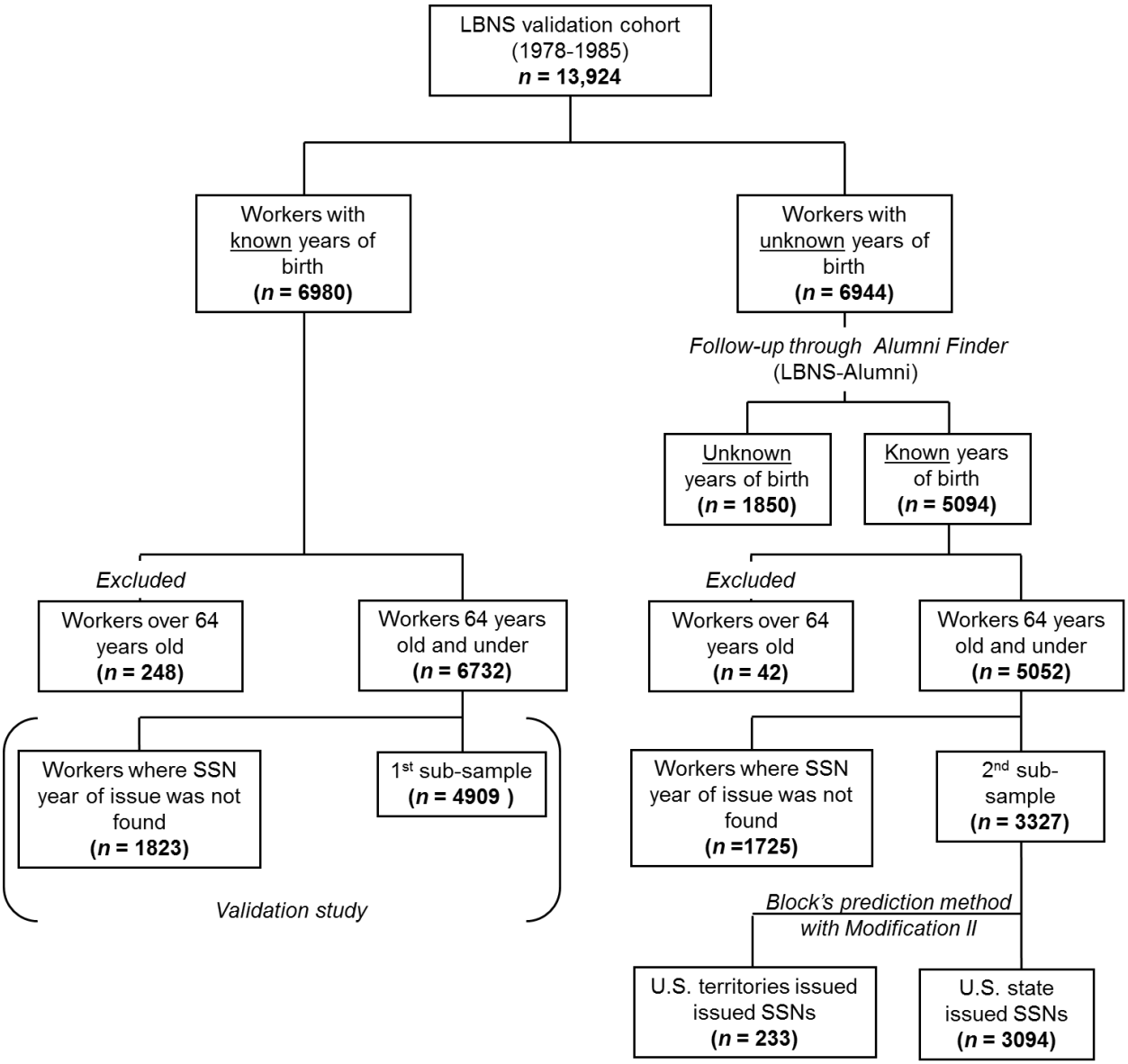


FIGURE 1. Outline of the Long Beach Naval Shipyard cohort (1978-1985) validation study of Block's method to predict years of birth using Social Security Numbers. LBNS, Long Beach Naval Shipyard; RRB, Railroad Board; SSN, Social Security Number.

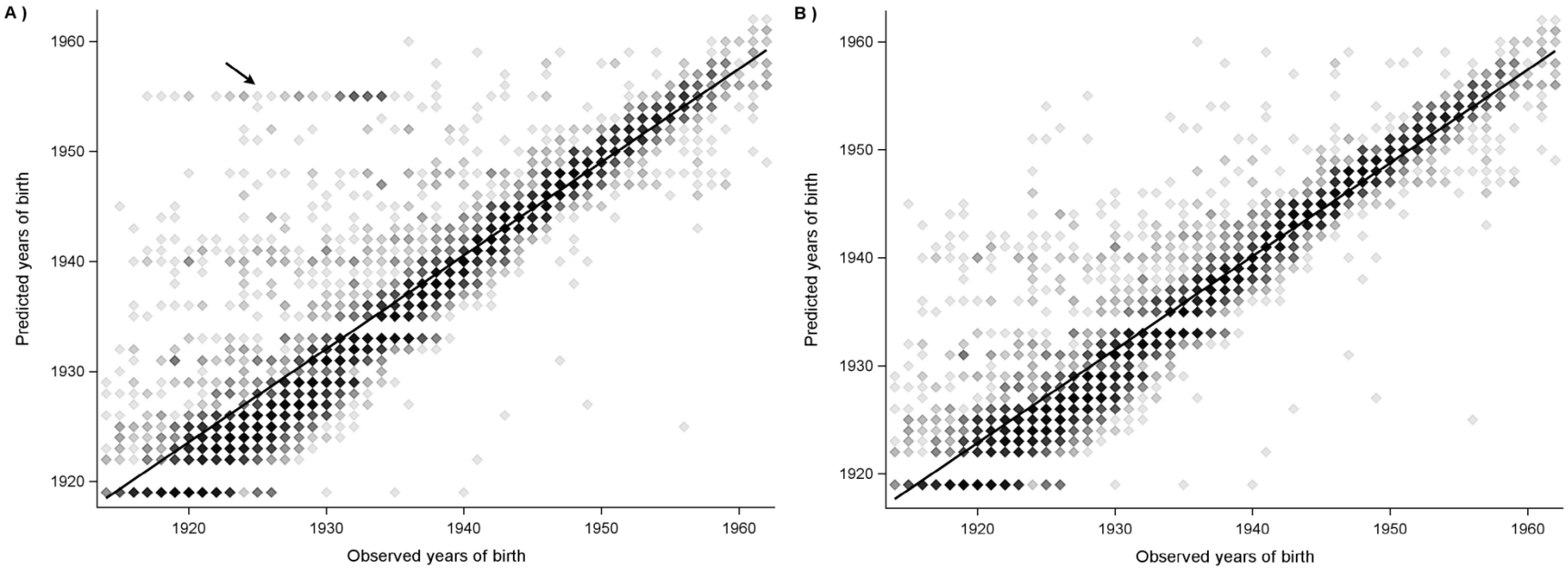


FIGURE 2. Relationships between predicted and observed years of birth in LBNS-VC workers (*n* = 6,980). A, unmodified Block's method; B, Block's method with modification II. Arrow is cluster of workers with U.S. territories-issued SSN.

DISCUSSIONS

Our results show that the age prediction method we describe in this paper yielded superior results than the original method by Block, et. al. Our data show that the correlation between the predicted and observed years of birth increased when workers with U.S. territory-issued SSN are removed from the analysis. Block, et. al. showed that Railroad Board SSNs were highly inaccurate in predicting the year of births. However, they did not examine the accuracy of U.S. territory-issued SSNs. In our validation study, 4.20% of the workers in the LBNS-VC have a U.S. territory-issued SSNs. The majority of the U.S. territory-issued SSN produced incorrect predicted years of birth values, and more than half had predicted years of birth with more than 5 years difference from the true value.

Overall, the accuracy in estimating the years of birth in our validation study was worse for older workers relative to younger workers. One source of error is due to the inaccurate age estimates when the SSN was issues.[91] The age at which individuals obtained their SSN varied widely in the first few years of the Social Security Administration.[122] After the majority of the U.S. workforce obtained their SSNs, the typical age at which SSN is obtained became less variable.[122,123] Although the distribution of SSN age-of-issue in the population is generally more predictable several years after the introduction of the SSN program, discrepancies existed in certain subgroups, such as adult immigrants entering the workforce.

The matrix described by Block, et. al. did not include SSNs obtained after 1978, and therefore, the information in the matrix may also not accurately characterize younger workers who most likely have obtained their SSN in later years of the program. Finally, in 1991, the majority of the U.S. states aloowed the parent of a newborn to request an SSN as part of the state's birth registration process.[122] In addition, in June 2011, the Social Security Administration

changed the method of assigning SSN referred to as "randomization."[124] Thus, the ability of Block's method to accurately predict the year of birth is limited to the SSN year-of-issuance.

The large population used in our validation study represents multiple groups of workers in variety of occupations at the shipyard. Although the majority of the LBNS employees were blue-collar workers, a portion of the cohort held professional degrees, which were mostly in engineering and architecture. Our study addresses the concern of the applicability of the prediction method to other populations including professional groups. We also performed subsequent analysis using "AlumniFinder" methodology to verify the results from the LBNS-VC. The result from this analysis is consistent with the initial findings (**Table 2**).

In conclusion, this study and other similar prediction methods are valuable in epidemiological studies where important data elements are missing such as age while SSN is more complete. It can be useful to researchers in the calculation of age-specific incidence and mortality rates. The method presented here was applied to occupational cohorts who are primarily white male workers. Future applications in nonoccupational populations as well as in predominantly female populations are warranted to determine if this method is equally applicable in other populations.

CHAPTER 4

Causes of Deaths, and Incidence of Cancers in the Long Beach Naval Shipyard Study Cohort

4.1. Introduction

Shipyard workers are often exposed to a wide range of physical and chemical hazards in the workplace. There is an abundance of evidence showing increase risk of lung cancer and mesothelioma in shipyard workers due to asbestos exposure. Although asbestos exposure is often connected in the shipyard industry, there are ample of other chemicals and physical elements present in a shipyard that could potentially contribute to increase risk of various diseases. Studies have assessed long-term health outcomes due to other occupational hazards present in the shipyard, including exposure to solvents, manganese, welding fumes as well as vibrations.

A previous study of 6,183 LBNS workers employed in 1977 examined pleural plaques and pulmonary abnormalities in chest x-rays in relation to asbestos exposure in the LBNS. The study found that older LBNS workers were more likely employed for a longer period in the shipyard, and had higher prevalence of pleural plaques.[119] However, a further assessment on the mortality experienced by LBNS workers as well as cancer incidence in this study cohort is warranted. The purpose of this chapter is to compare the causes of deaths and cancer incidence of LBNS workers employed between 1978 and 1985 to the general population of California. Due to the diverse occupations present in the shipyard, secondary exposure to multiple toxic substances are possible. As a result, the study also performed a separate analysis by different subgroups within the LBNS, such as different asbestos exposure levels as well as occupational groups.

4.2. Methods

Chapter 2 contains the detailed description of the general methods used for the study cohort.

4.2.1. Standardized mortality ratio

There were 13,141 LBNS workers included in the analysis. Workers with unknown years of birth, as well as workers hired at the age of ≤16 years old, and workers who were >64 years old during the first year of the study or were hired at the age of >64 years between 1978 and 1985 were excluded from the analysis. In addition, workers found in LBNS employee listings years after their deaths (n = 11), as well as workers without a year of birth (n = 571), were excluded in the study. Mortality information were derived from DSMF between 1978 to 2013, and from the AlumniFinder. Information on the causes of death were only available from the DSMF.

Causes of death were grouped into different categories based on the ICD-10. All causes of death coded using the ICD-9 and ICD-8 were converted to ICD-10. There were 3,683 deaths with available cause-of-death information, and there were 1,083 deaths where the cause-of-death information was not available. The number of deaths for each underlying cause-of-death category in this group were calculated based on the mortality distribution of the deaths with available cause-of-death information. The total number of deaths for each cause-of-death category was the sum of the number of deaths with available cause-of-death information and the calculated deaths for cases without available cause-of-death.

Age-specific standardized mortality ratio was calculated using the California population (1978-2013) as the standard population. The expected number of deaths were calculated for each year between 1978 to 2013. The age-specific mortality rates for men in California were used to calculate the expected number of deaths. The 95% confidence intervals were determined for the

SMR where a 95% confidence interval that excluded 1.0 indicates significance.

4.2.2. Standardized incidence ratio

Out of the 13,924 shipyard workers in the study cohort, 11,062 were included in the analysis. Workers who had missing years of birth and workers who did not meet the age inclusion were excluded in the analysis. In addition, workers that belonged to the main occupational group Office workers and Administrative personnel were excluded in the analysis. Information on cancer diagnosis were derived from the CCR. Tumors were defined using the ICD-O-3 and WHO's Classification of Tumours and Haematopoeitic and Lymphoid Tissues (2008). Only primary tumors diagnosed between 1988 and 2011 were included in the analysis. Tumors characterized as benign or borderline malignant were excluded. In addition, tumors reported from autopsy only or from death certificate only were also excluded.

The population in the state of California from 1988 to 2011 was utilized as the reference population to calculate the age-specific standardized incidence ratio for white males. The expected number of cancers for each year from 1988 to 2011 were calculated per five-year interval except for years prior to 1990 and after 2009, which were per two-year interval. The age-specific incidence rates in men in California were used to calculate the expected number of cancer in the LBNS study cohort. The 95% confidence intervals were determined for the SIR, where a 95% confidence interval that excluded 1.0 indicates significant. The age-specific SIRs for high asbestos and intermediate asbestos exposure groups were compared to the low asbestos exposure group (reference) for the mesothelioma and lung cancer using the chi-square test. A *P*-value of less than or equal 0.05 indicates significant difference between two exposure groups (i.e. low vs high, intermediate vs high).

4.3. Results

4.3.1. Age-specific standardized mortality ratio

The 13,141 workers in the study cohort after exclusions contributed a total of 293,730 person-years with an average of 22.4 ±10.9 years of follow-up. The average age-at-entry to the study was 38.6 ±12.1 years. After workers in the occupational category, 'Office workers and administrative personnel', were excluded (n = 11,062), the cumulative person-years of follow-up is 247,549 person-years of follow-up. No change was observed in the mean years of follow-up and the mean age-at-entry to the study.

4.3.1.1. Overall mortality in the LBNS study cohort

There were 3,683 deaths with available cause-of-death information, and 1,083 deaths without available cause-of-death information **(Appendix E)** in the Long Beach Naval shipyard cohort (n = 13,141). The total number of deaths in the LBNS study cohort was 4,766. Deaths were clustered into categories based on the causes of deaths. The five leading causes are Diseases of the circulatory system (n = 1,812), Neoplasms (n = 1,405), Diseases of the respiratory system (n = 415), Accidents, Suicides, and Homicides (n = 336), and Diseases of the digestive system (n = 189).

The specific causes of death for each of the five-leading cause-of-death categories are listed in **Appendix F**. Only deaths with available cause-of-death information are included in this list. A total of 1,400 deaths were due to the Diseases of the circulatory system. Over 55% (*n =793*) of these deaths were due to ischemic heart disease. There was a total of 321 deaths due to the Diseases of the respiratory system, and the most common specific cause-of-death in this category is chronic lower respiratory disease (38.94%). Out of the 260 deaths due to Accidents,

suicides, and homicides, the leading specific cause-of-death was fracture of the upper limb (15.77%), followed by poisoning by drugs, medicinals, and biological substances (14.62%). Lastly, there are 146 deaths due to the Diseases of the digestive system. The most common specific cause-of-death in this category was chronic liver disease and cirrhosis (39.04%), followed by alcoholic liver disease (20.55%).

Table 4.1 summarized the SMRs for the five-leading cause-of-death categories in the LBNS study cohort. There was no significant difference in the number of deaths due to the Diseases of circulatory system in the LBNS study cohort compared to the general population of California (SMR= 1.00 (0.95-1.05)). Neoplasms had an SMR of 1.09 (1.03-1.15), Diseases of the respiratory system had an SMR of 1.15 (1.04-1.26), and Accidents, suicides, and homicides had a statistically significant SMR of 1.60 (1.44-1.78). In addition, there was about a 2-folds (SMR= 2.00 (1.73-2.30)) excess deaths due to the Diseases of the digestive system in the LBNS study cohort compared to the expected deaths from this disease based on general population of California.

Table 4.1. Overall age-specific standardized mortality ratio in the LBNS study cohort (*N=13,141*)

Cause-of-death categories	Total deaths	Expected deaths	SMR (95% CI)
Diseases of circulatory system	1812	1812.93	1.00 (0.95-1.05)
Neoplasms[1]	1405	1288.69	1.09 (1.03-1.15)
Diseases of the respiratory system	415	361.37	1.15 (1.04-1.26)
Accidents, Suicides, Homicides	336	209.78	1.60 (1.44-1.78)
Diseases of the digestive system	189	94.68	2.00 (1.73-2.30)

[1] Includes benign tumors, non-malignant

4.3.1.2. Overall mortality in the LBNS study cohort by asbestos exposure groups

The LBNS study cohort was separated in to three asbestos exposure groups; low, intermediate and high. In the SMR analysis, the low and intermediate asbestos exposure (AE) groups were combined. Out of 13,141 shipyard workers included in the analysis, 5,878 workers were in the low/intermediate AE group and 5,616 workers were in the high asbestos exposure group. There was a total of 1,951 deaths in the low/intermediate AE group and a total of 2,089 deaths in the high AE group (**Appendix G)**. The five-leading cause-of-deaths in both low/intermediate AE group and high AE group were Diseases of the circulatory system, Neoplasms, Diseases of the respiratory system, Accidents, suicides, and homicides, and Diseases of the digestive system.

Generally, the SMR for each of the five most common cause-of-death categories was slightly higher in the high AE group compared to the SMR of the low/intermediate AE group (**Table 4.2**). Only the SMR for the Diseases of the circulatory system was not statistically significant in the low/intermediate AE group (SMR= 0.99 (0.92-1.07)). All five-leading cause-of-death categories in the high AE group were statistically significant. The number of deaths due to Neoplasms in the low/intermediate AE group was significantly higher (SMR= 1.09 (1.01-1.18)) compared to expected number of deaths in the general population of California. There was also a statistically significant excess number of deaths due to neoplasms in the high AE group (SMR= 1.36 (1.26-1.48)), and was slightly higher than the calculated SMR of the low/intermediate AE group. Both asbestos groups had over 2.5-folds excess number of deaths due to accidents, suicides, and homicides compared to the general population of California (SMR= 2.50 (2.09-2.99), and SMR= 2.77 (2.39-3.20)). In addition, both asbestos exposure groups had about 4.0-folds excess deaths in the LBNS study cohort due to Diseases of the

digestive system (SMR= 3.71 (2.96-4.56), and SMR= 4.16 (3.31-5.16)). The low/intermediate AE group had statistically significant SMR of 1.33 (1.14-1.53) for the Disease of the respiratory system, while the SMR in the high AE group for this category was slightly higher (SMR= 1.86 (1.60-2.14)).

Table 4.2. Age-specific standardized mortality ratio in the LBNS study cohort by asbestos exposure groups (*n = 11,494*)†

A. Low/intermediate asbestos exposure group (*N = 5,878*)

Cause-of-death categories	Low/intermediate asbestos exposure		
	Total deaths	Expected deaths	SMR (95% CI)
Diseases of circulatory system	743	747.90	0.99 (0.92-1.07)
Neoplasms[1]	587	536.83	1.09 (1.01-1.18)
Diseases of the respiratory system	175	131.89	1.33 (1.14-1.53)
Accidents, Suicides, Homicides	120	47.83	2.50 (2.09-2.99)
Diseases of the digestive system	82	22.20	3.71 (2.96-4.56)

[1] Includes benign tumors, non-malignant

B. High asbestos exposure group (*N = 5,616*)

Cause-of-death categories	High asbestos exposure		
	Total deaths	Expected deaths	SMR (95% CI)
Diseases of circulatory system	773	638.28	1.21 (1.13-1.30)
Neoplasms[1]	598	438.67	1.36 (1.26-1.48)
Diseases of the respiratory system	182	98.2	1.86 (1.60-2.14)
Accidents, Suicides, Homicides	181	65.36	2.77 (2.39-3.20)
Diseases of the digestive system	78	18.75	4.16 (3.31-5.16)

[1] Includes benign tumors, non-malignant

† 1,647 did not have assigned asbestos exposure group

4.3.1.3. Cancer-specific mortality in the LBNS study cohort

There was a total of 1,086 cancer-specific deaths with available cause-of-death information in the LBNS study cohort **(Appendix H)**. The total number of cancer-specific deaths is 1,405. The five-leading cancer-specific deaths in the LBNS were Malignant neoplasms of the respiratory and intrathoracic organs (*n = 502*), Malignant neoplasms of the digestive organs and peritoneum (*n = 333*), Malignant neoplasms of the lymphatic and hematopoietic tissue (*n =124*), Malignant neoplasms of the male genital organs (*n = 118*), and Malignant neoplasms of the ill-defined, other secondary, and unspecified sites (*n = 92*).

Table 4.3 summarized the cancer-specific SMRs for Malignant neoplasms of the respiratory and intrathoracic organs, Malignant neoplasms of the digestive organs and peritoneum, Malignant neoplasms of the lymphatic and hematopoietic tissue, Malignant neoplasms of the male genital organs, and Malignant neoplasms of the urinary tract. All five cancers had statistically significant SMRs. Malignant neoplasms of the urinary tract had the highest SMR of 3.64 (2.87-4.50), followed by the Malignant neoplasms of the lymphatic and hematopoietic tissue with an SMR of 2.48 (2.07-2.95). Malignant neoplasms of the digestive

Table 4.3. Cancer-specific age-specific standardized mortality ratio in the LBNS study cohort (*N=13,141*)

Type of neoplasms	Total deaths	Expected deaths	SMR (95% CI)
Malignant neoplasm of respiratory and intrathoracic organs	502	317	1.58 (1.45-1.73)
Malignant neoplasm of digestive organs and peritoneum	333	246	1.35 (1.22-1.51)
Malignant neoplasm of lymphatic and hematopoietic tissue	124	50	2.48 (2.07-2.95)
Malignant neoplasms of male genital organs	118	68	1.73 (1.44-2.07)
Malignant neoplasms of urinary tract	76	21	3.64 (2.87-4.50)

organs and peritoneum had the lowest SMR, which was 1.35 (1.22-1.51).

4.3.1.4. Cancer-specific mortality in the LBNS study cohort by asbestos exposure levels

There was a total of 587 cancer-specific deaths in the low/intermediate AE group, a total of 598 cancer-specific deaths in the high AE group (**Appendix I**). The five-leading cancer-specific deaths were Malignant neoplasm of the respiratory and intrathoracic organs (n = 210), Malignant neoplasms of the digestive organs and peritoneum (n = 129), Malignant neoplasms of the lymphatic and hematopoietic tissue (n = 61), Malignant neoplasms of male genital organs (n = 39), and Malignant neoplasms of urinary tract (n = 32). Similarly, Malignant neoplasms of the respiratory and intrathoracic organs (n =216), Malignant neoplasms of the digestive organs and peritoneum (n = 149), Malignant neoplasms of the lymphatic and hematopoietic tissue (n =49), and Malignant neoplasms of male genital organs (n =58) were also leading cancer-specific deaths in the high AE group, in addition to Malignant neoplasms of ill-defined, other secondary, and unspecified sites (n = 36).

