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Relationship Between PM2.5 Levels and Cancer Incidences in Interior Alaska

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This is to certify that the doctoral study by

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Walden University
2020

Abstract

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Sandra G. Lewis

Doctoral Study Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Public Health

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August 2020

Abstract

Exposure to high levels of ambient air particulates < 2.5 microns in diameter ($PM_{2.5}$) in the Fairbanks North Star Borough (FNSB) and the resulting impact on cancer incidence is the focus of this study. Climate, geography, and culture influence $PM_{2.5}$ levels, particularly during the long cold season. While this study considers lung cancer incidences from $PM_{2.5}$ exposure, the primary focus of the study is the incidences of all other types of cancers from exposure to $PM_{2.5}$, because of the limited research done on this topic. This quantitative, retrospective, cohort study considered the incidences of new cancer diagnoses in the population during a 10-year period (January 1, 2008-December 31, 2017). The 2 FNSB Zip Codes, designated "hot spots," frequently see spikes in $PM_{2.5}$ during the long cold season. These areas are densely populated and contain the EPA-regulated air quality monitors. Cancer diagnoses in the hot spot Zip Codes were compared to cancer diagnoses in outlying Zip Codes (non-hot spots) that experience less $PM_{2.5}$ and are more consistently within the EPA air quality guidelines. EPA monitors are not yet located in the non-hot spots. Cancer patient data were obtained from the Fairbanks Memorial Hospital Cancer Center. The results demonstrated that a strong association was found between $PM_{2.5}$ exposure and non-lung cancers (OR = 1.37; RR = 1.36; $p < 0.001$); and between $PM_{2.5}$ exposure and lung cancer (OR = 1.87; RR = 1.88; $p < 0.001$). These findings may be used to promote an increased awareness among FNSB residents of the potential impact on cancer diagnoses from inhaling high levels of $PM_{2.5}$, so residents may change their behavior in favor of alternatives to biomass burning to improve air quality.

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Dedication

This work is dedicated to the many thousands of my former college and university students of anatomy and physiology, who worked so hard to achieve their dreams of a career in the field of healthcare, whether in practice or in research. In this Pandemic time especially, it was your perseverance in your education and training, and is now your dedication to caring for others, that is giving people all around the world hope.

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Section 1: Foundation of the Study and Literature Review

Introduction

A serious public health problem exists in the Fairbanks North Star Borough (FNSB) area, located in the interior of Alaska. During the long cold season, which generally runs from mid-October through March (U.S. Climate Data, 2018), frequent spikes in air particulate matter equal to or less than 2.5 microns in diameter ($PM_{2.5}$) occur (FNSB Air Quality Division, n.d.). These spikes in fine particulate levels often exceed the United States Environmental Protection Agency (EPA) standard for $PM_{2.5}$. In 2006, the National Ambient Air Quality Standards (NAAQS) for $PM_{2.5}$ was lowered to not exceed 35 micrograms/m^3 for a 24-hour period. (EPA, 2006). In 2017, the FNSB was reclassified by the EPA from a moderate to a serious nonattainment area (EPA, 2017). According to the American Lung Association (2018), Fairbanks ranks number one in the nation for the number of people at risk for adverse health effects due to annual $PM_{2.5}$ levels. In December, 2012, in the small FNSB town of North Pole located just 20 miles south of Fairbanks, the daily average concentration for $PM_{2.5}$ was 170 micrograms/m^3 (Wang & Hopke, 2014), greatly exceeding the NAAQS standards. North Pole experiences more frequent spikes in $PM_{2.5}$ than any of the other areas of the FNSB, and thus is considered to be a "hot spot" for $PM_{2.5}$ during the cold season, as is the downtown Fairbanks zip code area (Alaska Department of Environmental Conservation Division of Air Quality, 2019). The speciation network of the EPA identifies seven major sources of $PM_{2.5}$ in the FNSB region including wood smoke (40.5%), sulfate (19.5%), gasoline (16.3%), diesel (14.3%), nitrate (4.5%), soil (3.4%) and road salt (1.5%). Wood smoke

contributions could be doubled during periods of air quality violations ($PM_{2.5}$ > 35 micrograms/m^3), and because wood is a primary source of heat in the Alaskan interior, it is the main contributor to unhealthy air during the cold season (Wang & Hopke, 2014).

There have been many studies linking the inhalation of high levels of $PM_{2.5}$ to respiratory, cardiovascular, and cerebrovascular health issues (Apte, Marshall, Cohen, & Brauer, 2015; Du, Xu, Chu, Guo, & Wang, 2016; West et al. 2016; Xing, Xu, Shi, & Lian, 2016). Other validated studies have linked $PM_{2.5}$ exposure during pregnancy to negative pregnancy outcomes (Stieb et al. 2016; Sun et al. 2015; Zhang et al. 2016). However, there have been few studies published on the carcinogenic effects of inhaling high levels of $PM_{2.5}$ beyond causing lung cancer, and many of the lung cancer studies encourage additional research in this area (Fu, Jiang, Lin, Liu, & Wang, 2015; Huang, Pan, Wu, Chen, E. & Chen, L. 2017; Poirier, Grundy, Khandwala, Friedenreich, & Brenner, 2017; Pun, Kazemiparkouhi, Manjourides & Suh, 2017).