Table 4.4 shows the SMR for the low/intermediate AE group and the high AE group. Malignant neoplasms of the urinary tract had the highest SMR for both asbestos groups followed by the Malignant neoplasms of the lymphatic and hematopoietic tissue. In the low/intermediate AE group, there was over 5-folds (SMR= 5.09 (3.96-6.55)) statistically significant excess deaths due to Malignant neoplasms of the lymphatic and hematopoietic tissue compared to the general population. The high AE group had a lower SMR due to Malignant neoplasms of the lymphatic and hematopoietic tissue than the low/intermediate AE group (SMR= 4.47 (3.35-5.88)). The Malignant neoplasms of the urinary tract in the high AE group had the highest SMR of 8.46 (5.95-11.60), while the low/intermediate AE group had a SMR of 6.24 (4.31-8.65) for this disease. In addition, in both asbestos exposure groups there was over 2-folds statistically

significant excess deaths due to Malignant neoplasms of the respiratory and intrathoracic organs (SMR= 2.15 (1.88-2.46), SMR= 2.12 (1.85-2.41)) as well as deaths due to Malignant neoplasms of the digestive organs and peritoneum (SMR= 2.26 (1.90-2.68), SMR= 2.16 (1.83-2.53)) in both asbestos exposure groups compared to the general population of California. There was almost a 3-folds (SMR= 2.79 (2.03-3.82)) statistically significant excess deaths due to Malignant neoplasms of the male genital organs in the low/intermediate A group compared to the general population. The high AE group had slightly higher SMR for the Malignant neoplasms of the male genital organs than the low/intermediate AE group (SMR= 3.19 (2.44-4.09)).

Table 4.4. Cancer-specific age-adjusted standardized mortality ratio in the LBNS study cohort by asbestos exposure groups (*N = 11,494*)[†]

A. Low/intermediate asbestos exposure group

Neoplasms	*Total n = 5,878*		
	Total deaths	**Expected deaths**	**SMR (95% CI)**
Malignant neoplasm of respiratory and intrathoracic organs	210	97.42	2.15 (1.88-2.46)
Malignant neoplasm of digestive organs and peritoneum	129	56.91	2.26 (1.90-2.68)
Malignant neoplasm of lymphatic and hematopoietic tissue	61	11.88	5.09 (3.96-6.55)
Malignant neoplasms of male genital organs	39	13.83	2.79 (2.03-3.82)
Malignant neoplasms of urinary tract	32	5.16	6.24 (4.31-8.65)

B. High asbestos exposure group

Neoplasms	*Total n = 5,616*		
	Total deaths	**Expected death**	**SMR (95% CI)**
Malignant neoplasm of respiratory and intrathoracic organs	216	102.01	2.12 (1.85-2.41)
Malignant neoplasm of digestive organs and peritoneum	149	69.10	2.16 (1.83-2.53)
Malignant neoplasms of male genital organs	58	18.22	3.19 (2.44-4.09)
Malignant neoplasm of lymphatic and hematopoietic tissue	49	10.93	4.47 (3.35-5.88)
Malignant neoplasms of urinary tract	34	4.02	8.46 (5.95-11.69)

† 1,647 did not have assigned asbestos exposure group

4.3.2. Cancer-specific age-adjusted standardized incidence ratio

4.3.2.1. Overall incidence of primary cancers in male LBNS shipyard workers

There was a total of 1,532 primary cancers in the LBNS study cohort (**Appendix J**). After excluding the main occupational group Office workers and administrative personnel, the total number of primary cancer in the cohort was reduced 1,277 (**Table 4.7**). The five most common primary cancers in this sample were prostate, lung, colorectal, digestive system (excluding colorectal), and urinary system. **Appendix K** shows the site-specific cancers for organ systems including cancer of the digestive system (excluding colorectal) and cancer of the urinary system. The distribution of primary cancer in the group 'Office workers and administrative personnel' is described in **Appendix L**. As expected the most common cancer in this occupational category was breast cancer (n = 45), followed by prostate cancer (n = 42).

There were 11,062 shipyard workers included in the SIR analysis. Occupations in the shipyard are predominantly populated by male workers, which are reflected by the data shown in

Appendix D. The occupational category, 'Office workers and administrative personnel' were excluded in the analysis because it had over 57% of women. Consequently, cancers in female reproductive system and breast cancer were excluded in the SIR analyses.

The overall cancer-specific SIR of the study cohort was 2.14 (2.02-2.26) (**Table 4.6**). Among the fifteen different cancer types examine, mesothelioma had the highest cancer-specific SIR of 12.08 (7.99-17.57). Aside from mesothelioma, ten cancer types on the list had statistically significant SIR of approximately 2.0 or higher; cancers of the brain and other nervous system, colorectal cancer, cancers of the digestive system excluding colorectal, cancers of endocrine system, lung cancer, myeloma, prostate cancer, and cancers of the urinary system.

4.3.2.2. Incidence of primary cancers in male Long Beach Naval shipyard workers stratified by asbestos exposure groups

For this analysis, the sample population was divided into three different asbestos exposure groups; low AE, intermediate AE, and high AE. There was a total of 166 primary tumors in the low AE group, 287 in the intermediate AE group, and 611 in the high AE group (**Appendix M**). The two most common primary tumors in the low AE group were prostate (37.95%) and lung (12.65%), followed by cancer of the urinary system (6.63%). Furthermore, two most common primary tumors in both intermediate AE and high AE group were also prostate (20.97% and 35.52%) and lung (16.38% and 15.06%), followed by colorectal cancer (12.54% and 10.64%).

Table 4.5. Primary cancers in the Long Beach Naval shipyard study cohort excluding Office workers and Administrative personnel (*N =11,062*)

Cancer type[1]	Count	Percent
Prostate	427	33.44
Lung	200	15.66
Colorectal	138	10.81
Digestive system excluding colorectal	113	8.85
Urinary system	103	8.07
Other[2]	52	4.07
Lymphoma	39	3.05
Skin excluding basal and squamous	37	2.90
Oral cavity and pharynx	29	2.27
Mesothelioma	25	1.96
Brain and other nervous system	22	1.72
Leukemia	24	1.88
Respiratory system	22	1.72
Myeloma	19	1.49
Breast and female reproductive system[3]	11	0.86
Endocrine system	10	0.78
Male reproductive system	6	0.47
Total	*1,277*	*100.00*

[1] **Appendix L** contained detailed list on site-specific primary tumors for Brain and other nervous system, Digestive system excluding colorectal, Endocrine system, Male reproductive system excluding prostate, Oral cavity and pharynx, Respiratory system excluding lung, skin excluding basal and squamous, and Urinary system.

[2] Other cancers include cancers of the bones and joints, soft tissue including heart, eye and orbit, Kaposi sarcoma, and miscellaneous cancers.

[3] Seven breast cancer, 1 cancer of the cervix uteri, 2 cancer of the corpus uteri, and 1 ovary cancer

Table 4.6. Cancer-specific age-specific standardized incidence ratio in male Long Beach Naval shipyard workers compared to the general population of California (n = 11,062)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	22	8.81	2.50 (1.60-3.72)
Colorectal	138	66.87	2.06 (1.74-2.43)
Digestive system excluding colorectal	113	50.43	2.24 (1.86-2.68)
Endocrine system	10	5.09	1.97 (1.00-3.50)
Leukemia	24	14.97	1.60 (1.05-2.35)
Lung	200	86.34	2.32 (2.01-2.65)
Lymphoma	39	27.90	1.40 (1.01-1.89)
Male reproductive system excluding prostate	6	7.44	0.81 (0.33-1.68)
Mesothelioma	25	2.07	12.08 (7.99-17.57)
Myeloma	19	7.06	2.69 (1.67-4.12)
Oral cavity and pharynx	29	19.84	1.46 (1.00-2.07)
Prostate	427	172.10	2.48 (2.25-2.72)
Respiratory system excluding lung	22	10.59	2.08 (1.33-3.09)
Skin excluding basal and squamous	37	37.87	0.98 (0.70-1.33)
Urinary system	103	50.67	2.03 (1.67-2.46)
Overall	*1,214*	*568.05*	*2.14 (2.02-2.26)*

† Primary cancers only

The highest statistically significant SIR in all three asbestos exposure groups was cancer of the mesothelioma (**Table 4.7**). An exposure-response pattern was observed for mesothelioma SIRs, where the low AE group had the lowest SIR of 9.11 (1.52-31.04) and the high AE group had a SIR of 11.46 (6.03-19.92). There was no statistical difference in SIRs between low asbestos exposure and intermediate asbestos exposure (*P*-value = 0.09), as well as between low and high asbestos exposure (*P*-value = 0.09). There was a statistically significant excess incidence of lung cancer (low AE SIR= 2.27 (1.44-3.41), intermediate AE SIR= 2.26 (1.68-2.99), high AE SIR= 2.29 (1.86-2.80)) and prostate cancer (low AE SIR= 3.41 (2.64-4.34), intermediate AE SIR= 2.07 (1.67-2.54), high AE SIR= 2.70 (2.36-3.08)) in all three asbestos exposure groups compared to the general population of California. Among the three asbestos

exposure groups, the intermediate AE group had the greatest excess incidence of cancers in the urinary system (SIR= 2.72 (1.90-3.78)). The low AE group had an SIR of 2.00 (2.17-2.97), and the high AE group had an SIR of 1.55 (1.11-2.12) for the cancers of the urinary system.

Interestingly, cancer of the brain and other nervous system was highest in the low AE group (SIR= 5.97 (2.41-12.36)). There was also a statistically significant excess incidence of cancer of the brain and other nervous system in the high AE group (SIR= 2.56 (1.35-4.45)) compared to the general population, but it was lower than the SIR in low AE group. A statistically significant SIR for myeloma was also observed in high AE (SIR= 3.31 (1.74-5.74)). There was a 2.0-fold (1.11-3.21) excess incidence of leukemia in the high AE group compared the general population. A statistically significant excess incidence of colorectal cancers and cancers of the digestive system were observed in both the intermediate AE and the high AE groups (SIR= 2.25 (1.60-3.09), SIR= 2.07 (1.37-3.01) and SIR= 2.06 (1.61-2.61), SIR= 2.39 (1.82-3.07)).

Table 4.7. Primary cancers in the Long Beach Naval shipyard cohort by asbestos exposure (n = 9,415)

A. Low asbestos exposure (n = 1,337)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	6	1.01	5.97 (2.41-12.36)
Colorectal	10	7.24	1.38 (0.70-2.46)
Digestive system excluding colorectal	10	5.52	1.81 (0.92-3.23)
Endocrine system	3	0.60	5.01 (1.27-13.61)
Leukemia	3	1.65	1.82 (0.46-4.95)
Lung	21	9.24	2.27 (1.44-3.41)
Lymphoma	6	3.18	1.89 (0.76-3.92)
Male reproductive system excluding prostate	1	0.93	1.08 (0.05-5.31)
Mesothelioma	2	0.22	9.11 (1.52-31.04)
Myeloma	3	0.77	3.90 (0.99-10.60)
Oral cavity and pharynx	8	2.22	3.61 (1.67-6.84)
Prostate	63	18.46	3.41 (2.64-4.34)
Respiratory system excluding lung	5	1.15	4.35 (1.59-9.64)
Skin excluding basal and squamous	6	4.30	1.40 (0.57-2.90)
Urinary system	11	5.49	2.00 (1.05-3.48)
Total	*158*	*61.98*	*2.55 (2.17-2.97)*

† Primary cancers only

B. Intermediate asbestos exposure (n = 2,462)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	3	2.07	1.45 (0.37-3.94)
Colorectal	36	15.98	2.25 (1.60-3.09)
Digestive system excluding colorectal	25	12.07	2.07 (1.37-3.01)
Endocrine system	3	1.19	2.53 (0.64-6.86)
Leukemia	3	3.55	0.85 (0.21-2.30)
Lung	47	20.75	2.26 (1.68-2.99)
Lymphoma	9	6.55	1.37 (0.67-2.52)
Male reproductive system excluding prostate	2	1.64	1.22 (0.20-4.03)
Mesothelioma	5	0.50	10.08 (3.66-22.17)
Myeloma	3	1.69	1.77 (0.45-4.83)
Oral cavity and pharynx	7	4.73	1.48 (0.65-2.93)
Prostate	86	41.54	2.07 (1.67-2.54)
Respiratory system excluding lung	3	2.54	1.18 (0.30-3.21)
Skin excluding basal and squamous	6	8.96	0.67 (0.27-1.39)
Urinary system	33	12.13	2.72 (1.90-3.78)
Total	*271*	*135.89*	*1.99 (1.77-2.24)*

† Primary cancers only

C. High asbestos exposure (n = 5,616)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	11	4.30	2.56 (1.35-4.45)
Colorectal	65	31.48	2.06 (1.61-2.61)
Digestive system excluding colorectal	57	23.89	2.39 (1.82-3.07)
Endocrine system	3	2.53	1.18 (0.30-3.23)
Leukemia	14	7.15	1.96 (1.11-3.21)
Lung	92	40.17	2.29 (1.86-2.80)
Lymphoma	18	13.63	1.32 (0.81-2.05)
Male reproductive system excluding prostate	3	3.89	0.77 (0.20-2.10)
Mesothelioma	11	0.96	11.46 (6.03-19.92)
Myeloma	11	3.33	3.31 (1.74-5.74)
Oral cavity and pharynx	12	9.53	1.26 (0.68-2.14)
Prostate	217	80.28	2.70 (2.36-3.08)
Respiratory system excluding lung	12	4.99	2.41 (1.30-4.09)
Skin excluding basal and squamous	18	18.41	0.98 (0.60-1.51)
Urinary system	37	23.85	1.55 (1.11-2.12)
Total	*581*	*268.39*	*2.16 (1.99-2.35)*

† Primary cancers only

4.3.2.3. Incidence of primary cancers in male LBNS shipyard workers by main occupational group

Appendix N summarizes the cancer-specific SIR for each of ten main occupational categories in the LBNS study cohort. For this analysis, the main occupational categories 'Boilermakers, insulators, pipecoverers, and pipefitters' were collapsed into one group. Similarly, the main occupational categories 'Sheet metal workers, structural workers, and welders' were also collapsed into a group (**Appendix O**). Six occupational groups had statistically significant excess incidence of mesothelioma compared to the general population of California. Occupational groups with excess incidence of lung cancer compared to the general population of California includes 'Architects and engineers', 'Electricians', 'Machinists', 'Painters', 'Riggers and equipment cleaners', 'Boilermakers, insulators, pipecoverers and

pipefitters', and 'Sheet metal workers, structural workers, and welders'. Occupational categories with a statistically significant SIR for colorectal cancer included 'Electronics and equipment mechanics', 'Electricians', 'Machinists', 'Riggers and equipment cleaners', 'Boilermakers, insulators, pipecoverers, and pipefitters', and 'Sheet metal workers, structural workers and welders'. Eight out of the ten occupational categories had statistically significant prostate cancer SIR.

Two occupational categories had statistically significant SIR for cancers of the Brain and other nervous system; 'Architects and engineers' (SIR= 5.24 (1.34-14.32)) and 'Painters' (SIR= 8.01 (2.06-22.07)). The occupational categories 'Electronics and equipment mechanics', 'Electricians', and 'Painters' had statistically significant excess incidence of myeloma compared to the general population (SIR= 5.39 (1.36-14.58), SIR= 4.12 (1.04-11.18), SIR= 10.56 (2.73-29.16)). In addition, 'Electronics and equipment mechanics' as well as 'Sheet metal workers, structural workers and welders' (SIR= 4.26 (1.57-9.47), SIR= 2.75 (1.28-5.22)) had statistically significant excess incidence of leukemia.

4.3.2.4. Incidence of primary cancers in male LBNS shipyard workers by asbestos exposure level and duration of employment

The study cohort was separated into two groups; workers with less than five-years duration of employment in LBNS, and workers employed in the shipyard for five or more years in LBNS. The duration of employment is defined as the total years of employment in the LBNS starting from the year of hire to the last year of employment or 1985, whichever came first. There was a total of 6,844 workers with less than five-years duration of employment, and 4,218 workers employed in LBNS for five or more years. Out of the 11,062 workers included in the

analysis, three had duration of employment that were less than zero and were excluded for further analysis. A total of 1,644 workers did not have a specified asbestos exposure group. After excluding these workers, there were 5,848 workers that had less than five-years duration of employment and 3,566 workers were employed in the LBNS for five or more years.

There was a statistically significant excess of prostate cancer incidence across all three asbestos exposure groups among workers employed in LBNS for a total of less than five years (SIR= 3.61 (2.56-4.97), SIR= 2.03 (1.48-2.70), SIR= 2.76 (2.30-3.28)) (**Table 4.8**). Colorectal cancer (SIR= 2.79 (1.81-4.12), SIR= 2.20 (1.58-2.98)), cancer of the digestive system (SIR= 2.23 (1.27-3.66), SIR= 2.81 (2.01-3.83)), lung cancer (SIR= 2.19 (1.42-3.24), SIR= 1.94 (1.41-2.60)), and cancer of the urinary system (SIR= 2.88 (1.76-4.46), SIR= 1.68 (1.08-2.51)) had statistically significant SIRs in both the intermediate asbestos exposure and high asbestos exposure groups. A statistically significant excess incidence of mesothelioma (SIR= 13.48 (5.89-26.63)) was observed among LBNS workers employed for less than five years in the high asbestos exposure group. Moreover, compared to the general population of California, there was a statistically significant excess incidence of myeloma (SIR= 3.83 (1.67-7.57)) in the high asbestos exposure group in this subgroup of LBNS workers.

Similar to the previous subgroup, among the group of workers employed in the shipyard for five or more years, there was statistically significant excess incidence of prostate cancer across all three asbestos exposure groups compared to the general population (SIR= 3.19 (2.16-4.54), SIR = 2.12 (1.55-2.82), SIR= 2.64 (2.15-3.21)). There was a statistically significant excess incidence of lung cancer (SIR= 2.34 (1.53-3.42)) in workers with intermediate asbestos exposure in the group with five or more years of duration of employment in the shipyard. The low and high asbestos exposure groups had approximately 2.7-folds (SIR= 2.73 (1.48-4.64),

SIR= 2.70 (2.03-3.53)) excess incidence of lung cancer compared the expected number based on the general population. There was a statistically significant excess of mesothelioma in the intermediate and high asbestos exposure groups (SIR= 16.67 (5.30-40.20), SIR= 9.09 (2.89-21.93)). There was also a excess of leukemia (SIR= 4.71 (2.19-8.94)) and cancers of the urinary system (SIR= 2.55 (1.48-4.11)) in the intermediate asbestos exposure group. The SIRs for cancer of the digestive system (SIR= 1.87 (1.17-2.83)) and colorectal cancer (SIR= 1.90 (1.98-2.73)) remained statistically significant in the high asbestos exposure groups employed for five or more years in the shipyard.

Table 4.8. Primary cancers in the Long Beach Naval shipyard cohort by asbestos exposure separated by the duration of employment (n = 9,415)

A. Duration of employment of less than five years

i. Low asbestos exposure (n = 871)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	4	0.57	7.04 (2.23-16.93)
Colorectal	3	3.91	0.77 (0.20-2.09)
Digestive system excluding colorectal	6	2.98	2.01 (0.82-4.19)
Endocrine system	3	0.35	8.54 (2.18-23.33)
Leukemia	1	0.91	1.10 (0.05-5.42)
Lung	9	4.84	1.86 (0.91-3.41)
Lymphoma	4	1.81	2.22 (0.70-5.33)
Male reproductive system excluding prostate	1	0.61	1.65 (0.08-8.09)
Mesothelioma	1	0.12	8.59 (0.42-41.10)
Myeloma	2	0.41	4.82 (0.82-16.12)
Oral cavity and pharynx	5	1.21	4.14 (1.51-9.16)
Prostate	35	9.68	3.61 (2.56-4.97)
Respiratory system excluding lung	5	0.61	8.24 (3.00-18.17)
Skin excluding basal and squamous	2	2.41	0.83 (0.14-2.74)
Urinary system	5	2.95	1.70 (0.62-3.76)

[†] Primary cancers only

ii. Intermediate asbestos exposure (n = 1,447)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	2	1.10	1.82 (0.30-6.01)
Colorectal	23	8.25	2.79 (1.81-4.12)
Digestive system excluding colorectal	14	6.27	2.23 (1.27-3.66)
Endocrine system	1	0.65	1.54 (0.08-7.59)
Leukemia	1	1.86	0.54 (0.03-2.65)
Lung	23	10.49	2.19 (1.42-3.24)
Lymphoma	3	3.50	0.86 (0.22-2.33)
Male reproductive system excluding prostate	2	0.97	2.07 (0.35-6.81)
Mesothelioma	1	0.25	3.96 (0.20-19.73)
Myeloma	1	0.88	1.14 (0.06-5.60)
Oral cavity and pharynx	2	2.46	0.81 (0.14-2.69)
Prostate	43	21.22	2.03 (1.48-2.70)
Respiratory system excluding lung	2	1.29	1.56 (0.26-5.12)
Skin excluding basal and squamous	4	4.78	0.84 (0.27-2.02)
Urinary system	18	6.26	2.88 (1.76-4.46)

† Primary cancers only

iii. High asbestos exposure (n = 3,530)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	6	2.47	2.43 (0.98-5.05)
Colorectal	38	17.30	2.20 (1.58-2.98)
Digestive system excluding colorectal	37	13.18	2.81 (2.01-3.83)
Endocrine system	2	1.47	1.36 (0.23-4.50)
Leukemia	8	3.97	2.02 (0.94-3.83)
Lung	42	21.67	1.94 (1.41-2.60)
Lymphoma	8	7.72	1.04 (0.48-1.97)
Male reproductive system excluding prostate	2	2.39	0.84 (0.14-2.76)
Mesothelioma	7	0.52	13.48 (5.89-26.63)
Myeloma	7	1.83	3.83 (1.67-7.57)
Oral cavity and pharynx	6	5.29	1.13 (0.46-2.36)
Prostate	120	43.54	2.76 (2.30-3.28)
Respiratory system excluding lung	7	2.71	2.58 (1.13-5.11)
Skin excluding basal and squamous	7	10.38	0.67 (0.29-1.33)
Urinary system	22	13.07	1.68 (1.08-2.51)

† Primary cancers only

B. Duration of employment of five or more years

i. Low asbestos exposure (n = 466)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	2	0.44	4.55 (0.76-15.02)
Colorectal	7	3.34	2.10 (0.92-4.15)
Digestive system excluding colorectal	4	2.55	1.57 (0.50-3.78)
Endocrine system	.	0.25	.
Leukemia	2	0.74	2.70 (0.45-8.93)
Lung	12	4.40	2.73 (1.48-4.64)
Lymphoma	2	1.38	1.45 (0.24-4.79)
Male reproductive system excluding prostate	.	0.32	.
Mesothelioma	1	0.10	10.00 (0.50-49.32)
Myeloma	1	0.36	2.78 (0.14-13.70)
Oral cavity and pharynx	3	1.01	2.97 (0.76-8.08)
Prostate	28	8.79	3.19 (2.16-4.54)
Respiratory system excluding lung	.	0.54	.
Skin excluding basal and squamous	4	1.90	2.12 (0.67-5.08)
Urinary system	6	2.55	2.35 (0.95-4.89)

[†] Primary cancers only

ii. Intermediate asbestos exposure (n = 1,015)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	1	0.97	1.03 (0.05-5.08)
Colorectal	13	7.73	1.68 (0.94-2.80)
Digestive system excluding colorectal	11	5.81	1.89 (1.00-3.29)
Endocrine system	2	0.53	3.77 (0.63-12.47)
Leukemia	8	1.70	4.71 (2.19-8.94)
Lung	24	10.27	2.34 (1.53-3.42)
Lymphoma	6	3.05	1.97 (0.80-4.09)
Male reproductive system excluding prostate	.	0.67	.
Mesothelioma	4	0.24	16.67 (5.30-40.20)
Myeloma	2	0.82	2.44 (0.41-8.06)
Oral cavity and pharynx	5	2.27	2.20 (0.81-4.88)
Prostate	43	20.33	2.12 (1.55-2.82)
Respiratory system excluding lung	1	1.25	0.80 (0.04-3.95)
Skin excluding basal and squamous	2	4.19	0.48 (0.08-1.58)
Urinary system	15	5.88	2.55 (1.48-4.11)

† Primary cancers only

iii. High asbestos exposure (n = 2,085)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	5	2.47	2.02 (0.74-4.49)
Colorectal	27	14.18	1.90 (1.98-2.73)
Digestive system excluding colorectal	20	10.71	1.87 (1.17-2.83)
Endocrine system	1	1.06	0.94 (0.05-4.65)
Leukemia	6	3.18	1.89 (0.86-3.92)
Lung	50	18.50	2.70 (2.03-3.53)
Lymphoma	10	5.91	1.69 (0.86-3.02)
Male reproductive system excluding prostate	1	1.51	0.66 (0.33-3.27)
Mesothelioma	4	0.44	9.09 (2.89-21.93)
Myeloma	4	1.50	2.67 (0.85-6.43)
Oral cavity and pharynx	6	4.24	1.42 (0.57-2.94)
Prostate	97	36.75	2.64 (2.15-3.21)
Respiratory system excluding lung	5	2.28	2.19 (0.80-4.86)
Skin excluding basal and squamous	11	8.03	1.37 (0.72-2.38)
Urinary system	15	10.78	1.39 (0.81-2.24)

† Primary cancers only

4.4. Discussion

As expected the leading causes of death in the LBNS study cohort were comparable to the leading causes of death in California. The cause-of-death categories that were most common in the LBNS study cohort included Disease of the circulatory system, Neoplasms, Diseases of the respiratory system, Accidents, suicides and homicides, and Diseases of the digestive system. According to the California Department of Public Health, in 2013 the most common specific causes of death in California included diseases of the heart, malignant neoplasm, stroke, chronic lower respiratory disease, and Alzheimer's disease.[125] There were excess deaths due to Neoplasms, Disease of the respiratory system, Accidents, suicides, and homicides, and Disease of the digestive system in the LBNS study cohort compared to the general population of California. Overall, LBNS workers with high asbestos exposure had higher SMRs for all five-leading cause-of-death categories compared to workers with low/intermediate asbestos exposure. Align with our previous findings have shown excess overall mortality and cancer specific deaths in workers exposed to asbestos.[8,9] A study on civilian workers in a U.S. Coast Guard shipyard showed an excess mortality from respiratory cancers, lung cancers, as well as mesothelioma, and a decrease in deaths from cardiovascular diseases.[8] Similar pattern was present in our study. Nevertheless, a study on workers in a U.S. naval shipyard in Japan by Kurumatani, et. al. found non-significant increase in mortality from cardiovascular disease.[126] In the LBNS study cohort, we found no difference in mortality from the Diseases of the circulatory system between the study cohort and the reference population.