From numerous studies conducted over the past 30-40 years, $PM_{2.5}$ is emerging as one of the most harmful substances that can be inhaled. This is because these fine particulates are so tiny that they bypass the mucociliary escalator found in healthy upper respiratory tracts in humans. This “escalator” using the pseudostratified ciliated columnar epithelium of the upper respiratory tract is able to capture larger particulates, such as those 10 microns in diameter and larger (PM_{10}), by trapping them in mucous secreted by the extensive mucous-secreting “goblet” cells of the epithelial lining, then, via ciliated action, the larger particulates are packaged up and moved upward toward the throat, where they are then swallowed and ultimately destroyed and/or eliminated by the

digestive system (Shei, Peabody, & Rowe, 2018). $PM_{2.5}$ however, are small enough to bypass the mucociliary escalator of the upper respiratory tract and are inhaled deep into the alveoli, where they cross the alveolar-capillary membranes and enter the bloodstream. Once in the capillaries and arteries, damage to the endothelial lining of the blood vessels begins, causing oxidative stress and inflammation of the tissues. $PM_{2.5}$ can directly damage vascular and cardiac endothelium and is also known to induce the release of interleukin-6 and proinflammatory cytokines that cause the liver to release C-reactive proteins, which further stimulate inflammation (Dai et al., 2016). $PM_{2.5}$ is also known to be more harmful than PM_{10} because the tiny size of the fine particulates actually gives them a much greater surface area for carrying toxins. Thus, by the physical nature alone of the tiny particulates, they are much more hazardous to human health than larger particulates (Xing et al., 2016). Additionally, epidemiological evidence has shown that injury to DNA and the induction of chromosomal abnormalities due to exposure to $PM_{2.5}$ are primary causes of lung cancer pathogenesis (Kim, Chen, Zhou, & Huang, 2018). Fine particulates are known to carry toxins that have carcinogenic properties such as polycyclic aromatic hydrocarbons (PAHs), arsenic, chromium, and nickel (Harrison, Smith, & Kibble, 2004). When carcinogens such as PAHs come into contact with DNA, a covalent bond between the DNA and the carcinogen can form, resulting in substitutions in nucleic acid nucleotides, deletions of nucleotides, and rearrangement of chromosomes during DNA replication, all contributing to the development of cancer (Demetriou et al. 2012). Fine particulates are strongly linked to lung cancer (Deng et al. 2013; Fu et al. 2015; Huang et al. 2017; Poirier et al. 2017; Wei et al. 2017). The World Health

Organization's (WHO) International Agency for Research on Cancer (2013) classified $PM_{2.5}$ as a level 1 human carcinogen for lung cancer, but the literature is sparse regarding the impact of $PM_{2.5}$ on non-lung type cancers. A number of studies have recommended additional research on the impact of $PM_{2.5}$, and its possible link to DNA alterations that might lead to cancers of various types beyond lung cancer (Andersen et al., 2018; Montrose et al. 2015; Parikh & Wei, 2016; Turner et al. 2017; Wei et al. 2017; Wong et al. 2016). Additionally, there is significant evidence to support a possible link between $PM_{2.5}$ and cancers of the breast, digestive system, lymphatic system, and hematopoietic systems, supporting the need for more studies on the link between exposure to high levels of $PM_{2.5}$ and cancers beyond lung cancers (Parikh & Wei, 2016; Pun et al. 2017; Wong et al. 2016).

As more is learned about the harmful effects of $PM_{2.5}$, particularly particulates resulting from biomass burning, it is expected that there will be positive changes in attitudes among people living in the FNSB toward responsible use of wood stoves, burn bans, and close adherence to air quality advisories.

Section 1 reveals the problem related to this study, the theoretical theory on which this study is based, a thorough review of scholarly studies that have addressed the numerous adverse health effects of breathing high levels of $PM_{2.5}$, definitions of the independent and dependent variables, and the research questions and hypotheses. Additionally, I address assumptions that will guide the study, the scope of the study and its limitations, and the study's significance.

Problem Statement

Breathing clean air is essential for optimal health. Inhaling polluted air can cause serious health conditions and can even lead to death. The long cold season in the Alaskan interior significantly reduces the quality of air, particularly in more populated areas such as in the towns of Fairbanks and North Pole, as opposed to outlying areas where many people, both wealthy and economically challenged live. In addition to more people contributing particulate matter to the air by burning wood, coal, and other substances for warmth, the climate, as well as the geography of the area, significantly influences the quality of air during the cold season.