Malignant neoplasm of the respiratory and intrathoracic organs was the most common cancer-specific cause-of-death in the LBNS study cohort. Among the five-leading cancer-specific causes of death in the study cohort, Malignant neoplasm of the urinary tract had the

highest SMR of 3.64 (2.87-4.50), followed by the Malignant neoplasm of the lymphatic and hematopoietic tissues (SMR= 2.48 (2.07-2.95)). Similar trend was observed in workers exposed to low/intermediate asbestos level as well as workers with high asbestos exposure. Excess mortality from malignant neoplasm of the urinary tract can be explained by exposure to other toxic substances in the shipyard. A previous study of shipyard workers in Genoa, Italy found excess deaths from bladder cancer.[127] Exposure to trichloroethylene (TCE), a type of solvent, had been previously associated to increase risk of kidney cancer mortality.[128] In addition, a meta-analysis study found association between occupational TCE exposure and kidney cancer risk, which was not observed using another solvent.[129] Exposure to cadmium has also been associated to increase risk of renal cancer.[130] These agents are common in many industries including the shipyard industry.

Various studies also showed elevated risk of lymphatic and hematopoietic malignancies in workers exposed to polycylic aromatic hydrocarbons.[130-132] A study by Brownson, et. al. found an increased risk of Hodgkin's disease in machinists, and increased risk of leukemia in mechanics.[132] In addition, an excess mortality from leukemia and aleukemia was observed on a group of mechanics with high exposure to fuels and solvents.[131] Furthermore, there is a suggestive evidence for a link between electrical occupation and risk of leukemia.[133-137] Studies by Pearce, et. al. found increased risk of leukemia among electrical workers in New Zealand.[138] Although Loomis, et. al. did not find an association between the risk of leukemia mortality and electrical workers in the U.S., there was sufficient evidence to suggest excess deaths from leukemia among electrical engineers and technicians, telephone workers, and electric power workers.[135]

Overall, there is an excess incidence of malignant neoplasms (excluding female related

cancers and breast cancer) in the study population. As expected, prostate cancer was the leading cancer in this population. Our findings showed that 13 out of the 15 specific cancers evaluated in the study had statistically significant elevated SIRs. These included mesothelioma, prostate, lung, and colorectal cancer. An exposure-response pattern was observed between the SIRs for mesothelioma and asbestos exposure level, but there was no statistical difference in SIRs for low asbestos exposure compared to the other two asbestos exposure groups. In general, the workers with low asbestos exposure had the lowest excess in incidence of mesothelioma among the three asbestos exposure groups, while the high asbestos exposure group had the highest excess in incidence of mesothelioma. An excess incidence of lung cancer was also observed in our study, however, unlike mesothelioma the SIR for lung cancer were similar across all three asbestos exposure groups. A recent study by Jarvholm, et. al. on Swedish construction workers found that after 20 years since their last recorded asbestos exposure, workers heavily exposed to asbestos had similar risk of lung cancer with workers in low or no asbestos exposure.[139] Similar to the findings reported by Jarvholm, et. al., our study population has almost 30 years of follow-up and most the workers are retired.

Aligned with previous findings, the excess incidence of most cancers in the study were more elevated in workers with longer duration of employment in the shipyard. Krstev, et. al. reported a large SMR for mesothelioma among U.S. Coast Guard shipyard workers with longer duration of employment.[8] A similar trend was observed by Albin, et. al. in evaluating mortality for lung cancer and colorectal cancer among asbestos cement workers.[9] In contrast, a study by Melkild, et. al. examining the incidence of lung cancer among workers in a Norwegian shipyard, showed decreased in excess incidence of lung cancer as the duration of employment increase.[82] Nevertheless, the excess incidence of lung cancer was constant as the duration of employment

increased.

Brain cancer was unexpectedly high in this population. Excess incidence of brain cancer was observed in both the low and high asbestos exposure group. Electronic magnetic field (EMF) and electrical workers has been linked to elevated risk of brain cancer.[135-137,140,141] However, other studies failed to find a positive association between brain cancer and exposure to EMF.[142,143] Interestingly, in our study excess of brain cancer was most prominent in Architects and Engineers, a finding that is difficult to interpret. Electricians as well as electronics and equipment mechanics, had non-significant elevated incidence of brain cancer. Nonetheless, specific types of engineers, such as electrical engineers, potentially have similar exposure to that of electricians and electronic mechanics.

In addition, excess incidence of lymphatic and hematopoietic malignancies was observed in the high asbestos exposure group. Myeloma cases were most evident in electrical workers (i.e. electronics and equipment mechanics, and electricians), and painters. Most occupational studies examining lymphatic and hematopoietic malignancies found a relationship between leukemia and electrical workers. However, the relationship between myeloma and electrical workers has not yet been established. Findings from a population-based case-control study found a non-significant elevated risk of multiple myeloma in electrical fitters as well as in related electrical and electronic workers.[144] Similar result was established in other studies with a similar nature.[145,146] In our study, excess incidence of leukemia was mostly observed in electronics and equipment mechanics, as well as in structural-relevant occupations (i.e. sheet metal workers, structural workers, and welders). A study of electrical workers from Los Angeles county observed a higher mortality from leukemia in electrical workers compared non-electrical workers.[134] EMF has been speculated to cause the increased risk of leukemia observed among

electrical workers.[134-136,138,141,143,147]

Metals such as cadmium and lead present in the shipyard are suspected to increase risk of several cancer types including prostate.[148-151] For example, a previous study suggests an association between prostate cancer and exposure to cadmium.[152] Specific metals (e.g. cadmium, lead, manganese, and zinc) as well as some solvents have endocrine disrupting potential.[153] Exposures to these metals and solvents in specific occupations at the LBNS shipyard may have contributed to the observed elevated incidence in other cancer such as prostate and endocrine-related cancers.

Overall, the excess mortality from various diseases and cancer, as well as the excess incidence of a wide range of malignancies in the LBNS study cohort served as evidence of the hazards from working in the shipyard. Excess incidence of non-asbestos related cancer such as brain cancer and leukemia indicated exposure to other hazardous substances in the shipyard. The simultaneous exposure from asbestos and these other occupational hazards plays a role in the excess mortality from a wide-variety of diseased as well as excess incidence of various cancers in the cohort. Further study is warranted to understand the impact of concurrent exposures to multiple occupational substances in worker's health and safety.

CHAPTER 5

The Risk of Colorectal Cancer Between Long Beach Naval Shipyard Workers Exposed to Low, Intermediate and High Asbestos Exposure

5.1 Introduction

Asbestos is known to cause lung cancer and mesothelioma, and is suggested to also cause colorectal cancer. However, the relationship between asbestos and colorectal cancer is yet to be clearly established. Pleural plaques, indicative of airborne asbestos exposure, were previously observed in LBNS workers. The study reported a significantly higher prevalence of pleural plaques in older workers who had a longer duration of employment.[119] The risk of lung cancer and colorectal cancer due to asbestos exposure as well as other asbestos-related malignancies has not yet been evaluated among LBNS workers. Thus, such study is warranted in this population.

Inhalation of asbestos fibers, which are irritants that activates the body's immune system to clear the fibers in the lungs, results to the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) leading to DNA damage.[154] Although the mechanism on how asbestos exposure causes cancer is not fully understood, chronic inflammation is speculated to play a key role in the development of asbestos-related malignancies, such as mesothelioma. Accumulation of asbestos fibers can result to formation of asbestos bodies causing chronic inflammation and induces pro-inflammatory and anti-inflammatory responses, which can initiate cancer development.[155] DNA damage caused by ROS is thought to be a contributing factor in the transformation of mesothelial cells and progression of mesothelioma.[156] Currently, studies that examine differences in tumor characteristics between shipyard workers exposed to asbestos and non-exposed shipyard workers are lacking in the literature.

The purpose of this study is to first examine the relationship between the risk of

colorectal cancer and varying levels of asbestos exposure (i.e. low, intermediate, high) in the LBNS workers employed between 1978 and 1985. Secondly, this chapter aims to compare colon and rectum tumor characteristics specifically focusing on tumor histology and stage at diagnosis across low, intermediate, and high asbestos exposure levels in LBNS workers diagnosed with colorectal cancer.

5.2. Methods

Chapter 2 contains the detailed description of the general methods used for the study cohort. *Chapter 2* also discussed the method used to determine the asbestos exposure level of the LBNS workers. Workers who did not belong to an asbestos exposure group were excluded from the analyses in this chapter.

5.2.1. Risk of colorectal cancer in low, intermediate and high asbestos exposure groups

The Kaplan-Meier (KM) method was used to examine the survival curve for length of time after initial employment in the shipyard until disease occurrences stratified by asbestos exposure. The log-rank test was utilized to compare the groups for the colorectal cancer outcome. A *P*-value less than 0.05 indicated statistical significant. The proportional hazard assumption was also assessed for both asbestos exposure and duration of employment using the log of the negative log plot (**Appendix P**). Violation of the proportional hazard assumption was observed in both variables. Thus, results from the Cox proportional hazard should be interpreted with caution. Furthermore, a secondary analysis on lung cancer and asbestos exposure was also performed.

5.2.2. Histology and stage of diagnosis of colorectal tumors in the Long Beach Naval shipyard

Information on the histological types for the colorectal tumors were derived from the CCR data coded using the ICD-O-3. Histological types were collapsed based on the histological categories presented by Stewart, et. al.[157] The variable SUMSTAGE from the CCR, which is defined as the "summary stage at the time of diagnosis,"[158] was used for the stage at cancer diagnosis. *In situ* and localized tumors were considered as early stage, while regional and remote tumors were categorized as late stage. A chi-squared test was calculated to examine the relationship between histological types or stage-at-diagnosis and asbestos exposure group. A *P*-value less than or equal to 0.05 indicates that the two variables are related.

5.3. Results

5.3.1. Colorectal cancer risks in the Long Beach Naval shipyard

After workers with unknown asbestos exposure were excluded, there was a total of 9,349 workers in the analysis. Out of the 138 colorectal cancer diagnoses in the LBNS study cohort. **Figure 5.1** depicts the distribution of age-at-diagnosis for colorectal cancer in the shipyard. Eight (5.8%) tumors were diagnosed before the age of 50 years. The mean age-at-diagnoses for colorectal cancer tumors in the shipyard was 65.4±10.3 years old. Tumors with unknown asbestos exposure were excluded in the analysis. Only 111 tumors were included in the analysis (**Table 5.1**). Twenty-seven colorectal cancer cases did not have assigned asbestos exposure group. Out of 111 colorectal tumors, 65 (58.56%) were in the high asbestos exposure group. There were 10 (9.01%) colorectal cancer cases in the low asbestos group, 36 (32.43%) cases in the intermediate group. **Figure 5.2** illustrates the KM curve for the length of time after initial

employment in the shipyard until occurrence of colorectal cancer by asbestos exposure group. No difference in time-to-disease occurrence was observed across the three different asbestos exposure groups (log-rank *P*-value = 0.16) for colorectal cancer even after adjusting for the duration of employment (log-rank *P*-value = 0.33) (**Figure 5.3**).

The univariate Cox regression showed that there was no significant association found between colorectal cancer risk and asbestos exposure levels comparing the high and intermediate asbestos exposure group to the low asbestos exposure group (reference group) (**Table 5.2**). The analysis combining high and intermediate asbestos groups also produced a non-statistically significant result on the relationship between asbestos exposure and the risk of colorectal cancer.

For the secondary outcome, out of the 200 lung tumors diagnosed in the LBNS study cohort during the years of follow-up, 159 were included in the analysis (**Appendix Q**). A total of 40 lung cancers had unknown asbestos exposure level. As expected, our findings showed no significant difference in KM time-to-disease occurrence curve across the three different asbestos exposure groups in the KM analysis (log-rank *P*-value = 0.69) (**Appendix R**).

5.3.2. Characteristics of colorectal tumors in the Long Beach Naval shipyard workers

Overall, 63.0% of the 111 colorectal cancer cases were diagnosed in the late stage. For this analysis, the low and intermediate asbestos exposure groups were combined due to the small number of cases. The low/intermediate asbestos exposure group had 58.7% colorectal cancers diagnosed at a late stage, and 67.7% of the colorectal cancer cases in the high asbestos exposure group were diagnosed at a late stage (**Table 5.3**). The *P*-value of 0.42 signifies that there was no relationship between stage-at-diagnosis and asbestos exposure. Approximately 96% of colorectal cancers in the low/intermediate asbestos exposure group were adenocarcinoma (**Table 5.4**). The

high asbestos exposure group had slightly lower proportion of adenocarcinoma compared to the low/intermediate asbestos exposure group. Five percent of the colorectal cancer cases in this group were carcinoid tumors, and 1.5% was squamous cell carcinomas. Our study findings showed no relationship between histological types and asbestos exposure (*P*-value = 0.73).

Figure 5.1. Distribution of age-at-diagnosis for colorectal cancer in the Long Beach Naval shipyard

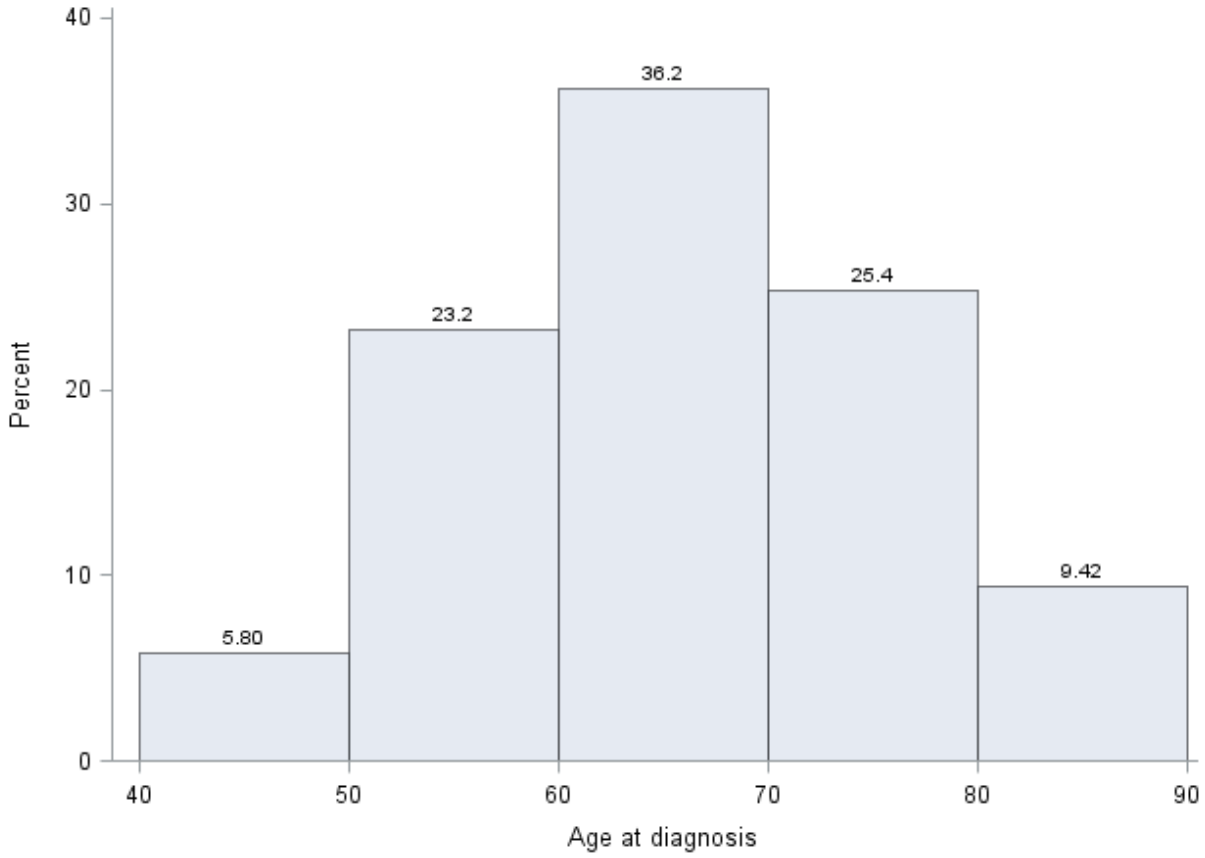


Table 5.1. Colorectal cancer stratified by asbestos exposure groups (n = 9,415)

Exposure to asbestos	Count	Percent
Low	10	9.01
Intermediate	36	32.43
High	64	58.56
Total	*111*	*100.00*

Table 5.2. Cox proportional hazards analysis for incidence of colorectal cancer stratified by the duration of employment in the LBNS (n = 9,349)

Model	Hazard Ratio	95% CI
Univariate		
low	reference	
intermediate	1.89	0.94-3.80
high	1.54	0.79-2.99
Model 1[a]		
low	reference	
intermediate	1.90	0.94-3.82
high	1.54	0.79-2.99
Model 2[b]		
low	reference	
intermediate/high	1.56	0.81-2.98

[a] Stratified by duration of employment
[b] Two asbestos exposure group (low vs intermediate/high), stratified by duration of employment

FIGURE 5.2. Kaplan-Meier survival curve for length of time after initial employment in the shipyard until occurrence of colorectal cancer stratified by asbestos exposure

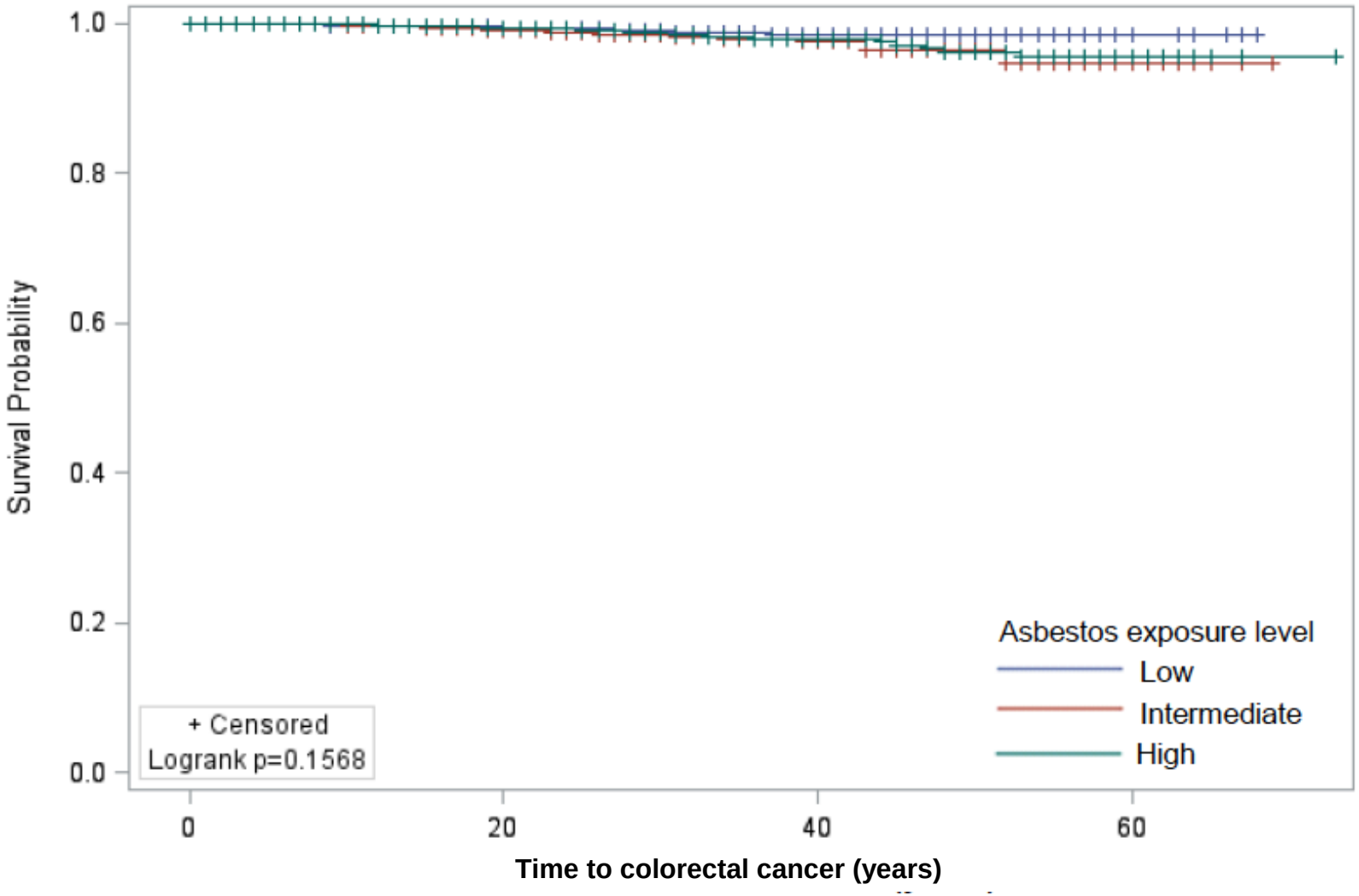


FIGURE 5.3. Kaplan-Meier survival curve for length of time after initial employment in the shipyard until occurrence of colorectal cancer stratified by asbestos exposure and duration of employment

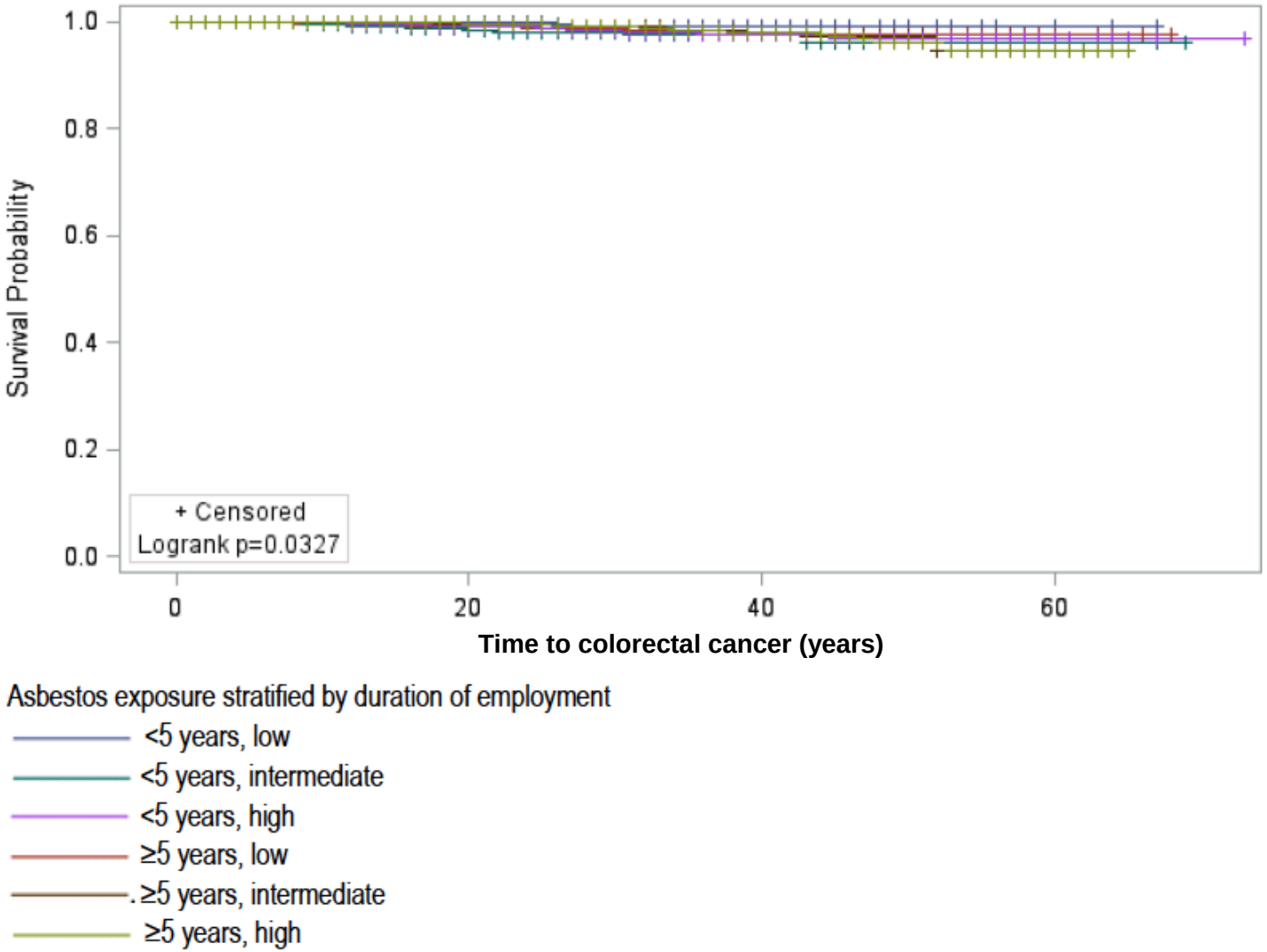


Table 5.3. Distribution of stage-at-diagnosis for colorectal cancer in the Long Beach Naval shipyard (n = 111)

Stage at diagnosis	Low/Intermediate		High	
	Count	Percent	Count	Percent
Early	19	41.3	21	32.31
Late	27	58.7	44	67.69
Total	*46*	*100*	*65*	*100*

Chi-squared test *P*-value = 0.42

Table 5.4. Distribution of histological types for colorectal tumors in the Long Beach Naval shipyard (n = 111)

Histological types	Low/Intermediate		High	
	Count	%	Count	%
Carcinoma, NOS	1	2.17	2	3.08
Squamous cell carcinoma, NOS	0	0	1	1.54
Adenocarcinoma	44	95.65	59	90.77
Carcinoid tumor, malignant	1	2.17	3	4.62
Total	*46*	*100*	*65*	*100*

Chi-squared test *P*-value = 0.73

5.4 Discussion

5.4.1. Risk of colorectal cancer and lung cancer between low, intermediate, and high asbestos exposed workers at the Long Beach Naval shipyard

Our study found no difference in time to colorectal cancer occurrence between the three asbestos exposure groups in LBNS. Similarly, we found no difference in KM curves between the asbestos exposure groups for the lung cancer outcome. This result is consistent from the previous SIR analysis presented in *Chapter 4*. Based from our previous analysis, workers in the LBNS experienced higher cases of cancer compared to the general population of California. However, we observed similar SIR for colorectal cancer and lung cancer across three asbestos exposure group. The hazard ratio assessing colorectal cancer between the low asbestos exposure group (reference group) and high as well as intermediate exposure group both resulted to non-significant elevated risks of colorectal cancer.

Previous findings on the relationship between colorectal cancer risk and asbestos exposure were conflicting. Early studies on building trade insulation workers by Selikoff, et. al., who observed increased risk of gastrointestinal cancers in this wokrers[24,42], encouraged subsequent investigation on the risk of colorectal cancer as well as other gastrointestinal cancers and exposure to asbestos. A Swedish study observed increased risk of colorectal cancer only in asbestos cement workers with highest cumulative dose of asbestos.[9] Similarly, studies from Jakobsson, et. al. found excess risk of colorectal cancer in their study population of cement workers.[12,159,160] A Dutch study of asbestos cement workers also found excess risk of colorectal cancer in men employed in the early production period.[13]

Shipyard studies have contradicting results on the relationship between colorectal cancer and asbestos exposure. An early study by Puntoni, et. al. found elevated risk of colon cancer

excluding rectum among shipyard workers in Genoa, Italy.[161] Nevertheless, a more recent study of the ship repairers, refitters and construction workers in the same area found no excess mortality from colorectal cancer among workers in the shipyard compared to the general population of Genoa, Italy.[127] This recent finding aligns with previous results from various epidemiological studies. A 2011 study of Japanese workers at a U.S. Navy shipyard in Japan also found no excess mortality due to colorectal cancer. However, the study lack statistical power due to the size of the cohort.[17] Furthermore, a Finnish studies on shipyard and machine shop male workers found no pronounced excess cases of colorectal cancer in the shipyard workers compared to the general population.[16] Additionally, Krstev, et. al. also did not find excess mortality of colorectal cancer among civilian workers in the U.S. Coast Guard even after adjusting for the duration of employment in the shipyard.[8] Nonetheless, a study on the Royal Norwegian Navy observed a borderline significant SIR for colorectal cancer in the non-engines crews.[4] Similarly, our study found elevated colorectal cancer SIR in workers with intermediate and high asbestos exposure. However, we found no difference in colorectal cancer risk between workers with varying asbestos exposure groups in the shipyard. Asbestos exposure could potentially increase colorectal cancer in workers exposed to the substance. However, in a shipyard setting, most workers are exposed to asbestos at some level; yet, the role that concentration and the duration plays remains unclear.

Our non-significant finding on the risk of lung cancer between shipyard workers exposed to low levels of asbestos and intermediate/high asbestos exposed group may be due to the indirect exposures to asbestos by workers employed in the shipyard who were not in the trades that commonly use asbestos. Several studies in shipyards, including our current findings, reported asbestos-related cancers in workers whose trades were traditionally not exposed to

asbestos such as boilermakers and structural workers.[80-82,162] In short, all shipyard employees are exposed to asbestos regardless of the occupation, and therefore all are at a higher risk of asbestos-related malignancies.

In addition, it is also possible that our non-significant findings reflect previous reports on the risk of lung cancer after cessation of asbestos exposure. A recent study by Jarvholm, et. al. found that after approximately 20 years since last asbestos exposure the risk for lung cancer in high asbestos exposure group was similar to the low exposure group.[139] Asbestos exposure level in the study was estimated using incidence of pleural mesothelioma. Occupations commonly associated with heavy exposure to asbestos were found in the high asbestos exposure group. Findings by Jarvholm, et. al. was consistent with an Italian study, which observed high overall SMR for lung cancer in asbestos cement workers, who were followed-up for over 50 years since cessation of asbestos exposure.[163] SMR for lung cancer peaked on the 30-39 years since cessation of the exposure, and slightly declined in the subsequent years. However, contradictory to these studies, a Taiwanese study of shipbreaking workers with a 24-year follow-up found a exposure-response trend for lung cancer risk comparing low, medium, and high asbestos exposure to a matched population control.[56] Our study had an average of 22.4 ±10.9 years of follow-up, which provides sufficient latency period to observe a asbestos-related malignancies to develop. However, it is possible that due to the long latency the risk of lung cancer in high asbestos exposure group declined over the years.

In the past 30 years, colorectal cancer incidence in the United States has decreased, attributed largely to increased screening.[164] The U.S. Preventive Services Task Force recommended screening for colorectal cancer beginning at the age of 50 until age 75.[165] In the LBNS shipyard cohort, approximately 94% of colorectal tumors were diagnosed at age 50 or

older. In this study, the true incidence of colorectal cancer due to asbestos exposure cannot be determined since screening would have prevented polyps to progress to tumors.

5.4.2. Colorectal tumor characteristics and asbestos exposure

Overall, our findings showed a higher proportion of late stage-at-diagnosis in the high asbestos exposure group. There was no statistically significant relationship observed between stage-at-diagnosis and asbestos exposure groups. A comparable percent of adenocarcinoma was observed in the LBNS low/intermediate asbestos exposure group (95.65%). Meanwhile, the LBNS group with high asbestos exposure had about 6% lower adenocarcinoma cases. About 3% of the cases were carcinoma, NOS and about 5% were carcinoid tumor, malignant. There was no statistically significant difference found between the two groups of asbestos exposures in relation to histological types.

The distribution of the histological categories in our study reflects the findings reported by Stewart, et. al. on microscopically confirmed colorectal cancer cases in the U.S. between 1998 and 2011.[157] According to Stewart, et. al., in the white male subgroup of the U.S. population, 95.65% of colorectal cancer cases were adenocarcinoma. In general, sporadic colorectal cancer cases are mostly adenocarcinoma.[166] As expected, the majority of colorectal tumors in the LBNS were adenocarcinoma. Nevertheless, further examination is necessary to assess the histological characteristics of workers in the high asbestos group, which had a higher proportion of other histological types compared to the proportion in the low/intermediate exposure as well as the U.S. population.

Non-sporadic colorectal cancers, such as familial colorectal cancer as well as colorectal cancer due to chronic inflammation, have different mechanism compared to sporadic cancer

cases. The mechanism behind colorectal cancer due to chronic inflammation, such as that observed in inflammatory bowel disease (IBD) individuals, is not well understood. However, studies have shown that cancer that developed from this pathway is pathologically different than sporadic tumors. For example, colorectal cancer in IBD individuals are diagnosed in a younger age. In addition, studies showed that mutations commonly observed in sporadic cancers are less frequent in cancer associated with chronic inflammation[167-169].

An animal study showed that inhaled asbestos can induce inflammation in the lungs.[170] Case studies have repeatedly observed asbestos bodies present in the lungs of individuals who were previously exposed to asbestos. Asbestos bodies are accumulation of asbestos fibers that have become encapsulated with protein rich in ferritin, which results to the production of ROS.[171,172] There are also reported cases of asbestos bodies in the colon of individuals who were exposed to asbestos.[173,174] The mechanism behind migration of asbestos from environment to the colon remains unclear. Aside from direct ingestion of asbestos fibers, mucocialliary escalators could facilitate the migration of asbestos fibers from the lungs, by removing asbestos fibers in the airway, then swallowed and excreted in the feces.[175] These asbestos fibers could potentially remain in the gastrointestinal tract and cause inflammation. Chronic inflammation in the colon can lead to colorectal cancer if not treated. Due to a different mechanism from sporadic tumors, exposure to asbestos could potentially present different tumor characteristics perhaps more comparable to that of individuals suffering from chronic inflammation in the colon.

CHAPTER 6

The Risk of Lung Cancer Between Long Beach Naval Shipyard Workers Exposed to Welding Fumes and Unexposed Workers

6.1 Introduction

Lung cancer is the leading cause of cancer death worldwide in both men in women. Although smoking contributes to 80-90% of lung deaths, a portion of lung cancer incidence is due to environment and occupational exposures. In the 1990, the International Agency for Research on Cancer classified welding fumes in the Group 2B category of carcinogens, indicating that there is a limited evidence in humans on the carcinogenicity of welding fumes, and there is inadequate evidence in experimental animals.[176] Welding fumes are formed from the burning of the electrode and heating of the base metal. It has a diverse composition that is determined by the welding process and the base metals. For instance, high levels of nickel and hexavalent chromium, which are known carcinogens, are emitted during stainless steel welding, and not commonly present in fumes of mild-steel welding.[177]

There is a large body of evidence demonstrating a link between welders and lung cancer. Nevertheless, these results vary across different epidemiological studies. It has been suggested that the observed increased in lung cancer among welders could be attributed to stainless steel welding.[77] However, recent studies also showed an increase of lung cancer risk in mild-steel welders.[79,178,179] In addition, a study by Moulin, et. al. involving stainless steel welders and mild-steel welders showed no difference in SMR between the two groups.[68]

Previous studies of lung cancer in shipyard welders reports inconsistent findings. A study on shipyard workers by Melkild, et. al. found increased incidence of lung cancer among

welders.[82] Danielson, et. al. reported no clear relationship between exposure to welding fumes and lung cancer.[80] However, an increase of lung cancer risk was reported in welders with five or more years of employment compared to non-welders. Currently, assessment of lung cancer risk in shipyard workers exposed to welding fumes is inadequate. Welding fumes in the shipyard setting is not limited to workers who carries the specific job title of "welder". Several other job titles such as pipefitters and sheet metal workers also use welding routinely. In addition, it is important to consider that workers in the shipyard are also indirectly exposed to asbestos fibers. Therefore, study of welding fumes exposure and lung cancer in the shipyard industry should not be limited to shipyard welders only, and their asbestos exposure status should also be considered. The purpose of this study is to measure the association between lung cancer risk (lung cancer incidence and mortality rates) and various levels of exposure to welding fumes (exposed vs unexposed) in the LBNS. Workers will be grouped based on their welding fumes exposure and asbestos exposure. We will also examine this relationship by duration of employment in the shipyard.

6.2. Methods

Chapter 2 contains the detailed description of the general methods used for the study cohort.

6.2.1. Cancer-specific age-adjusted standardized incidence ratio in male Long Beach Naval shipyard workers stratified by welding fumes clusters and duration of employment

Workers who had missing years of birth, workers who did not meet the age inclusion, workers with unknown asbestos exposure were excluded in the analysis. In addition, workers that belonged to the main occupational group Office workers and Administrative personnel were

excluded in the analysis. Information on cancer diagnosis were derived from the CCR. Tumors were defined using the ICD-O-3 and WHO's Classification of Tumours and Haematopoeitic and Lymphoid Tissues (2008). Only primary tumors diagnosed between 1988 and 2011 were included in the analysis. Tumors characterized as benign or borderline malignant were excluded. In addition, tumors reported from autopsy only or from death certificate only were also excluded.

The population in the state of California from 1988 to 2011 was utilized as the reference population to calculate the age-specific standardized incidence ratio for white males. The expected number of cancers for each year from 1988 to 2011 were calculated per five-year interval except for years prior to 1990 and after 2009, which were per two-year interval. The age-specific incidence rates in men in California were used to calculate the expected number of cancer in the LBNS study cohort. The 95% confidence intervals were determined for the SIR, where a 95% confidence interval that excluded 1.0 indicates significant.

6.2.2. Exposure to welding fumes

Occupations with tasks involving welding fumes were identified using the information from an occupational health database (Haz-Map: https://hazmap.nlm.nih.gov). The Haz-Map database contains a wide variety of occupational agents, the diseases linked to these agents, as well as, the jobs and hazardous job tasks. The relationships between the occupational agents, hazardous job tasks and the diseases linked to the agents are based on current scientific evidence. All information from the Haz-Map database is based on several resources including textbooks, journal articles, the Documentation of the Threshold Limit values, and other electronic databases such as the Hazardous Substances Data Bank, which is managed by the National Library of Medicine.

Each of the occupational category in the LBNS study cohort, excluding ‘Other’ and ‘Office & Administrative personnel’, were grouped as either exposed or unexposed to welding fumes, based on the Haz-Map list of “high risk job tasks associated” with welding. An occupational category was considered exposed to welding fumes if it consisted of workers with major job tasks that included ‘welding.’ Data from the Haz-Map were verified using official information from the Naval Sea Systems Command website (http://www.navsea.navy. mil) (**Table 6.1**).

Three clusters of welding fumes exposure were formed. The first cluster (Cluster I) contained workers who were not exposed to welding fumes and asbestos. The low asbestos exposure was considered as not exposed to asbestos. Workers in the intermediate and high asbestos exposure group were considered as exposed to asbestos. Consequently, the second cluster (Cluster II) consisted of worker who were not exposed to welding fumes, but were exposed to asbestos. Lastly, workers exposed to both substances were placed in the third cluster (Cluster III). Workers who did not have an asbestos exposure group and workers in the occupational categories ‘Office worker and administrative personnel’ and ‘Other’ were excluded in the analysis.

Table 6.1. List of occupational categories in the Long Beach Naval shipyard clustered by exposure to welding fumes and asbestos

Clusters	Occupational categories	Exposed to welding fumes[a]	Exposed to asbestos[a]
I	Architects, Engineers	0	0
	Office workers, Administrative personnel	0	0
	Painters	0	0
II	Electricians	0	1
	Electronics & equipment mechanics	0	1
	Machinist	0	1
	Insulators	0	1
	Transportation & motor vehicle operators	0	1
	Riggers & equipment cleaners	0	1
	Warehousemen	0	1
III	Welders	1	1
	Sheet metal workers	1	1
	Structural workers	1	1
	Boilermakers	1	1
	Pipefitters	1	1

[a] 0 is not exposed, 1 is exposed

6.2.2. Kaplan-Meier for occurrence of lung cancer

The KM method was examined for lung cancer by exposure to welding fumes. The log-rank test was utilized to compare the KM curve between the three different welding fumes exposure clusters. A *P*-value less than 0.05 indicated statistical significant. The time to lung cancer survival curve by welding fumes exposure clusters was further adjusted for duration of employment in the shipyard was calculated.

6.3. Results

6.3.1. Age-specific standardized incidence ratio of cancer in the Long Beach Naval shipyard stratified by welding fumes and duration of employment

There was a total of 9,349 workers included in the analysis. Workers with unknown

asbestos exposure status as well as workers in main occupational groups 'Office workers/Administrative personnel' and 'Other' were excluded in the analysis. Cluster I had a total of 1,277 workers (**Table 6.2**). There were 4,591 workers in cluster II, and 3,481 in cluster III. **Table 6.2** includes the distribution of cancers by welding fumes clusters stratified by duration of employment. Out of the 9,349 workers, 3,531 workers had a duration of employment of less than five years, and 5,818 workers had a duration of employment of five or more years in the shipyard.

Briefly there was a total of 159 lung cancers. Cluster II had the highest number of lung cancer cases. **Table 6.3** presents the overall age-adjusted SIR for each of the welding fumes cluster. Excess incidence of mesothelioma, lung, and prostate were observed in all three clusters. Compared to the general population of California, the first cluster, which has no exposure to welding fumes and asbestos had elevated incidence of brain cancer (SIR= 6.33 (2.56-13.14)), in addition to excess incidence of myeloma (SIR= 4.16 (1.06-11.34)), cancer of the oral cavity and pharynx (SIR= 3.84 (1.79-7.30)), and cancer of other respiratory system excluding lung (SIR=3.71 (1.18-8.93)). Workers in cluster II, who were not exposed to welding fumes, but were exposed to asbestos, had the highest number of cancer types with statistically significant SIR among the three clusters. As expected, the second cluster had the highest excess of mesothelioma (SIR=14.35 (1.74-24.29). Aside from lung cancer (SIR= 2.22 (1.77-2.76)) and prostate cancer (SIR=2.41 (2.06-2.79)), Cluster II had excess incidence of brain cancer (SIR= 3.01 (1.58-5.22)), colorectal cancer (SIR= 2.24 (1.73-2.86)), cancer of the digestive system excluding colorectal (SIR= 2.27 (1.69-2.99)), myeloma (SIR= 3.46 (1.76-6.17)), cancer of the respiratory system excluding lung (SIR= 2.30 (1.17-4.11)), and cancer of the urinary system (SIR= 2.27 (1.69-2.99)). Similarly, the last cluster which contained workers exposed to both welding fumes and

asbestos also have statistically significant excess incidence of lung cancer (SIR= 2.33 (1.79-2.98)), mesothelioma (SIR= 6.47 (2.05-15.56)), prostate cancer (SIR= 2.64 (2.22-3.11)), colorectal cancer (SIR= 2.03 (1.47-2.73)), and cancer of the digestive system (SIR= 2.20 (1.12-3.92)). Moreover, there was a 2.20-folds (1.12-3.92) excess cases of leukemia in cluster III compared to the general population.

Table 6.2. Distribution of lung cancer cases in the Long Beach Naval shipyard by welding fumes clusters and duration of employment (n = 9,349)

Welding fumes clusters	Count (%)	Number of lung cancer cases (%)	Duration of employment of less than 5 years		Duration of employment of 5 or more years	
			Count (%)	Number of lung cancer cases (%)	Count (%)	Number of lung cancer cases (%)
I	1,277 (13.6%)	21 (13.2%)	440 (12.5%)	12 (14.0%)	837 (14.4%)	9 (12.3%)
II	4,591 (49.1%)	78 (49.1%)	1,767 (50.0%)	41 (47.7%)	2,824 (48.5%)	37 (50.7%)
III	3,481 (37.2%)	60 (37.7%)	1,324 (37.5%)	33 (38.4%)	2,157 (37.1%)	27 (37.0%)
Total	*9,349*	*159*	*3,531*	*86*	*5,818*	*73*

Table 6.3. Primary cancers in the Long Beach Naval shipyard cohort by welding fumes clusters (n = 9,349)

A. Group with no asbestos exposure and no welding fumes exposure (n = 1,277)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	6	0.95	6.33 (2.56-13.14)
Colorectal	9	6.79	1.33 (0.65-2.43)
Digestive system excluding colorectal	7	5.17	1.35 (0.59-2.68)
Endocrine system	2	0.57	3.54 (0.59-11.59)
Leukemia	2	1.55	1.29 (0.22-4.26)
Lung	21	8.63	2.43 (1.55-3.66)
Lymphoma	6	2.99	2.00 (0.81-4.17)
Male reproductive system excluding prostate	1	0.89	1.13 (0.06-5.54)
Mesothelioma	2	0.21	9.76 (1.60-31.47)
Myeloma	3	0.72	4.16 (1.06-11.34)
Oral cavity and pharynx	8	2.08	3.84 (1.79-7.30)
Prostate	60	17.24	3.48 (2.68-4.45)
Respiratory system excluding lung	4	1.08	3.71 (1.18-8.93)
Skin excluding basal and squamous	6	4.04	1.48 (0.60-3.09)
Urinary system	11	5.14	2.14 (1.13-3.72)

[†]Primary cancers only

B. Group with asbestos exposure and with no exposure to welding fumes (n = 4,591)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	11	3.66	3.01 (1.58-5.22)
Colorectal	61	27.24	2.24 (1.73-2.86)
Digestive system excluding colorectal	47	20.7	2.27 (1.69-2.99)
Endocrine system	4	2.13	1.87 (0.60-4.53)
Leukemia	8	6.14	1.30 (0.61-2.47)
Lung	78	35.11	2.22 (1.77-2.76)
Lymphoma	17	11.58	1.47 (0.88-2.30)
Male reproductive system excluding prostate	2	3.12	0.64 (0.11-2.12)
Mesothelioma	12	0.84	14.35 (7.74-24.29)
Myeloma	10	2.89	3.46 (1.76-6.17)
Oral cavity and pharynx	14	8.22	1.70 (0.97-2.79)
Prostate	169	70.23	2.41 (2.06-2.79)
Respiratory system excluding lung	10	4.34	2.30 (1.17-4.11)
Skin excluding basal and squamous	11	15.76	0.70 (0.37-1.21)
Urinary system	47	20.69	2.27 (1.69-2.99)

†Primary cancers only

C. Group exposed to both asbestos and welding fume (n = 3,481)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	3	2.70	1.11 (0.28-3.02)
Colorectal	41	20.19	2.03 (1.47-2.73)
Digestive system excluding colorectal	38	15.24	2.49 (1.79-3.39)
Endocrine system	2	1.58	1.26 (0.21-4.18)
Leukemia	10	4.55	2.20 (1.12-3.92)
Lung	60	25.77	2.33 (1.79-2.98)
Lymphoma	10	8.59	1.16 (0.59-2.08)
Male reproductive system excluding prostate	3	2.40	1.25 (0.32-3.40)
Mesothelioma	4	0.62	6.47 (2.05-15.56)
Myeloma	4	2.12	1.88 (0.60-4.55)
Oral cavity and pharynx	5	6.03	0.83 (0.30-1.84)
Prostate	136	51.50	2.64 (2.22-3.11)
Respiratory system excluding lung	6	3.18	1.89 (0.76-3.92)
Skin excluding basal and squamous	13	11.60	1.12 (0.62-1.87)
Urinary system	21	15.26	1.38 (0.87-2.07)

[†]Primary cancers only

To adjust for duration of employment in the shipyard, the cohort was stratified into two groups; workers who were employed less than five-years in the shipyard, and workers with five or more years of employment in the shipyard. Excess incidence of lung cancer was observed in workers with five or more years of duration of employment for all three clusters of welding fumes exposure (**Table 6.4**). In addition, elevated excess of prostate cancer was observed in all six subgroups. In cluster I, as observed in the overall analysis, there was a statistically significant excess incidence of brain cancer, cancer of oral cavity and pharynx, and cancer of the respiratory system excluding lung. An excess of incidence of cancer of the endocrine system (SIR= 6.00 (1.62-9.81)) in the group with less than five-years duration of employment was also observed. In addition, there was a 2.4-folds (1.93-6.52) excess incidence of cancer of the urinary system in the group with five or more years of employment in the shipyard.

Excess incidence of mesothelioma was observed in the two groups of duration of employment in cluster II. In addition, as observed in the overall analysis, the SIR for colorectal cancer, cancer of the digestive system excluding colorectal, and cancer of the urinary system were all statistically significant. SIR of the cancer of the brain, myeloma, and cancer of the respiratory system were only statistically significant in the group with less than five-years duration of employment. In the group with five and more years of duration of employment, a statistically significant excess incidence of lymphoma (SIR= 2.35 (1.27-4.00)) was observed.

Approximately 6.0-folds excess incidence of mesothelioma (SIR=6.07 (1.02-20.02), SIR= 2.73 (1.91-22.79)) was observed in both duration of employment subgroups in cluster III. Although both subgroups had statistically significant excess incidence of lung cancer, the group with workers employed in the shipyard for five or more years had a higher SIR (SIR=1.98 (1.33-2.83) vs SIR= 2.73 (1.91-3.79)). Elevated incidence of cancer of the digestive system excluding

colorectal and prostate were observed in both subgroups of duration of employment. However, excess incidence of colorectal cancer was only observed in the group with less than five-years duration of employment.

6.2.2. Lung cancer-free survival curve in workers exposed to welding fumes

Figure 6.1 illustrates the KM curve for length of time after initial employment in the shipyard until occurrence of colorectal cancer stratified by welding fumes clusters. There was no difference in time to disease occurrence across the three different clusters (log-rank *P*-value = 0.95). A similar finding was observed after adjusting for the duration of employment (log-rank *P*-value = 0.91) (**Figure 6.2**).

Table 6.4. Primary cancers in the Long Beach Naval shipyard cohort by welding fumes clusters and duration of employment (n = 9,349)

A. Less than five-years duration of employment

i. Group with no asbestos exposure and no welding fumes exposure (n = 440)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	4	0.54	7.47 (2.35-17.87)
Colorectal	3	3.65	0.82 (0.21-2.24)
Digestive system excluding colorectal	3	2.78	1.08 (0.27-2.94)
Endocrine system	2	0.33	6.00 (1.02-20.02)
Leukemia	1	0.85	1.17 (0.06-5.80)
Lung	9	4.50	2.00 (0.98-3.67)
Lymphoma	4	1.70	2.35 (0.75-5.68)
Male reproductive system excluding prostate	1	0.58	1.72 (0.09-8.50)
Mesothelioma	1	0.11	9.25 (0.45-44.84)
Myeloma	2	0.39	5.17 (0.86-16.94)
Oral cavity and pharynx	5	1.13	4.42 (1.62-9.81)
Prostate	33	8.98	3.67 (2.57-5.10)
Respiratory system excluding lung	4	0.57	7.08 (2.23-16.93)
Skin excluding basal and squamous	2	2.26	0.88 (0.15-2.92)
Urinary system	5	2.75	1.82 (0.67-4.03)

[†]Primary cancers only

ii. Group with asbestos exposure and with no exposure to welding fumes (n = 1,767)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	7	2.04	3.43 (1.50-6.79)
Colorectal	35	14.70	2.38 (1.68-3.27)
Digestive system excluding colorectal	29	11.25	2.58 (1.76-3.65)
Endocrine system	1	1.23	0.81 (0.04-4.01)
Leukemia	3	3.36	0.89 (0.23-2.43)
Lung	37	18.54	2.00 (1.43-2.72)
Lymphoma	5	6.48	0.77 (0.28-1.71)
Male reproductive system excluding prostate	2	1.91	1.05 (0.18-3.46)
Mesothelioma	6	0.44	13.53 (5.53-28.36)
Myeloma	7	1.57	4.47 (1.95-8.82)
Oral cavity and pharynx	6	4.49	1.34 (0.54-2.78)
Prostate	92	37.53	2.45 (1.99-2.99)
Respiratory system excluding lung	6	2.31	2.60 (1.05-5.40)
Skin excluding basal and squamous	5	8.81	0.57 (0.21-1.26)
Urinary system	27	11.15	2.42 (1.62-3.47)

[†]Primary cancers only

iii. Group exposed to both asbestos and welding fumes (n = 1,324)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	1	1.49	0.67 (0.34-3.31)
Colorectal	26	10.89	2.39 (1.59-3.45)
Digestive system excluding colorectal	25	8.23	3.04 (2.01-4.42)
Endocrine system	2	0.90	2.23 (0.37-7.34)
Leukemia	6	2.48	2.42 (0.98-5.03)
Lung	27	13.67	1.98 (1.33-2.83)
Lymphoma	6	4.76	1.26 (0.51-2.62)
Male reproductive system excluding prostate	2	1.44	1.39 (0.23-4.59)
Mesothelioma	2	0.33	6.07 (1.02-20.02)
Myeloma	1	1.14	0.87 (0.04-4.33)
Oral cavity and pharynx	2	3.27	0.61 (0.10-2.02)
Prostate	73	27.35	2.67 (2.11-3.34)
Respiratory system excluding lung	4	1.70	2.36 (0.75-5.68)
Skin excluding basal and squamous	6	6.39	0.94 (0.38-1.95)
Urinary system	13	8.21	1.58 (0.88-2.64)

[†]Primary cancers only

B. Five years or more duration of employment

i. Group with no asbestos exposure and no welding fumes exposure (n = 837)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	2	0.41	4.85 (0.82-16.12)
Colorectal	6	3.14	1.91 (0.77-3.97)
Digestive system excluding colorectal	4	2.40	1.67 (0.53-4.02)
Endocrine system	.	0.23	.
Leukemia	1	0.70	1.43 (0.07-7.05)
Lung	12	4.14	2.90 (1.57-4.93)
Lymphoma	2	1.30	1.54 (0.26-5.08)
Male reproductive system excluding prostate	.	0.30	.
Mesothelioma	1	0.10	10.28 (0.50-49.32)
Myeloma	1	0.34	2.98 (0.15-14.51)
Oral cavity and pharynx	3	0.95	3.15 (0.80-8.59)
Prostate	27	8.28	3.26 (2.19-4.68)
Respiratory system excluding lung	.	0.51	.
Skin excluding basal and squamous	4	1.79	2.24 (0.71-5.39)
Urinary system	6	2.40	2.50 (1.93-6.52)

[†]Primary cancers only

ii. Group with asbestos exposure and with no exposure to welding fumes (n = 2,824)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	4	1.62	2.47 (0.78-5.96)
Colorectal	26	12.54	2.07 (1.38-2.99)
Digestive system excluding colorectal	18	9.45	1.90 (1.16-2.95)
Endocrine system	3	0.91	3.31 (0.84-8.97)
Leukemia	5	2.78	1.80 (0.66-3.99)
Lung	41	16.58	2.47 (1.80-3.32)
Lymphoma	12	5.10	2.35 (1.27-4.00)
Male reproductive system excluding prostate	.	1.21	.
Mesothelioma	6	0.39	15.28 (6.24-32.00)
Myeloma	3	1.33	2.26 (0.57-6.14)
Oral cavity and pharynx	8	3.73	2.15 (1.00-4.07)
Prostate	77	32.71	2.35 (1.87-2.92)
Respiratory system excluding lung	4	2.03	1.97 (0.63-4.75)
Skin excluding basal and squamous	6	6.95	0.86 (0.35-1.80)
Urinary system	20	9.53	2.10 (1.32-3.18)

[†]Primary cancers only

iii. Group exposed to both asbestos and welding fumes (n = 2,157)

Cancer type[†]	Observed	Expected	SIR (95% CI)
Brain and other nervous system	2	1.21	1.66 (0.28-5.46)
Colorectal	15	9.30	1.61 (0.94-2.60)
Digestive system excluding colorectal	13	7.00	1.86 (1.03-3.10)
Endocrine system	.	0.69	.
Leukemia	4	2.07	1.93 (0.61-4.66)
Lung	33	12.10	2.73 (1.91-3.79)
Lymphoma	4	3.83	1.04 (0.33-2.52)
Male reproductive system excluding prostate	1	0.96	1.04 (0.05-5.14)
Mesothelioma	2	0.29	6.91 (1.16-22.79)
Myeloma	3	0.98	3.06 (0.78-8.33)
Oral cavity and pharynx	3	2.75	1.09 (0.28-2.97)
Prostate	63	24.15	2.61 (2.02-3.32)
Respiratory system excluding lung	2	1.48	1.35 (0.23-4.46)
Skin excluding basal and squamous	7	5.21	1.34 (0.59-2.66)
Urinary system	8	7.06	1.13 (0.53-2.15)

[†]Primary cancers only

Figure 6.1. Kaplan-Meier survival curve for length of time after initial employment in the shipyard until occurrence of lung cancer in the Long Beach Naval shipyard study cohort stratified by welding fumes exposure clusters

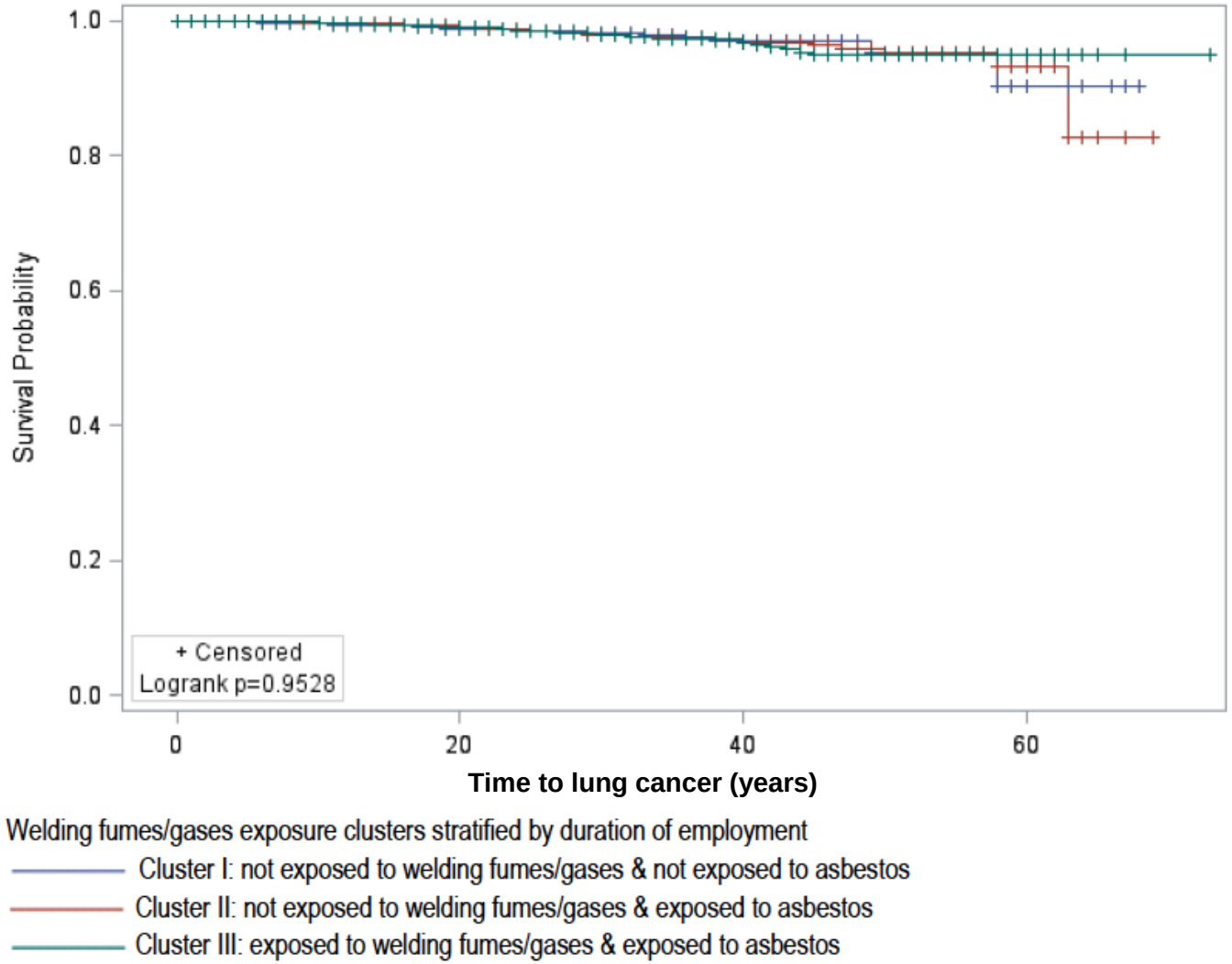
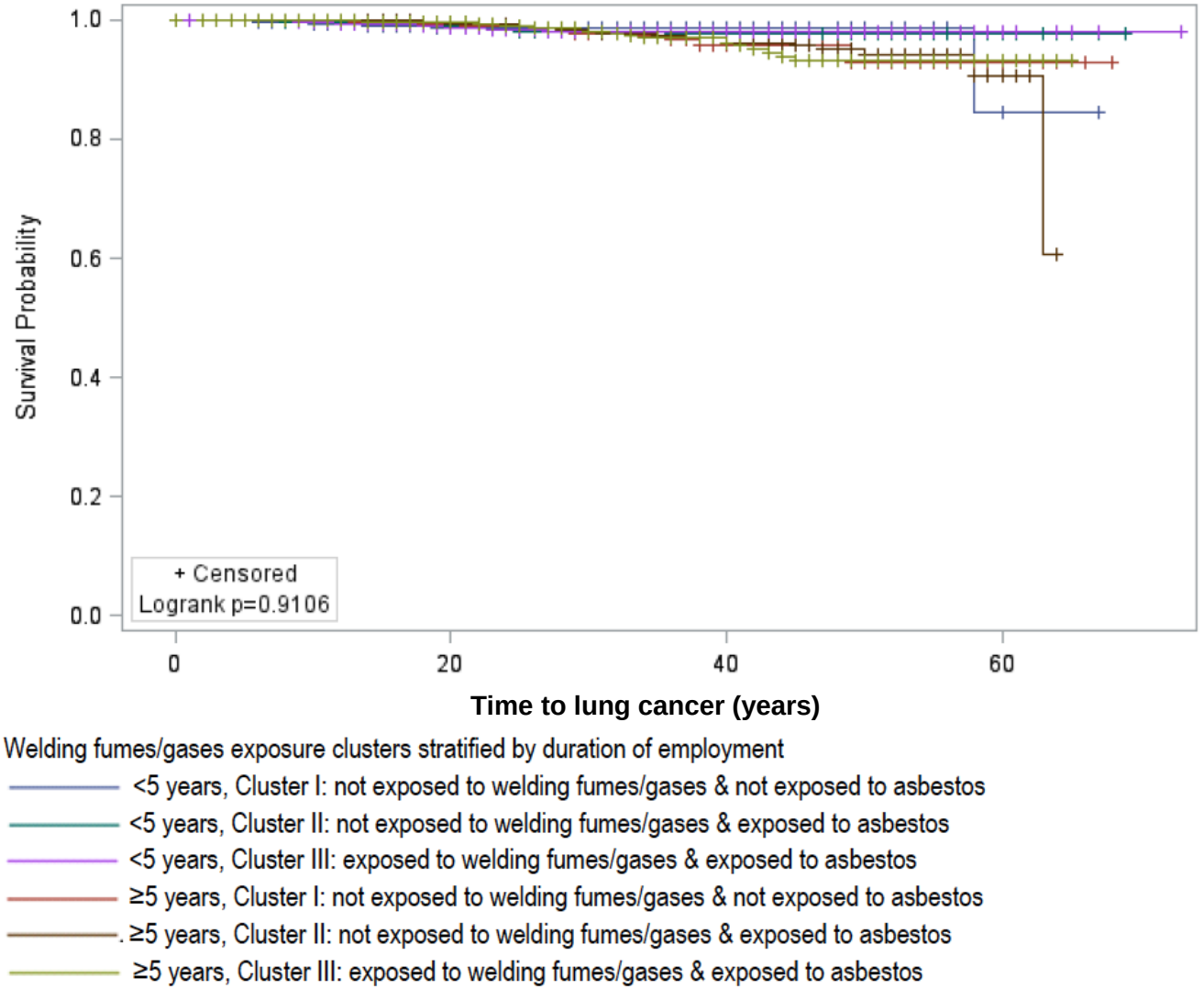


Figure 6.2. Kaplan-Meier survival curve for length of time after initial employment in the shipyard until occurrence of lung cancer stratified by welding fumes exposure clusters and duration of employment in the shipyard



6.4. Discussion

Our present study found excess lung cancer incidence for all three clusters of exposure to welding fumes. In general, a higher SIR for lung cancer was observed among workers with five or more years of employment in the shipyard. The survival analysis showed no difference in time to colorectal cancer occurrence between the three clusters of welding fumes exposure, which persisted after adjusting for the duration of employment.

The types of welding fumes that welders are exposed to depends on the type of materials used. For example, stainless-steel welding is associated with a high exposure of chromium and nickel, which not present in fumes produced by mild steel welding.[176,177,180,181] Consistent findings showed increased risk of lung cancer in stainless-steel welders.[77,179,182] However, it is unclear whether lung cancer is associated with mild-steel welders.

An assessment of mild-steel welders and non-welders in the same Illinois manufacturing plant found no difference in risk of lung cancer between the two groups.[183] After ten-year follow-up with these population Steenland, et. al. found a statistically significant excess mortality due to lung cancer in the mild-steel welders, while there was no change in SMR among the non-welders.[78] Moulin, et. al. reported excess mortality due to lung cancer in mild-steel welders, which was not observed in stainless-steel welders. In addition, the excess in mortality from lung cancer increased in workers with twenty or more years of duration of employment as well as in workers with twenty years of more of time since first exposure to welding fumes.[68] In contrast, a recent meta-analysis by Ambroise, et. al. found similar excess risk of cancer in both the stainless-steel welders and mild-steel welders.[79] Similar findings was reported by Lauritsen, et. al. among stainless steel and mild-steel workers using a nested case-referent study.[184] Data on the type of metal and welding process used in the LBNS are not available. Nevertheless, in general, welding

in the shipyard industry, more specifically shipbuilding, mostly involves mild steel welding.[180] Tola, et. al. observed elevated risk of lung cancer in mild-steel welders in the shipyard.[81] Similar to our study, the author also observed increased lung cancer in other occupations in the shipyard.

Our study did not have information on smoking use. Potential confounding due to smoking is likely to mask the effect of exposure to welding fumes. A recent study only observed increased risk of lung cancer in worker exposed to welding fumes who were also light smokers, but not in heavy smokers.[185] The author elucidated that the observed difference between smoking strata may be explained by the strong effect of smoking to lung cancer. A previous case-control study by Mannetje, et. al. also found increased risk of lung cancer among welders in Central and Easter Europe and the United Kingdom after adjusting for smoking and asbestos exposure.[70] The author reported that adjusting for asbestos exposure had little effect to the risk estimate, an indication that confounding from asbestos is minimal in the population. However, the population used in the study was not restricted to shipyard welders, where a secondary exposure to high levels of asbestos is more likely due to the confined spaces on the shipyard, as well as the wide spread use of asbestos materials for insulation within the vessels. Danielsen, et. al. reported excess lung cancers among welders as well as excess mesothelioma, which were not observed in the non-welder group.[162] In our present study, excess incidence of mesothelioma was observed in the group exposed to welding fumes. Lung cancer cases observed in this cohort are possibly due to asbestos exposure alone or a result of an aggregate exposure to hazardous agents including welding fumes and asbestos fibers.

CHAPTER 7

Summary and Conclusions

7.1. Overall summary

In summary, our present study showed excess incidence and mortality of a wide variety of cancers in the shipyard workers. In addition, workers in the study had elevated incidence and mortality of cancers that are associated with exposure to other occupational agents such as polycylic aromatic hydrocarbons, organic solvents as well as metals. Increased SIRs and SMRs were observed in workers with longer duration of employment in the shipyard, which are consistent from previous studies. Excess incidence of mesothelioma were observed in all three asbestos exposure groups. The SIR of lung cancer were similar across the three groups of asbestos exposure. Consistent from previous findings, our study found excess incidence and mortality of colorectal cancer among the shipyard workers. However, there was no difference in the time to colorectal cancer survival curve, as well as the Cox proportional hazard between asbestos exposure groups. In our present analysis, the relationship between lung cancer and exposure to welding fumes is unclear.

7.2. Strengths and limitations of the study

The LBNS study cohort has almost 30 years of follow up and is a large cohort suitable to assess long-term adverse health outcomes due to asbestos exposure as well as other exposures in the LBNS shipyard. One of the major advantages of using a historical cohort study design is the ability to examine multiple outcomes for a specific exposure. In addition, recall bias is unlikely in the cohort study since cases are not identified by disease status. The use of a historical study cohort allows the ability to examine diseases that have a long latency period such as cancer,

which may otherwise be costly and inefficient if a prospective cohort design is utilized. Furthermore, the LBNS study cohort is comprise of workers who belonged to various shop numbers in the shipyard with a variety of occupations. Workers with low asbestos exposure (i.e. architects, engineers, and engineering technicians) and workers who are seldom or are never exposed to welding fumes based on their job-related tasks, served as internal controls for our study.

In occupational cohort studies, it is a common practice to compare occupational cohorts to the general population, mostly because there is a lack of internal control. In most instances, information on the exposure and information on specific job titles are not available. There are two biases that we need to be aware when using occupational cohorts and using the general population as a reference group. First, there could be a dilution effect where the inclusion of unexposed or low exposed workers in the study when pooled data are used, which could result to a bias towards the null.[186] Consequently, in our present study, we included a separate analysis stratifying workers into three different asbestos exposure groups — low, intermediate and high exposures. Second, occupational cohort studies are prone to comparison bias.[186] In general, individuals in occupational cohorts are healthier than the general population, a phenomenon known as healthy worker effect (HWE). A more in depth discussion of HWE will be presented later in this chapter.

Another limitation of our study is the lack of information on smoking in the LBNS study cohort. A previous population-based study of U.S. workers using the National Health Data Survey from 1978 to 1980 shows that blue collar workers, such as shipyard workers, typically smokes more than the general population of the United States.[183,187] In our study, we assumed that there is no significant difference in the use of smoking between the shipyard workers. It is

probable that the excess mortality and incidence of lung cancer among shipyard workers in all three asbestos exposure groups may be attributable to smoking. In addition, we expected to see a linear exposure-response trend between the three asbestos exposure groups for lung cancer, which we did not observe. A possible explanation is that a high prevalence of other risk factors, such as smoking, in the low asbestos exposure group could lead to a flattening of exposure-response curve in the high exposure group[188], which could have contributed to the lack of expose-response trend in our present study.

Previous studies of asbestos exposure and lung cancer have used incidence of mesothelioma as a biomarker for asbestos exposure.[139] However, this does not tell us the level of asbestos exposure. The concentration of asbestos sufficient to increase a person's risk of asbestos-related malignancies is unknown. In our present analysis, all three asbestos exposure levels had excess incidence of mesothelioma and lung cancer. Individual susceptibility to asbestos exposure may also play a role in risk of asbestos-related malignancies. Chronic inflammation is suggested to contribute in the development of asbestos-related malignancies. Further study is needed to elucidate the role of pro- and anti-inflammatory responses in relation to asbestos-related malignancies.

Another limitation of occupational studies is the lack of information on the exposure experience outside the study. In the LBNS study cohort we do not have information about the exposure experience by the workers after the end of the study. In addition, the healthy worker effect is a common source of selection bias in occupational studies, where individuals who are healthy enough to work are selected into the workforce. Occupational cohort tends to be healthier than the general population. Nevertheless, the effect of HWE declines with time since first hire and with age.[189,190] All workers in the LBNS study cohort were employed in the

shipyard between 1978 and 1980. The effect of HWE in the LBNS study cohort is likely negligible since at least 26 years had passed. In addition, to address healthy worker survivor effect, where workers with ill health are more likely to drop out from the workforce[188], we stratified by duration of employment in our analyses. Many investigators reasoned that HWE is of little concern assessing cancer outcomes since cancer is a silent disease with long latency until clinical manifestation.[189,190] Thus, it is unlikely that individuals are selected out from the recruitment and retention to the workforce.

Exposure misclassification is another limitation of the study. Workers in the LBNS study cohort were assigned into three different asbestos exposure groups based on their shops and occupation categories. Welding fumes exposure were also assigned based on the worker's occupational category. Since not all workers had job titles, the subgroup of works with shop numbers and job titles were utilized to assign all workers into an occupational category. Asbestos exposure assignment was done by utilizing the data on shop numbers and job title of the same subgroup of workers. Thus, it is possible that a non-differential misclassification occurred in the level of assigning workers into the different occupational categories and in assigning each occupational group with corresponding asbestos and welding fumes exposure status. A non-differential misclassification would dilute the effect and bias the result towards the null.

Lastly, most the workers in the shipyard are non-Hispanic white males. Our present study has incomplete information on race and gender. However, in the pilot study less than 10% of the population were women. In the analysis of the LBNS study cohort, we excluded occupations that are traditionally populated with female workers. Consequently, the findings in our study may only be valid in this population of shipyard workers.

7.3. Conclusion

At the present, asbestos is still widely used internationally, and from a report by the WHO, deaths due to asbestos exposure continue to rise globally.[49] The WHO added that developing countries should prepare for an increase in asbestos-related diseases. Studies on asbestos-related malignancies remains relevant to identify other cancers that are associated with asbestos exposure.

Chrysotile asbestos was used as an insulation material in the first 40 floors of the North Tower. The U.S. Environmental Protection Agency observed elevated asbestos levels in the air in the earliest days after September 11.[191] Asbestos were also found in settled dust in Ground Zero, as well as, dust on apartments and other buildings.[191] First responders, individuals who were in Ground Zero when the towers collapsed, as well as, workers involved in the cleaning of the debris are at are increased risk of asbestos-related malignancies. Thus, identifying and having a better understanding about other adverse health outcomes of asbestos continues to be an important task.

The Long Beach Naval shipyard was opened from 1943 to 1997 and employed over 40,000 workers during this time, and most these shipyard workers are retired. Our findings showed increased in asbestos-related malignancies and other types of cancers in these workers. Identification of other adverse health outcomes, aside from lung cancer and mesothelioma, associated to asbestos exposure continues to be important for identifying high-risk populations, including workers who were not directly exposed to asbestos.

Consistent with previous reports on asbestos exposure in the shipyard, we found excess mesothelioma, lung and other types of cancers in the LBNS. Based on our result, it is unclear whether asbestos exposure increase risks of colorectal cancer. The presence of asbestos exposure

in this population as well as the lack of information on smoking between welding fumes exposure clusters obstruct the association between exposure to welding fumes and lung cancer. Overall, this study showed that employment in the LBNS by itself increased a person's risk to a variety of cancers including asbestos-related malignancies. Based on our findings asbestos exposure is not confined in one specific occupation or shop numbers. It is likely that indirect exposure to asbestos often occur in the shipyard setting. The majority of the occupational exposure assessment done in the shipyard do not account for exposure to multiple agents. Often workers are exposed to multiple agents simultaneously. However, most occupational exposure lacks information about worker's specific exposures. Studies should strive to adjust for multiple exposures whenever possible. In addition, studies that examine the interaction of different occupational agents in the shipyard is warranted.

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APPENDIX A

EXTENT OF ASBESTOS EXPOSURE AND MANUAL LABOR BY POSITION
(ORGANIZED BY SHOP NUMBER)

Shop Number	Occupation	Code	Work Grade
001	Laborer (Group II)	(0) -M	
	Warehouseman	(1) -M	WG6907
002	Automotive Mechanic/ Worker	(3) +M	WG5823
	Bicycle Repairman	(1) -M	WG4844
	Crane Operator	(0) -L	WG5725
	Electrician	(0) -M	WG2805
	Electromotive Equip. Mech/Worker	(0) -M	WG5876
	Forklift Operator	(0) -L	WG5704
	Heavy Mobile Equip.Mech.	(2) +H	WG5803
	Heavy Mobile Equip. Mech. Inspector	(1) -M	WG5803
	Mobile Equip. dispacher	(0) -L	WG5701
	Mobile Equip. Servicer	(2) +M	WG5806
	Motor Vehicle Operator	(1) -M	WG5703
	Painter	(0) -H	WG4102
	Straddle Truck Opr.	( ) -M	WG5720
	Welder	(2) +H	WG3703
003	Air Conditioning Equip. Mechanic	(0) -H	WG5306-10
	Boiler Plant Operator	(3) +L	WG5402
	Carpenter	(1) -H	WG4607
	Electric Power Controller	(0) -M	WG5407
	Electrician (Power Plant)	(0) -H	WG2805
	Fireman	(3) +M	
	Instrument Mech./Worker	(0) -M	WG3359
	Locksmith	(0) -M	WG5311/3817
	Maint..Machinist	(0) -H	WG3414
	Maint.Sched. (General)	( ) -L	WD6701-7
	Painter	(0) -H	WG4102
	Pipefitter	(4) AH	WG4204
	Plasterer	(3) +H	WG3605
	Plumber	(2) +M	WG4206
	Power Plant Controlman	(2) +M	WG5407/2808
	Tractor Operator	(1) -M	WG5705
	Utilities Foreman	(0) -L	WG4701-10
006	Electrician	(0) -M	WG2803
	Elex. Mech. Maint.	(0) -M	WG2663
	Ind. Elec. Cont. Mech.	(0) -L	WG2663
	Instrument Mech./Worker	(0) -M	WG3359
	Marine Machinist	(3) AH	WG3414
	Maint. Machinist	(0) -H	WG3414
	Oiler	(1) -M	WG5323
	Saw Filer	(0) -L	WG4812-9

NOTE:
A job title may appear in more than one shop

Shop Number	Occupation	Code	Work Grade
006	Saw Smith	(0) -L	WG4812-11
	Tool & Cutter Grinder	(0) -L	WG3417
	Toolmaker	(0) -L	WG3416
	Tools & Parts Attend.	(0) -L	WG6904
	Toolroom Mechanic	(0) -M	WG4801
007	Air Cond. Equip. Mech.	(0) -H	WG5306
	Asphalt Worker	(0) -H	WG3653, WG3753
	Boiler Plant Operator	(3) +L	WG5402-10
	Cable Splicer	( )	WG
	Carpenter	(1) -H	WG4607
	Electrician (HV)	(0) -M	WG2805
	Elect. Equip. Repairer	(0) -M	WG2854
	Electrical Worker	(0) -M	WG
	Electronics Mechanic	(0) -M	WG2614
	Elevator Mechanic	(0) -M	WG5313
	Forklift Operator	(0) -M	WG5704
	Gardener	(0) -M	WG5003-6
	Grounds Leader	(0) -L	WG4701
	Heavy Laborer	(0) -H	WG
	Insulator	(4) AH	WG4203, WG3610
	Laborer	(0) -M	WG3502
	Locksmith	(0) -M	WG5311. WG3817
	Maintenance Mach.	(0) -H	WG3414
	Painter	(0) -H	WG4102
	Pest Controller	(0) -M	WG5026
	Pipefitter	(4) AH	WG4204
	Plasterer	(3) +H	WG3605
	Plumber	(2) +M	WG4206
	Public Works Foreman	(0) -L	WG4701-9
	Rigger	(3) AH	WG5210
	Roofer	(0) -H	WG3609-9
	Sheetmetal Mechanic	(2) +H	WG3806
	Sign Painter	(0) -L	WG4104
	Tractor Operator	(1) -M	WG5705
	Welder	(2) +H	WG3703
	Wharfbuilder	(0) -H	WG4639
011	Driller	(2) +H	WG3907
	Loftsman	(0) -M	WG6206, WG5221
	Pneumatic Tools Opr. (s/s)	(2) +H	WG3815, WG3801
	PTO (Test Spec.)	(1) -H	WG3801
	Riveter	( )	WG3815
	Shipfitter	(2) +H	WG3820
017	Forklift Operator	(0) -M	WG5704
	Sheetmetal Mechanic	(2) +H	WG3806

Shop Number	Occupation	Code	Work Grade
023	Helper Blacksmith		Grade II-3(1950's)
026	Welder	(2) +H	WG3703
028	Mechanical Syst. Insp.	(1) -M	WG6201
030	Ship Progressman	(1) -L	WG6701-8
	Ship Scheduler	(0) -L	WG6701-8
031	Boiler Plant Operator	(3) +L	WG5407
	Instrument Mechanic	(0) -M	WG3359
	Machine Tool Operator	(0) -M	WG3431
	Machinist	(0) -M	WG3414
	Num. Cont. Mach. Tool Pr.	(0) -L	WG3401
	Power Plant Controlman	( ) +M	WG5407
	Tool & Cutter Grinder	(0) -L	WG3417
	Toolmaker	(0) -L	WG3416
033	Boiler Syst. Insp.(SHIPS)	(2) +M	WG3808-10
	Electrical Syst. Insp.	(0) -M	WG2805-13
	Elec.Fire Cont.Syst.Insp.	(0) -M	WG2617
	Inspector(Ship's Hull)	(0) -M	WG6294
	Machine Parts Insp.	(0) -M	WG3413-10
	Mechanical Syst. Insp.	(1) -M	WG6201-12,13
	Metals Insp. Instructor	(1) -L	WG3801
	Painting Insp.	(0) -M	WG4102
	Shipfitting Insp.	(2) +M	WG3820-13
	Welding Insp.	(2) +M	WG3703
034	Elex. Mech.	(0) -M	WG
035	Metals Inspector	(1) -M	WG3801
036	Electronics Mech.	(0) -M	WG2614
	Electronics Mech. Crypto	(0) -M	WG2619
	Fire Control Mech.	(0) -M	WG2613
	Machinist(S/W)	(1) -M	WG3414, WG3404
	Optical Inst. Repairer	(0) -M	WG3306
	Ordnance Equip. Mech.	(0) -M	WG6641
038	Marine Machinist	(3) AH	WG3414
040	Custodial Work Insp.	( ) -M	WG3566
041	Blacksmith	(2) +H	WG3704, WG3830
	Boilermaker	(4) AH	WG3808
	Forger(Heavy)	(1) -H	WG3704
	Molder(Foundry,Forge)	(2) +H	WG3714

Shop Number	Occupation	Code	Work Grade
050	Warehouseman	(1) -M	WG6907
051	Armature Winder	(1) -M	WG2809
	Electrician	(1) -M	WG2805
	Electrical Eq. Rep.	(0) -M	WG2854
	Elex. Int. Syst. Mech.	(0) -M	WG2650
	Electroplater	(0) -L	WG3711
	Engraved Plate Maker	(0) -L	WG4401
	Gyrocompass Mech.	(0) -M	WG3361-11
	Instrument Mech./Worker	(0) -M	WG3359
	Janitor	(0) -M	WG3566
	Machine Tool Operator	(0) -M	WG3431
056	Air Cond. Equip. Mech.	(3) +H	WG5306
	Coppersmith	(1) -H	WG3804
	Insulator	(4) AH	WG4203, WG3610
	Pipefitter	(4) AH	WG4204
	Shipfitter	(2) +H	WG3820
057	Instrument Mechanic	(0) -M	WG3359
	Insulator	(4) AH	WG4203, WG3610
064	Carpenter	(1) -H	WG4607
	Millman (see Carpenter)		
	Molder (Plastics)	(0) -M	WG4351, WG4352
	Patternmakers	(0) -L	WG4616
	Shipwright	(2) +H	WG5220
	Woodworker(see Carpenter)		
066	Elex. Meas. Equip. Mech.	(0) -M	WG2602
	Electronics Mechanic	(0) -H	WG2614
067	Electrical Equip. Insp.	(0) -M	WG2805-11
	Elex. Mech.	(0) -H	WG2614
	Elex. Mech.(Crypto)	(0) -M	WG2619
	Elex Worker	(0) -M	WG2614
	Elex. Meas. Eq. Mech.	(0) -M	WG2602
	Electroplater	(0) -L	WG3711
	Instrument Mechanic	(0) -M	WG3359
	Radio Mechanic	(0) -M	WG2608-11
	Teletype Equip. Mech.	(0) -M	WG2509
071	Cement Finisher	(2) +H	WG3602
	Painter,Tile&Plate Setter	(0) -H	WG
	Sandblaster	(0) -M	WG5423-7
	Sign Painter	(0) -L	WG4104
	Silkscreen Process Wkr.	(0) -L	WG4419

Shop Number	Occupation	Code	Work Grade
072	Engine & Pump Opr.	(1) -H	WG5401,WG5419
	Equipment Cleaners:		WG5417,WG7009
	Buffer&Polisher	(3) AH	
	Calker&Chipper	(3) AH	
	Floor Tile Remover	(4) AH	
	Foundry Chipper	(3) AH	
	Metal Cleaner	(3) AH	
	Scaler&Buffer	(3) AH	
	Tank Cleaner	(3) AH	
	Equipment Planner	(0) -L	
	Fabric Worker	(0) -L	WG3105
	Heavy Laborer	( ) -H	WG3502
	Laborer	(0) -M	WG3502
	Rigger	(3) AH	WG5210
	Ship Maintenance Mech.	(2) +H	WG5925-7
091	Elex. Mech.(Crypto)	(0) -M	WG2619
092	Boilermaker Instructor	(4) AM	WG3808-12
	Sheetmetal Mech. Instruc.	(2) +M	WG3806-12
	Summer Aid	( ) -L	YV3506
095	Electrician Instructor	(0) -H	WG2805
	Summer Aid	(1) -M	YV3506
097	Prod.Shop Planner/Rigger	( ) -L	
	Working Aid	(0) -	WB3502
099	Electrician	(2) +M	WG2805
	Pipefitter	(4) AH	WG4204
	Service Ship Frm.	(0) -L	WG6201-15
	Service Shop Frm.	(0) -L	WG4701-13
	Tool&Cutter Grinder	(0) -L	WG3417
304	Marine Engineer	(1) -L	GS870
306	Equip. Spec.(General)	( ) -L	GS1670
	Production Sup.	( ) -L	GS1670
310	Computer Operator	(0) -L	GS332
	Computer Specialist	(0) -L	GS334
	Computer Syst. Analyst	(0) -L	GS334
	Data Transcriber	(0) -L	

Shop Number	Occupation	Code	Work Grade
310	Digital Comp.Syst.Opr.	(0) -L	GS332
	EAM Operator	(0) -L	GS359
	Labor Relations Spec.	( ) -L	GS233
313	Calibration&Meas QC Spec.	( )	GS1961-9
	Chemist	(2) +M	GS806
	Metals Inspector	(1) -M	WG3801
	QA Spec.	(1) -L	GS1910-11
	Trainees	( ) -M	
314	Management Analyst	(0) -L	GS343
315	Employee Relations Spec.	( ) -L	GS230
	Photographer	(0) -L	GS1060
319	Chief Engineer	(1) -L	GS801
	Electronics Engr.	(1) -L	GS855
	Electronics Tech.	(1) -L	GS856
	Supv. General Engr.	(1) -L	GS801
320	File Clerk	(0) -L	GS305
	Visual Information Spec		GS1084-9,10,11,12
322	Clerk Typist	(0) -L	GS322
	Equipment Spec.(SHIPS)	( ) -L	GS1670
	Prod. Controller	( ) -L	GS1152
324	Accountant	(0) -L	GS510
	Auditor	(0) -L	GS510
	Electrical Engr.	(1) -L	GS850
	Electrical Tech.	(1) -L	GS856
	Equipment Spec.	( ) -L	GS1670
	Mechanical Engineer	(1) -L	GS830
330	Engineering Tech.	(1) -L	GS802
	Marine Trans. Spec.	( ) -L	GS2150
	Supv. Prod. Cont.(SHIPS)	( ) -L	GS1152
334	Materials Engineer	( )	GS806
	Metallurgist	( )	GS1321-9
	Physical Scientist	( )	GS1301-13

Shop Number	Occupation	Code	Work Grade
338	Production Supt.	( ) -L	GS1601-13
340	Clerk	(0) -L	GS301
	Photographer	(0) -L	GS1060
350	Equipment Spec.(Marine)	( ) -L	GS1670-9
	Mail Clerk	(0) -L	GS305
	Messenger	(0) -L	GS302
	Supply Clerk	(0) -L	GS2005
	Supply Tech.	(0) -L	GS2005
360	Accountant	(0) -L	GS510
	Auditor	(0) -L	GS510
	Budget Analyst	(0) -L	GS560
	Shipyard Prod. Supt.	( ) -L	GS1601
	Time & Leave Clerk	(0) -L	GS590
393	File Clerk	(0) -L	GS305
	Sy Prod Supt		GS1601-15
394	Training Administrator	(0) -L	GS1712
395	Sy Prod Supt		GS1601-14
Fiscal Dept.	Timekeeper	(0) -L	GS590
P&C Dept.	Accts. Maint. Clerk	(0) -L	GS520
Planning/Design	Electronics Engr.	(1) -L	GS855
	Elec. Engr. Tech.	(1) -L	GS802
	Engr. Draftsman	(1) -L	GS818
	Naval Arch. Tech.	(1) -L	GS802
	Student Trainee(gen.engr)	( ) -L	GS899-3
	Supv. Naval Arch.	(1) -L	GS871
POME	Office Services Supv.	(0) -L	GS342
	Photographer	(0) -L	GS1060
	Utilities Supv.	(0) -L	GS1601

Shop Number	Occupation	Code	Work Grade
Production	Ind. Engr. Tech.	(1) -L	GS895
	Management Ass't.	(0) -L	GS344
	Management Tech.	(0) -L	GS344
QA Office	Physical Science Tech.	( )	GS1311
	QA Insp. Spec.(Metrology)	( )	GS1960
Administration	Dig. Comp. Syst. Opr.	(0) -L	GS332
	Teletypist	(0) -L	GS385
Supply	Office Machine Opr.	(0) -L	GS
	Warehouseman	(1) -M	WG6907

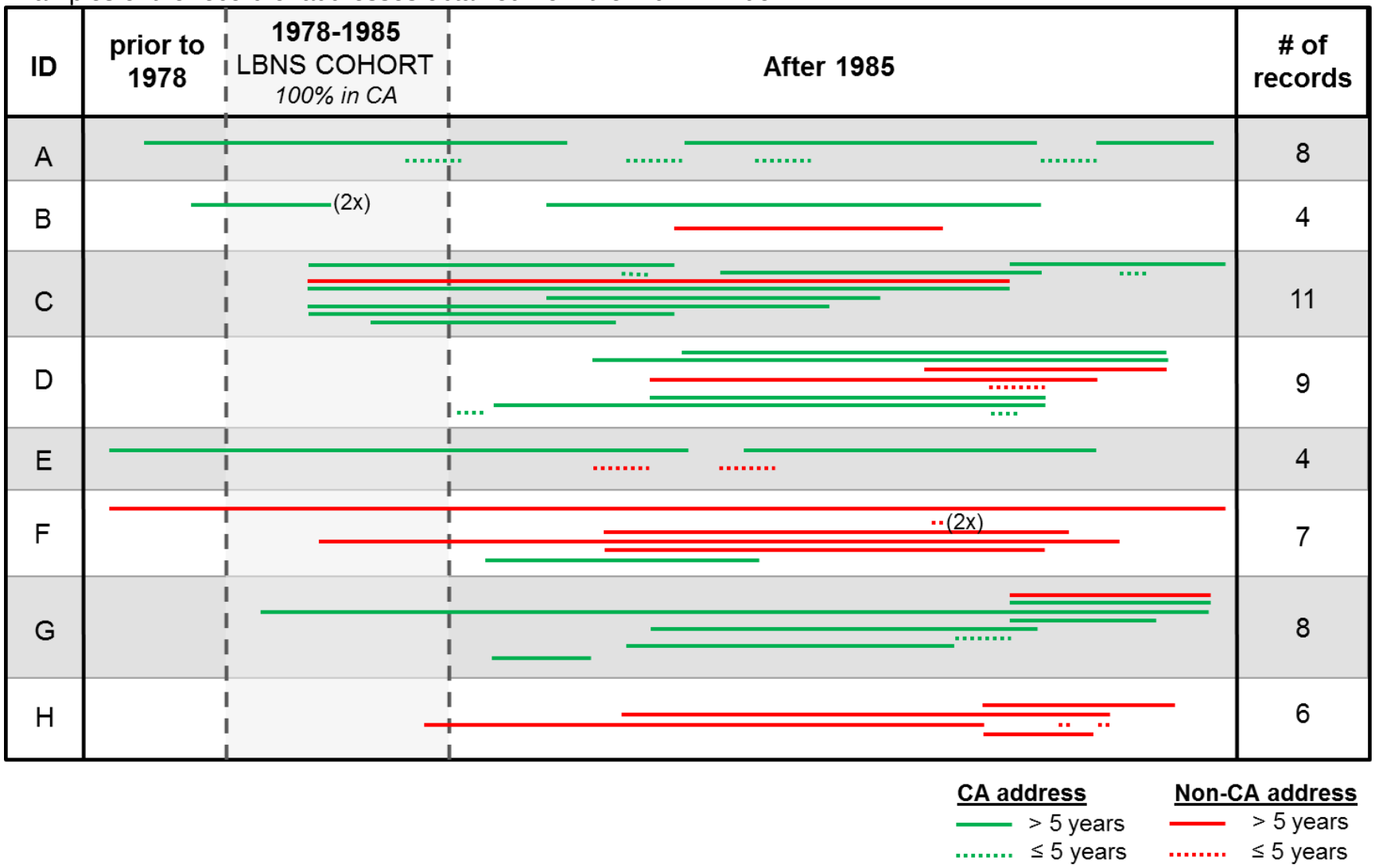
APPENDIX B

Distribution of workers by asbestos exposure levels based on their shop numbers and job titles

Major job group	Shops	Asbestos Exposure (*n* = 2,922)					
		Low	%	Intermediate	%	High	%
Architect, Engineer	319	13	**92.9**	1	7.1	0	0
	324	87	**100**	0	0	0	0
Boilermaker	41	0	0	0	0	149	100
Electrician	51	6	2.4	240	**97.2**	1	0.4
	99	0	0	44	**100**	0	0
Electronics and equipment mechanic	36	0	0	56	**100**	0	0
	67	0	0	13	7.6	158	**92.4**
Insulator, Pipecoverer	57	0	0	0	0	82	**100**
Machinist	31	9	4.5	192	**95.5**	0	0
	38	0	0	0	0	126	**100**
Office worker, Administrative personnel	> 99 (except 319, 324)	431	**98.9**	5	1.1	0	0
Painter	71	56	**90.3**	5	8.1	1	1.6
Pipefitter	56	0	0	0	0	225	**100**
Rigger, Equipment Cleaner	72	3	2.7	18	16.2	90	81.1
Sheet metal worker	17	0	0	0	0	192	**100**
Structural worker	11	0	0	2	0.9	216	**99.1**
	64	0	0	6	9.2	59	**90.8**
Transportation and motor vehicle operator	2	24	31.2	32	41.5	21	27.3
Warehouseman	50	0	0	67	**100**	0	0
Welders	26	0	0	1	0.3	291	**99.7**
Total		629		682		1,611	

APPENDIX C

Examples of the record of addresses obtained from the AlumniFinder



APPENDIX D

Distribution of sexual orientation by main occupational group in Long Beach Naval shipyard study cohort (n = 13,712)

Main occupational group[†]	Sex	Count	Percent
Architects, Engineers	Male	297	90.27
	Female	32	9.73
Missing n = 442			
Boilermakers	Male	195	98.98
	Female	2	1.02
Missing n = 242			
Electricians	Male	454	96.80
	Female	15	3.20
Missing n = 634			
Electronics and equipment mechanics	Male	386	95.07
	Female	20	4.93
Missing n = 488			
Insulators	Male	108	93.91
	Female	7	6.09
Missing n = 220			
Machinists	Male	629	98.59
	Female	9	1.41
	Total	638	100.00
Missing n = 763			
Office workers, administrative personnel	Male	343	**42.24**
	Female	469	**57.76**
Missing n = 1362			
Painters	Male	233	97.08
	Female	7	2.92
Missing n = 341			
Pipefitters	Male	445	99.11
	Female	4	0.89
Missing n = 528			
Riggers, Equipment cleaners	Male	338	99.71
	Female	1	0.29
Missing n = 425			
Sheet metal workers	Male	202	98.06
	Female	4	1.94
Missing n = 266			
Structural workers	Male	449	98.46
	Female	7	1.54
Missing n = 559			
Transportation and mobile vehicle operators	Male	201	97.10
	Female	6	2.90
Missing n = 210			
Warehousemen	Male	127	94.78
	Female	7	5.22
Missing n = 143			
Welders	Male	267	97.80
	Female	6	2.20
Missing n = 437			

[†]The main occupational group 'Others' that was not included in the table has 595 males, 23 females, and 764 missing.

APPENDIX E

Deaths classified by cause-of-death categories in the Long Beach Naval shipyard[a] (n = 13,141)

Cause-of-death categories	Deaths with available cause-of-death	Percent	Calculated deaths for cases without available cause-of-death	Total number of deaths
Diseases of circulatory system[b]	1,400	38.01	412	1,812
Neoplasms[b, c]	1,086	29.49	319	1,405
Diseases of the respiratory system[b]	321	8.72	94	415
Accidents, Suicides, Homicides[b]	260	7.06	76	336
Diseases of the digestive system[b]	146	3.96	43	189
Endocrine, nutritional and metabolic diseases	140	3.80	41	181
Diseases of the nervous system	100	2.72	29	129
Infections and parasitic diseases	74	2.01	22	96
Mental and behavioral disorders	74	2.01	22	96
Diseases of the genitourinary system	55	1.49	16	71
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	9	0.24	3	12
Diseases of the musculoskeletal system and connective tissue	8	0.22	2	10
Diseases of the blood	6	0.16	2	8
Congenital malformations, deformations and chromosomal abnormalities	2	0.05	1	3
Diseases of the eye and adnexa	1	0.03	0	1
Diseases of the skin and subcutaneous tissue	1	0.03	0	1
Total[d]	3,683	100.00	1,083	4,766

[a] Excluded workers with unknown years of birth, workers hired at the age of ≤16 years old, and workers who were >64 years old during the first year of the study or were hired at the age of >64 years between 1978 and 1985.Also, excluded workers found in LBNS employee listings years after death (*n* = 11).

[b] Specific cause-of-death list found in **APPENDIX F**

[c] Includes benign tumors, non-malignant

APPENDIX F

Specific cause-of-deaths for diseases of the circulatory, respiratory, and digestive systems as well as accidents, suicides, and homicides categories

A. Specific cause-of-deaths for the diseases of the circulatory system

Specific cause-of-death	Count†	Percent
Ischemic heart diseases	793	56.64
Other forms of heart disease	245	17.50
Cerebrovascular diseases	179	12.79
Hypertensive diseases	107	7.64
Diseases of arteries, arterioles and capillaries	51	3.64
Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified	12	0.86
Chronic rheumatic heart diseases	7	0.50
Pulmonary heart disease and diseases of pulmonary circulation	6	0.43
Total	*1,400*	*100.00*

† Only includes deaths with available cause-of-death information.

B. Specific cause-of-deaths for the diseases of the respiratory system

Specific cause-of-death	Count†	Percent
Chronic lower respiratory diseases	125	38.94
Influenza and pneumonia	98	30.53
Chronic obstructive pulmonary disease and allied conditions	61	19.00
Lung diseases due to external agents	12	3.74
Other diseases of respiratory system	12	3.74
Other respiratory diseases principally affecting the interstitium	9	2.80
Other diseases of the respiratory system	2	0.62
Acute respiratory infections	1	0.31
Other diseases of the pleura	1	0.31
Total	*321*	100.00

† Only includes deaths with available cause-of-death information.

C. Specific cause-of-deaths for accidents, suicides, and homicides

Specific cause-of-death	Count[†]	Percent
Fracture of the upper limb	41	15.77
Poisoning by drugs, medicinals, and biological substances	38	14.62
Injury to nerves and spinal cord	33	12.69
Intracranial injury, excluding those with skull fracture	21	8.08
Intentional self-harm	19	7.31
Slipping, tripping, stumbling and falls	16	6.15
Accidental poisoning by and exposure to noxious substances	13	5.00
Superficial Injury	9	3.46
Assault	7	2.69
Not specified	6	2.31
Other land transport accidents	5	1.92
Crushing Injury	4	1.54
Pedal cycle rider injured in transport accident	4	1.54
Motorcycle rider injured in transport accident	4	1.54
Sequelae of external causes of morbidity and mortality	4	1.54
Open wound of head, neck, trunk	3	1.15
Open wound of upper limb	3	1.15
Contusion With Intact Skin Surface	3	1.15
Pedestrian injured in transport accident	3	1.15
Car occupant injured in transport accident	3	1.15
Exposure to inanimate mechanical forces	3	1.15
Accidental non-transport drowning and submersion	3	1.15
Fracture of spine and trunk	2	0.77
Sprains and strains of joints and adjacent muscles	2	0.77
Internal injury of chest, abdomen, and pelvis	2	0.77
Toxic effects of substances chiefly nonmedicinal as to source	2	0.77
Fracture of lower limb	1	0.38
Dislocation	1	0.38
Injury to blood vessels	1	0.38
Certain traumatic complications and unspecified injuries	1	0.38
Accidental exposure to other specified factors	1	0.38
Contact with heat and hot substances	1	0.38
Surgical and other medical procedures as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure	1	0.38
Total	*260*	*100.00*

[†] Only includes deaths with available cause-of-death information.

D. Specific cause-of-deaths for the diseases of the digestive system

Specific cause-of-death	Count[†]	Percent
Chronic liver disease and cirrhosis	57	39.04
Alcoholic liver disease	30	20.55
Fibrosis and cirrhosis of liver	9	6.16
Vascular disorders of intestine	6	4.11
Duodenal ulcer	5	3.42
Acute pancreatitis	4	2.74
Diseases of pancreas	4	2.74
Paralytic ileus and intestinal obstruction without hernia	4	2.74
Cholecystitis	3	2.05
Diverticula of intestine	3	2.05
Gastric ulcer	3	2.05
Other diseases of digestive system	3	2.05
Cholelithiasis	2	1.37
Hepatic failure, not elsewhere classified	2	1.37
Other disorders of liver	2	1.37
Diseases of esophagus	1	0.68
Diverticular disease of intestine	1	0.68
Gastritis and duodenitis	1	0.68
Gastrojejunal ulcer	1	0.68
Intestinal obstruction without mention of hernia	1	0.68
Other diseases of gallbladder	1	0.68
Other diseases of intestine	1	0.68
Umbilical hernia	1	0.68
Ventral hernia	1	0.68
Total	*146*	*100.00*

[†] Only includes deaths with available cause-of-death information.

APPENDIX G

Deaths classified by cause-of-deaths categories in the Long Beach Naval shipyard study cohort by asbestos exposure groups (n = 11,494)

A. Low/intermediate asbestos exposure group

Cause-of-death categories	*Total n = 5,878*			
	Deaths with available cause-of-death	**Percent**	**Calculated deaths for cases without available cause-of-death**	**Total number of deaths**
Diseases of circulatory system	577	38.06	166	743
Neoplasms[1]	456	30.08	131	587
Diseases of the respiratory system	136	8.97	39	175
Accidents, Suicides, Homicides	93	6.13	27	120
Diseases of the digestive system	64	4.22	18	82
Endocrine, nutritional and metabolic diseases	63	4.16	18	81
Diseases of the nervous system	40	2.64	11	51
Infections and parasitic diseases	31	2.04	9	40
Mental and behavioral disorders	26	1.72	7	33
Diseases of the genitourinary system	21	1.39	6	27
Diseases of the musculoskeletal system and connective tissue	4	0.26	1	5
Diseases of the blood	3	0.2	1	4
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	2	0.13	1	3
Total	*1,516*	*100.00*	*435*	*1,951*

[1] Includes benign tumors, non-malignant

B. High asbestos exposure group

Cause-of-death categories	*Total n = 5,616*			
	Deaths with available cause-of-death	**Percent**	**Calculated deaths for cases without available cause-of-death**	**Total number of deaths**
Diseases of circulatory system	586	37.02	187	773
Neoplasms[1]	453	28.62	145	598
Diseases of the respiratory system	138	8.72	44	182
Accidents, Suicides, Homicides	137	8.65	44	181
Diseases of the digestive system	59	3.73	19	78
Endocrine, nutritional and metabolic diseases	53	3.35	17	70
Diseases of the nervous system	46	2.91	15	61
Mental and behavioral disorders	37	2.34	12	49
Infections and parasitic diseases	36	2.27	11	47
Diseases of the genitourinary system	24	1.52	8	32
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	5	0.32	2	7
Diseases of the musculoskeletal system and connective tissue	4	0.25	1	5
Diseases of the blood	3	0.19	1	4
Congenital malformations, deformations and chromosomal abnormalities	1	0.06	0	1
Diseases of the eye and adnexa	1	0.06	0	1
Total	*1,583*	*100.00*	*506*	*2,089*

[1] Includes benign tumors, non-malignant

APPENDIX H

Cancer-specific deaths in the LBNS study cohort (n = 13,141)

Neoplasms	Deaths with available cause-of-death	Percent	Calculated number of cancer-specific death for cases without available cause-of-death	Total number of deaths
Malignant neoplasm of respiratory and intrathoracic organs	388	35.73	114	502
Malignant neoplasm of digestive organs and peritoneum	257	23.66	76	333
Malignant neoplasm of lymphatic and hematopoietic tissue	96	8.84	28	124
Malignant neoplasms of male genital organs	91	8.38	27	118
Malignant neoplasms of ill-defined, other secondary and unspecified sites	71	6.54	21	92
Malignant neoplasms of urinary tract	59	5.43	17	76
Malignant neoplasms of mesothelial and soft tissue	25	2.30	7	32
Malignant neoplasm of lip, oral cavity, and pharynx	23	2.12	7	30
Malignant neoplasms of breast	19	1.75	6	25
Melanoma and other malignant neoplasms of skin	15	1.38	4	19
Malignant neoplasms of eye, brain and other parts of central nervous system	11	1.01	3	14
Malignant neoplasms of female genital organs	10	0.92	3	13
Malignant neoplasms of bone and articular cartilage	7	0.64	2	9
Neoplasms of uncertain behavior	7	0.64	2	9
Neoplasms of unspecified nature	4	0.37	1	5
Malignant neoplasms of thyroid and other endocrine glands	2	0.18	1	3
Benign neoplasms, except benign neuroendocrine tumors	1	0.09	0	1
Total	*1,086*	*100.00*	*319*	*1,405*

APPENDIX I

Cancer-specific deaths in the LBNS study cohort by asbestos exposure groups (n = 11,494)

A. Low/intermediate asbestos exposure group

Type of neoplasms	*Total = 5,878*			
	Deaths with available cause-of-death	**Percent**	**Calculated number of cancer-specific deaths for cases without available cause-of-death**	**Total number of deaths**
Malignant neoplasm of respiratory and intrathoracic organs	163	35.75	47	210
Malignant neoplasm of digestive organs and peritoneum	100	21.93	29	129
Malignant neoplasm of lymphatic and hematopoietic tissue	47	10.31	14	61
Malignant neoplasms of male genital organs	30	6.58	9	39
Malignant neoplasms of urinary tract	25	5.48	7	32
Malignant neoplasms of ill-defined, other secondary and unspecified sites	21	4.61	6	27
Malignant neoplasms of breast	14	3.07	4	18
Malignant neoplasm of lip, oral cavity, and pharynx	14	3.07	4	18
Malignant neoplasms of eye, brain and other parts of central nervous system	10	2.19	3	13
Malignant neoplasms of female genital organs	9	1.97	3	12
Melanoma and other malignant neoplasms of skin	6	1.32	2	8
Malignant neoplasms of mesothelial and soft tissue	6	1.32	2	8
Malignant neoplasms of bone and articular cartilage	5	1.10	1	6
Neoplasms of uncertain behavior	4	0.88	1	5
Benign neoplasms, except benign neuroendocrine tumors	1	0.22	0	1
Malignant neoplasms of thyroid and other endocrine glands	1	0.22	0	1
Total	*456*	*100.00*	*131*	*587*

B. High asbestos exposure group

Type of neoplasms	*Total n = 5,616*			
	Deaths with available cause-of-death	**Percent**	**Calculated number of cancer-specific deaths for cases without available cause-of-death**	**Total number of deaths**
Malignant neoplasm of respiratory and intrathoracic organs	164	36.20	52	216
Malignant neoplasm of digestive organs and peritoneum	113	24.94	36	149
Malignant neoplasms of male genital organs	44	9.71	14	58
Malignant neoplasm of lymphatic and hematopoietic tissue	37	8.17	12	49
Malignant neoplasms of ill-defined, other secondary and unspecified sites	27	5.96	9	36
Malignant neoplasms of urinary tract	26	5.74	8	34
Malignant neoplasms of mesothelial and soft tissue	11	2.43	4	15
Malignant neoplasm of lip, oral cavity, and pharynx	8	1.77	3	11
Malignant neoplasms of eye, brain and other parts of central nervous system	7	1.55	2	9
Malignant neoplasms of breast	5	1.10	2	7
Melanoma and other malignant neoplasms of skin	5	1.10	2	7
Malignant neoplasms of bone and articular cartilage	2	0.44	1	3
Malignant neoplasms of thyroid and other endocrine glands	2	0.44	1	3
Malignant neoplasms of female genital organs	1	0.22	0	1
Neoplasms of uncertain behavior	1	0.22	0	1
Total	*453*	*100.00*	*145*	*598*

APPENDIX J

Primary cancers in the LBNS study cohort including Office workers and Administrative personnel (n = 13,141)

Cancer	Count	Percent
Prostate	469	30.61
Lung	231	15.08
Colorectal	163	10.64
Digestive system excluding colorectal cancer	120	7.83
Urinary system	118	7.70
Breast and female reproductive system	80	5.22
Other†	72	4.70
Skin excluding basal and squamous	53	3.46
Lymphoma	48	3.13
Oral cavity and pharynx	34	2.22
Leukemia	29	1.89
Brain and other nervous system	25	1.63
Mesothelioma	27	1.76
Respiratory system excluding lung	23	1.50
Myeloma	21	1.37
Endocrine system	11	0.72
Male reproductive system excluding prostate	8	0.52
Total	*1,532*	100.00

† Other cancers include cancers of the bones and joints, soft tissue including heart, eye and orbit, Kaposi sarcoma, and miscellaneous cancers.

APPENDIX K

Site-specific primary cancers in the LBNS study cohort (n = 11,062)

Organ system	Site	Count	Percent
Brain and other nervous system	Brain	15	68.18
	Cranial nerves other nervous system	7	31.82
Total		*22*	
Digestive system excluding colorectal	Esophagus	12	10.62
	Stomach	35	30.97
	Small intestine	5	4.42
	Liver	17	15.04
	Intrahepatic bile duct	3	2.65
	Gallbladder	1	0.88
	Other biliary	4	3.54
	Pancreas	34	30.09
	Peritoneum, omentum and mesentery	1	0.88
	Other digestive organs	1	0.88
Total		*113*	
Endocrine system	Thyroid	8	80.00
	Other endocrine including thymus	2	20.00
Total		*10*	
Male reproductive system excluding prostate	Testis	4	66.67
	Penis	1	16.67
	Other male genital organs	1	16.67
Total		*6*	
Oral cavity and pharynx	Lip	2	6.90
	Tongue	6	20.69
	Salivary gland	3	10.34
	Floor of mouth	1	3.45
	Gum and other mouth	5	17.24
	Nasopharynx	3	10.34
	Tonsil	8	27.59
	Hypopharynx	1	3.45
Total		*29*	
Respiratory system excluding lung	Larynx	22	100.00
Total		*22*	
Skin excluding basal and squamous	Melanoma of the skin	32	86.49
	Other non-epithelial skin	5	13.51
Total		*37*	
Urinary system	Urinary bladder	68	66.02
	Kidney and renal pelvis	35	33.98
Total		*103*	

Appendix L

Primary cancers in the main occupational group, Office workers and Administrative personnel (n = 2,079)

Cancer	Count	Percent
Breast	45	17.65
Prostate	42	16.47
Lung	31	12.16
Colorectal	25	9.80
Female reproductive system	24	9.41
Other†	20	7.84
Skin excluding basal and squamous	16	6.27
Urinary system	15	5.88
Lymphoma	9	3.53
Digestive system excluding colorectal	7	2.75
Oral cavity and pharynx	5	1.96
Leukemia	5	1.96
Brain and other nervous system	3	1.18
Male reproductive system	2	0.78
Myeloma	2	0.78
Mesothelioma	2	0.78
Larynx	1	0.39
Endocrine system	1	0.39
Total	*255*	*100.00*

† Other cancers include cancers of the bones and joints, soft tissue including heart, eye and orbit, Kaposi sarcoma, and miscellaneous cancers.

APPENDIX M

Primary cancers in the LBNS study cohort by asbestos exposure groups (n = 9,414)

A. Low asbestos exposure group (*N = 1,337*)

Cancer type	Count	Percent
Prostate	63	37.95
Lung	21	12.65
Urinary system	11	6.63
Colorectal	10	6.02
Digestive system excluding colorectal cancer	10	6.02
Oral cavity and pharynx	8	4.82
Brain and other nervous system	6	3.61
Lymphoma	6	3.61
Other[1]	6	3.61
Skin excluding basal and squamous	6	3.61
Respiratory system excluding lung cancer	5	3.01
Endocrine system	3	1.81
Leukemia	3	1.81
Myeloma	3	1.81
Breast and female reproductive system	2	1.20
Mesothelioma	2	1.20
Male reproductive system excluding prostate	1	0.60
Total	*166*	*100.00*

[1] Other cancers include cancer of the bones and joints, soft tissue including heart, eye and orbit, Kaposi sarcoma, and miscellaneous cancers.

B. Intermediate asbestos exposure group (*N = 2,462*)

Cancer type	Count	Percent
Prostate	86	29.97
Lung	47	16.38
Colorectal	36	12.54
Urinary system	33	11.50
Digestive system excluding colorectal	25	8.71
Other[1]	11	3.83
Lymphoma	9	3.14
Oral cavity and pharynx	7	2.44
Skin excluding basal and squamous	6	2.09
Breast and female reproductive system	5	1.74
Mesothelioma	5	1.74
Brain and other nervous system	3	1.05
Endocrine system	3	1.05
Leukemia	3	1.05
Myeloma	3	1.05
Respiratory system excluding lung	3	1.05
Male reproductive system excluding prostate	2	0.70
Total	*287*	*100.00*

[1] Other cancers include cancer of the bones and joints, soft tissue including heart, eye and orbit, Kaposi sarcoma, and miscellaneous cancers.

C. High asbestos exposure group (*N = 5,616*)

Cancer type	Count	Percent
Prostate	217	35.52
Lung	92	15.06
Colorectal	65	10.64
Digestive system excluding colorectal	57	9.33
Urinary system	37	6.06
Other[1]	24	3.93
Lymphoma	18	2.95
Skin excluding basal and squamous	18	2.95
Leukemia	14	2.29
Brain and other nervous system	13	2.13
Oral cavity and pharynx	12	1.96
Respiratory system excluding lung	12	1.96
Mesothelioma	11	1.80
Myeloma	11	1.80
Breast and female reproductive system	4	0.65
Endocrine system	3	0.49
Male reproductive system excluding prostate	3	0.49
Total	*611*	*100.00*

[1] Other cancers include cancer of the Bones and joints, Soft tissue including heart, Eye and orbit, Kaposi sarcoma, and Miscellaneous.

APPENDIX N

Cancer-specific age-standardized incidence ratio in the male LBNS workers compared to the general population of California by main occupational group (n = 11,062)

A. Architects and engineers (*n = 742*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	3	0.57	5.24 (1.34-14.32)
Colorectal	5	4.10	1.22 (0.45-2.70)
Digestive system excluding colorectal	3	3.13	0.96 (0.24-2.61)
Endocrine system	1	0.34	2.92 (0.15-14.51)
Leukemia	2	0.94	2.13 (0.36-7.03)
Lung	11	5.21	2.11 (1.11-3.67)
Lymphoma	4	1.81	2.21 (0.70-5.33)
Mesothelioma	1	0.12	8.06 (0.42-41.10)
Oral cavity and pharynx	4	1.26	3.18 (1.01-7.66)
Prostate	33	10.52	3.14 (2.20-4.35)
Respiratory system excluding lung	2	0.65	3.08 (0.52-10.17)
Skin excluding basal and squamous	5	2.45	2.04 (0.75-4.52)
Urinary system	8	3.11	2.57 (1.19-4.88)

† Primary cancers only

B. Electronics and equipment mechanics (*n = 863*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	1	0.71	1.41 (0.07-6.94)
Colorectal	13	5.18	2.51 (1.40-4.18)
Digestive system excluding colorectal	7	3.99	1.75 (0.77-3.47)
Leukemia	5	1.17	4.26 (1.57-9.47)
Lung	11	6.67	1.65 (0.87-2.87)
Lymphoma	4	2.24	1.78 (0.57-4.31)
Mesothelioma	2	0.16	12.71 (2.10-41.30)
Myeloma	3	0.56	5.39 (1.36-14.58)
Oral cavity and pharynx	3	1.60	1.88 (0.48-5.10)
Prostate	38	13.50	2.81 (2.02-3.82)
Respiratory system excluding lung	2	0.83	2.40 (0.40-7.96)
Skin excluding basal and squamous	2	3.08	0.65 (0.11-2.15)
Urinary system	11	3.96	2.78 (1.47-4.83)

† Primary cancers only

C. Electricians (*n = 1,063*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	3	0.89	3.36 (0.86-9.17)
Colorectal	12	6.85	1.75 (0.95-2.98)
Digestive system excluding colorectal	11	5.20	2.12 (1.11-3.68)
Endocrine system	1	0.52	1.94 (0.10-9.48)
Leukemia	1	1.53	0.66 (0.03-3.22)
Lung	26	8.88	2.93 (1.95-4.23)
Lymphoma	6	2.83	2.12 (0.86-4.41)
Male reproductive system excluding prostate	2	0.71	2.84 (0.47-9.31)
Mesothelioma	3	0.21	14.18 (3.63-38.88)
Myeloma	3	0.73	4.12 (1.04-11.18)
Oral cavity and pharynx	4	2.04	1.96 (0.62-4.73)
Prostate	35	17.93	1.95 (1.38-2.68)
Skin excluding basal and squamous	3	3.88	0.77 (0.20-2.10)
Urinary system	10	5.21	1.92 (0.97-3.42)

† Primary cancers only

D. Machinists (*n = 1,361*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	3	1.06	2.83 (0.72-7.70)
Colorectal	20	7.79	2.57 (1.61-3.89)
Digestive system excluding colorectal	13	5.93	2.19 (1.22-3.65)
Endocrine system	1	0.62	1.61 (0.08-7.95)
Leukemia	1	1.77	0.57 (0.03-2.79)
Lung	17	9.97	1.71 (1.03-2.67)
Lymphoma	2	3.36	0.60 (0.10-1.97)
Mesothelioma	2	0.24	8.42 (1.40-27.53)
Myeloma	2	0.83	2.42 (0.40-7.96)
Oral cavity and pharynx	4	2.37	1.69 (0.54-4.07)
Prostate	50	20.00	2.50 (1.88-3.27)
Respiratory system excluding lung	3	1.24	2.42 (0.62-6.58)
Skin excluding basal and squamous	5	4.56	1.10 (0.40-2.43)
Urinary system	17	5.91	2.88 (1.73-4.51)

† Primary cancers only

E. Transportation and mobile vehicle operators (*n = 405*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	1	0.38	2.64 (0.13-12.98)
Colorectal	3	3.35	0.89 (0.23-2.44)
Digestive system excluding colorectal	7	2.44	2.86 (1.25-5.67)
Lung	5	4.49	1.11 (0.41-2.47)
Lymphoma	2	1.20	1.67 (0.28-5.51)
Mesothelioma	2	0.11	18.23 (3.05-60.07)
Oral cavity and pharynx	1	0.91	1.10 (0.05-5.42)
Prostate	13	8.74	1.49 (0.83-2.48)
Respiratory system excluding lung	2	0.52	3.82 (0.64-12.71)
Skin excluding basal and squamous	3	1.64	1.83 (0.47-4.98)
Urinary system	7	2.53	2.76 (1.21-5.47)

† Primary cancers only

F. Painters (*n = 535*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	3	0.37	8.01 (2.06-22.07)
Colorectal	4	2.68	1.49 (0.47-3.60)
Digestive system excluding colorectal	4	2.04	1.96 (0.62-4.73)
Endocrine system	1	0.22	4.48 (0.23-22.42)
Lung	10	3.42	2.93 (1.49-5.21)
Lymphoma	2	1.18	1.69 (0.28-5.60)
Male reproductive system excluding prostate	1	0.35	2.86 (0.14-14.09)
Mesothelioma	1	0.08	12.34 (0.63-61.65)
Myeloma	3	0.28	10.56 (2.73-29.16)
Oral cavity and pharynx	4	0.82	4.85 (1.55-11.77)
Prostate	27	6.72	4.02 (2.70-5.77)
Respiratory system excluding lung	2	0.43	4.67 (0.78-15.37)
Skin excluding basal and squamous	1	1.59	0.63 (0.03-3.10)
Urinary system	3	2.03	1.48 (0.38-4.02)

† Primary cancers only

G. Riggers and equipment cleaners (*n = 720*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	2	0.54	3.69 (0.62-12.24)
Colorectal	8	4.01	1.99 (0.93-3.79)
Digestive system excluding colorectal	9	3.02	2.98 (1.45-5.47)
Endocrine system	1	0.31	3.21 (0.16-15.91)
Leukemia	1	0.91	1.10 (0.05-5.42)
Lung	18	5.21	3.46 (2.11-5.35)
Lymphoma	4	1.71	2.34 (0.74-5.64)
Mesothelioma	3	0.12	24.13 (6.36-68.04)
Myeloma	2	0.42	4.73 (0.80-15.73)
Oral cavity and pharynx	2	1.20	1.66 (0.28-5.51)
Prostate	31	10.17	3.05 (2.11-4.27)
Respiratory system excluding lung	2	0.64	3.11 (0.52-10.32)
Skin excluding basal and squamous	1	2.29	0.44 (0.02-2.15)
Urinary system	5	3.03	1.65 (0.60-3.66)

† Primary cancers only

H. Boilermakers, insulators, pipecoverers, and pipefitters (*n = 1,664*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	2	1.20	1.66 (0.28-5.51)
Colorectal	23	8.34	2.76 (1.79-4.07)
Digestive system excluding colorectal	18	6.40	2.81 (1.72-4.36)
Endocrine system	1	0.73	1.36 (0.07-6.76)
Leukemia	2	1.93	1.03 (0.17-3.42)
Lung	25	10.47	2.39 (1.58-3.47)
Lymphoma	6	3.82	1.57 (0.64-3.27)
Male reproductive system excluding prostate	1	1.19	0.84 (0.04-4.14)
Mesothelioma	5	0.25	20.13 (7.33-44.33)
Myeloma	3	0.89	3.38 (0.86-9.17)
Oral cavity and pharynx	2	2.61	0.77 (0.13-2.53)
Prostate	57	20.99	2.71 (2.08-3.49)
Respiratory system excluding lung	2	1.32	1.51 (0.25-5.01)
Skin excluding basal and squamous	5	5.14	0.97 (0.36-2.16)
Urinary system	13	6.32	2.06 (1.14-3.42)

† Primary cancers only

I. Sheet metal workers, structural workers, and welders (*n = 2,131*)

Cancer type†	Observed	Expected	SIR (95% CI)
Brain and other nervous system	3	1.70	1.76 (0.45-4.80)
Colorectal	22	13.01	1.69 (1.09-2.52)
Digestive system excluding colorectal	22	9.76	2.25 (1.45-3.36)
Endocrine system	1	0.98	1.02 (0.05-5.03)
Leukemia	8	2.91	2.75 (1.28-5.22)
Lung	37	16.67	2.22 (1.59-3.03)
Lymphoma	5	5.40	0.93 (0.34-2.05)
Male reproductive system excluding prostate	2	1.47	1.36 (0.23-4.50)
Mesothelioma	2	0.40	4.97 (0.84-16.52)
Myeloma	1	1.36	0.73 (0.04-3.63)
Oral cavity and pharynx	4	3.82	1.05 (0.33-2.53)
Prostate	87	33.29	2.61 (2.11-3.21)
Respiratory system excluding lung	5	2.04	2.45 (0.90-5.43)
Skin excluding basal and squamous	8	7.31	1.10 (0.51-2.08)
Urinary system	10	9.83	1.02 (0.52-1.81)

† Primary cancers only

J. Warehousemen (*n = 266*)

Cancer type†	Observed	Expected	SIR (95% CI)
Colorectal	4	2.22	1.80 (0.57-4.35)
Digestive system excluding colorectal	2	1.64	1.22 (0.20-4.03)
Endocrine system	1	0.13	7.53 (0.38-37.94)
Lung	4	3.00	1.33 (0.42-3.22)
Prostate	8	5.87	1.36 (0.63-2.59)
Respiratory system excluding lung	1	0.35	2.85 (0.14-14.09)
Skin excluding basal and squamous	1	1.10	0.90 (0.04-4.48)
Urinary system	2	1.69	1.19 (0.20-3.91)

† Primary cancers only

APPENDIX O

Modified grouping of the main occupations in the Long Beach Naval shipyard study cohort (n = 13,141)

Main occupational groups[†]	Count	Percent
Office workers and administrative personnel	2,079	17.58
Architects, engineers	742	6.27
Electronics and equipment mechanics	863	7.30
Electricians	1,063	8.99
Machinists	1,361	11.51
Transportation and mobile vehicle operators	405	3.42
Painters	535	4.52
Riggers, equipment cleaners	720	6.09
Boilermakers, insulators, pipecoverers, pipefitters	1,664	14.07
Sheet metal workers, structural workers, welders	2,131	18.02
Warehousemen	266	2.25
Total[‡]	*11,829*	*100.00*

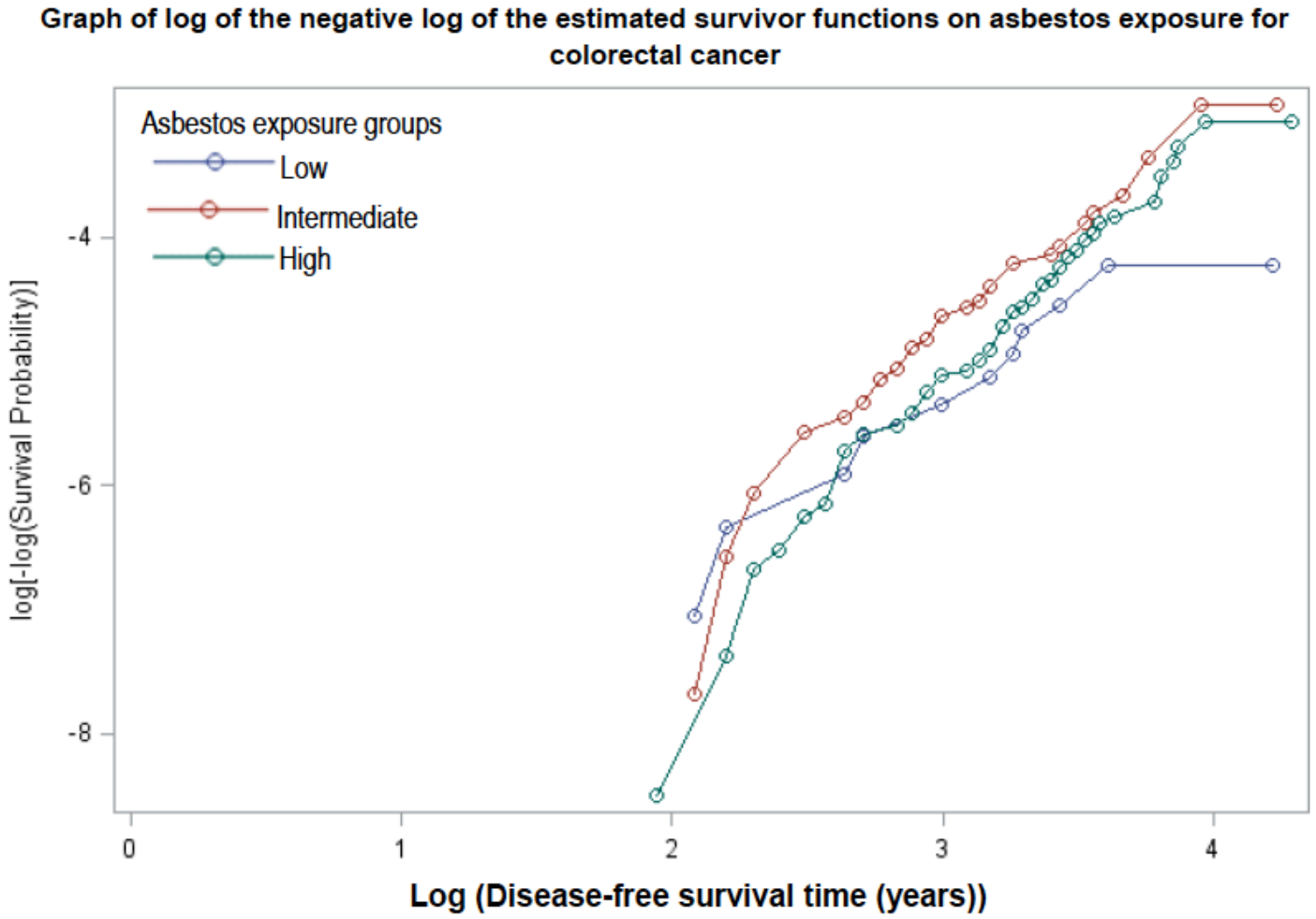
[†] Groups modified by collapsing seven main occupational groups into two groups

[‡] Not including workers in group 'Others' (*n = 1,312*)

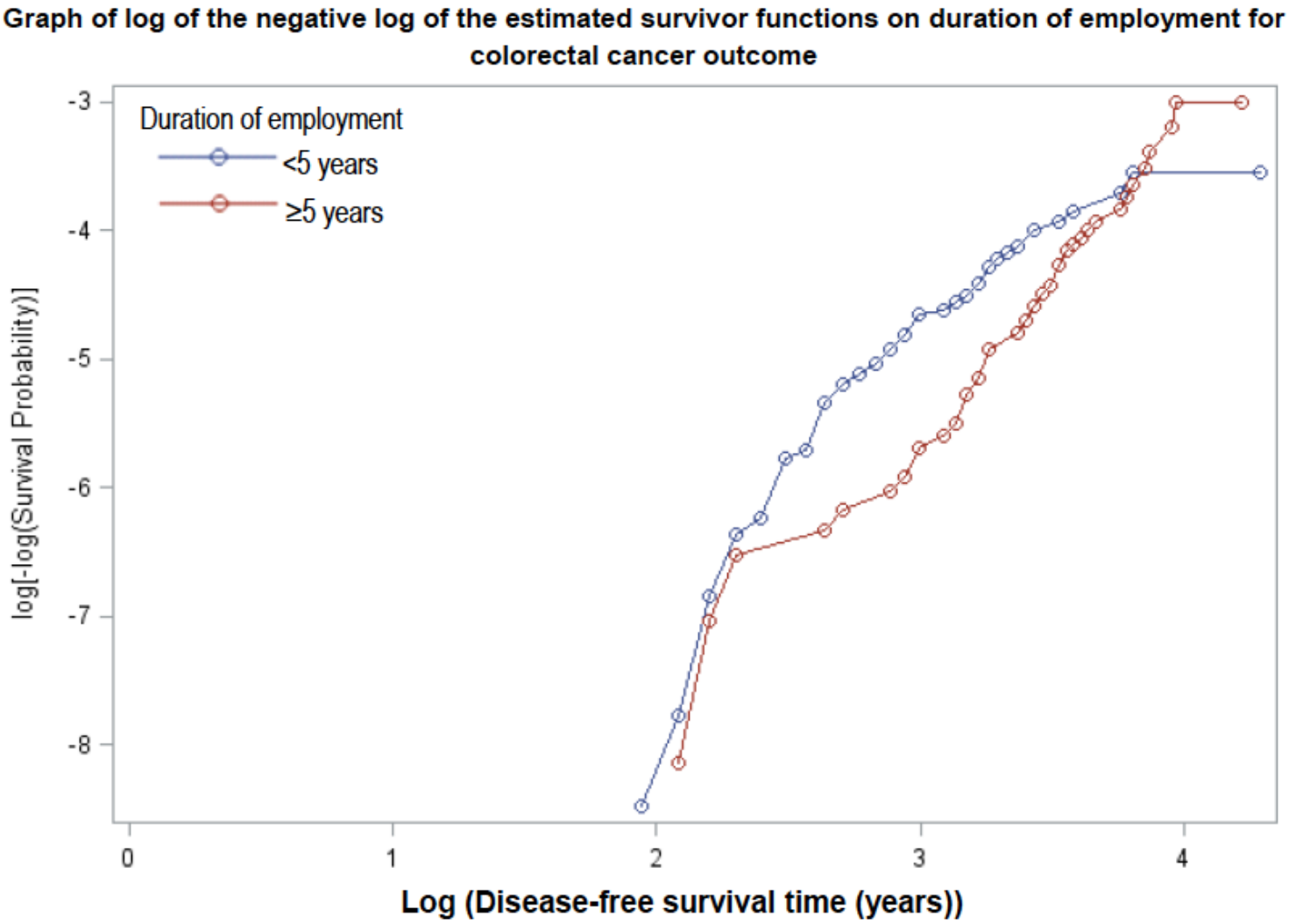
APPENDIX P

Graphs of log of the negative log of the estimated survivor functions to check proportional hazard assumptions for the outcomes colorectal cancer and lung cancer

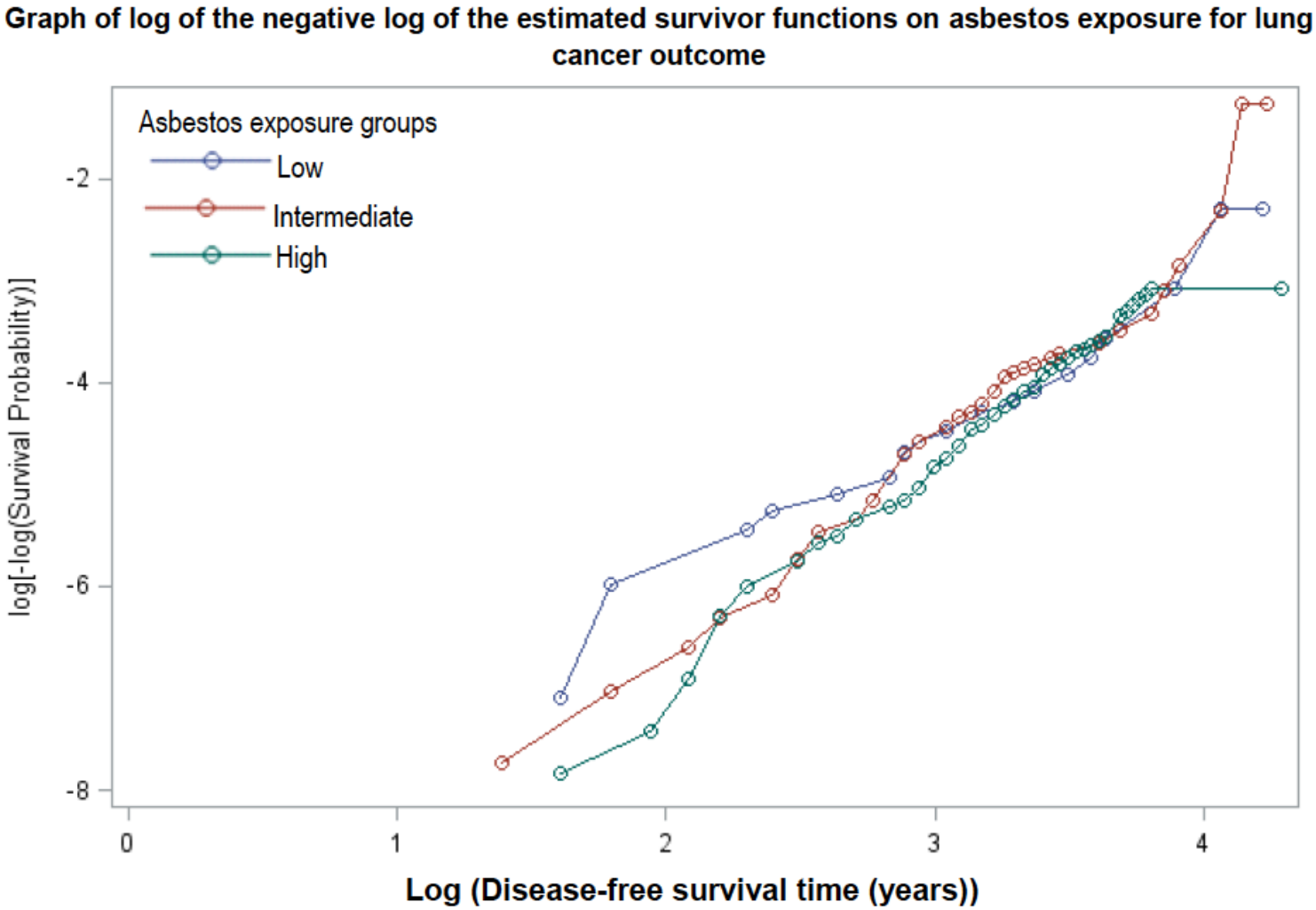
A.



B.


Graph of log of the negative log of the estimated survivor functions on duration of employment for colorectal cancer outcome
Duration of employment
<5 years
≥5 years
log[-log(Survival Probability)]
-3
-4
-5
-6
-7
-8
0
1
2
3
4
Log (Disease-free survival time (years))

C.


Graph of log of the negative log of the estimated survivor functions on asbestos exposure for lung cancer outcome
Asbestos exposure groups
Low
Intermediate
High
log[-log(Survival Probability)]
-2
-4
-6
-8
0
1
2
3
4
Log (Disease-free survival time (years))

Appendix Q

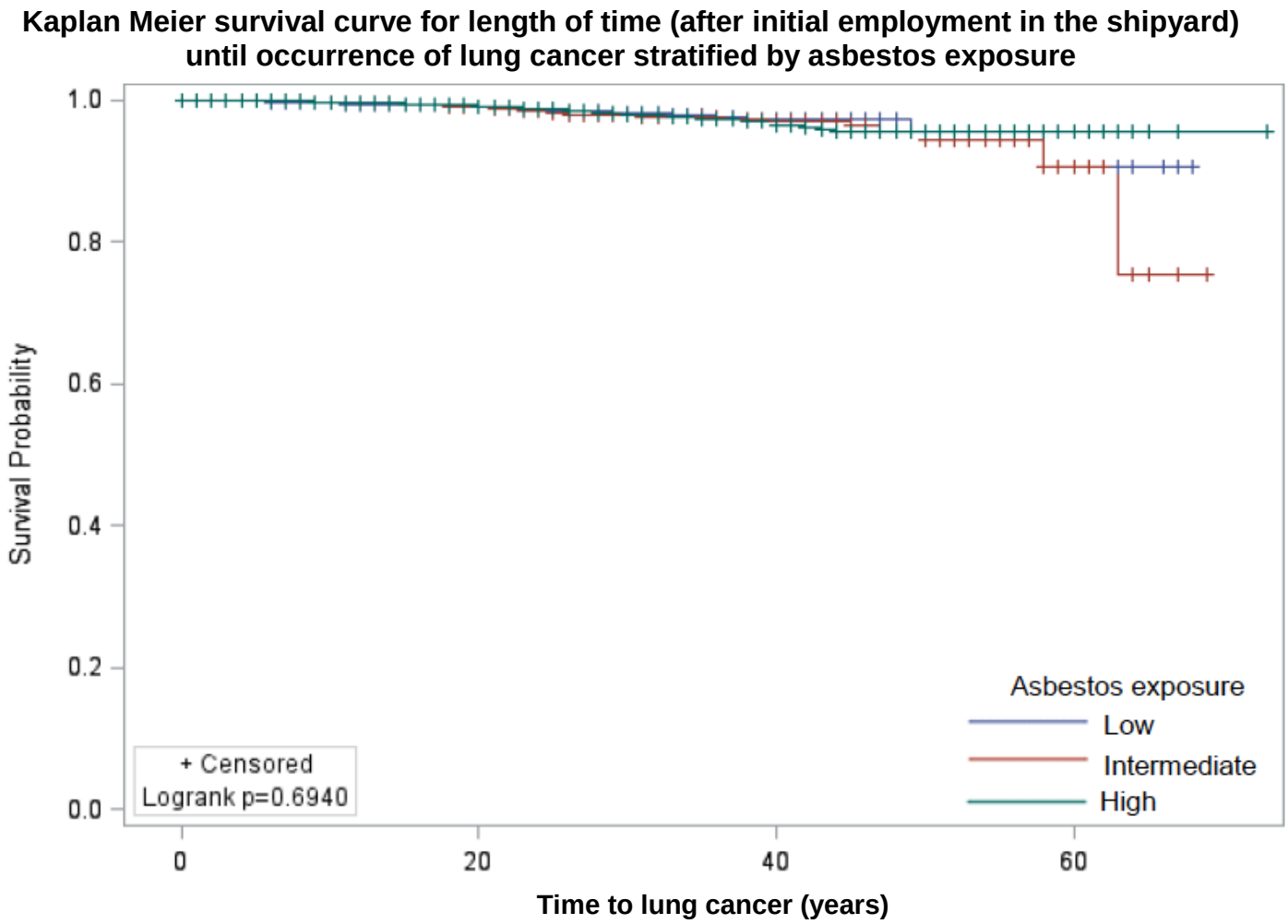
Lung cancer stratified by asbestos exposure groups (n = 9,349)

Exposure to asbestos	Count	Percent
Low	21	13.21
Intermediate	46	28.93
High	92	57.86
Total	*159*	*100.00*

APPENDIX R

Kaplan-Meier curve for lung cancer in the Long Beach Naval shipyard cohort by asbestos exposure and duration of employment

A.



B.

Kaplan Meier survival curve for length of time (after initial employment in the shipyard) until occurrence of lung cancer stratified by asbestos exposure and duration of employment