The climate in the Fairbanks area during the cold season is cold, dry, and desert-like. Temperatures during the cold season typically don't rise above zero for months and can reach as low or lower than -40$_{o}$ F. Local rivers usually freeze in October and will usually support the weight of a person by October 27th. Rivers continue to remain frozen and are safe for travel by car, plane, dog sled, and other means, usually until about the first part of April. River ice break-up usually occurs early in May. Cold snaps can last from 1 to 3 weeks and are often accompanied by the formation of ice fog, causing low visibility and trapping fine particulates at the surface. Because daylight is limited from mid-fall throughout the winter, temperatures generally don't rise significantly during the day, further contributing to the problem (National Climate Data Center, n.d.).

Geographically, Fairbanks is located in the Alaskan interior at the confluence of the Tanana and Chena Rivers in the Tanana Valley. Both the city of Fairbanks and the town of North Pole are surrounded on three sides by hills reaching as high as 2,000 feet

above sea level (National Climate Data Center, n. d.). This geography causes severe temperature inversions during the cold season. These temperature inversions are very effective at trapping air particulates in the very cold air at breathing level during the cold season and further contribute significantly to the $PM_{2.5}$ levels during cold snaps. The more densely populated areas of downtown Fairbanks, and the town of North Pole in particular, experience the highest levels of cold season $PM_{2.5}$ spikes (area hot spots). $PM_{2.5}$ levels above the NAAQS of 35 micrograms/m_3/24 hours in these hot spot areas during the cold season are due primarily to the residential burning of wood and other biomass for heat (Huff, 2017). Gaining a better understanding of cancer incidences that may be influenced by frequent elevated $PM_{2.5}$ levels that are due to cold season biomass burning and its contributions to severe increases in $PM_{2.5}$ levels, together with $PM_{2.5}$ exposure due to summer wildfires, could contribute to understanding the impact of $PM_{2.5}$ exposure on all types of cancers. However, the major confounders to this study include tobacco smoking and the latency period between exposure and cancer diagnoses. These are addressed in the section presenting limitations to this study.

It is expected that consequent to having a better understanding of potential adverse health effects of breathing high levels of $PM_{2.5}$, and particularly $PM_{2.5}$ comprised primarily of wood smoke particulates, policies that regulate the residential burning of wood would be enhanced, voluntarily abided by residents, yet enforced if needed. Policy development, adherence to policy, and enforcement of policy, will most likely occur if the population is educated about the health dangers from breathing high levels of $PM_{2.5}$.

The findings of this study were able to contribute to the limited number of previously published studies that have considered to what extent inhaling high levels of $PM_{2.5}$ have on the incidence of cancers beyond lung cancers. The literature review in this section has illustrated how research is revealing similarities in the etiology of many adverse health effects from $PM_{2.5}$. However, to date, a significant gap remains in the effect of $PM_{2.5}$ on non-lung cancers, particularly in high latitude, cold climate areas such as the FNSB.

Purpose of Study

This study's purpose was to determine if there is a significant difference in the incidence of both lung cancer and all type cancer incidences in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in the FNSB areas that are non-hot spots.

Research Questions and Hypotheses

RQ1: Is there a significant difference in the incidence of all cancer types other than lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots?

$H_0$1: There is no significant difference in the incidence of all cancer types other than lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots.

H_a1: There is a significant difference in the incidence of all cancer types other than lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB that are non-hot spots.

RQ2: Is there a significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots?

$H_0$2: There is no significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots.

H_a2: There is a significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots.

RQ2 served as a validation study question because $PM_{2.5}$ is already recognized as a cause of lung cancer. (Huang, et al., 2017; Poirier, et al., 2017; Wei et al., 2017).

Theoretical Foundation of the Study

The theory on which this study was based was Bandura's social cognitive theory (SCT; 1986). The SCT began in the 1960s as the social learning theory. In 1986 it was developed into the current SCT. The primary concept of the SCT is reciprocal determinism in which there is a reciprocal and dynamic interaction between human cognition, the environment, and human behavior (in terms of a person's response to stimuli in order to achieve goals). The SCT takes into consideration many aspects of the social ecological model in addressing individual behavior changes (Bandura, 1986).

Application of the SCT continues to effect positive cultural changes globally as it addresses the influences on human agency, including self-motivation and individual cognition, which, in this case, is knowledge of the carcinogenesis of $PM_{2.5}$ and

consequent behavioral changes such as voluntary decrease or elimination of biomass burning. The interaction of human agency along with the influences of socioenvironmental factors can lead to significant positive individual and social changes. (Bandura, 2018). The SCT framework aligned well with this study because it addressed physical environmental factors over which people can choose to exercise control in order to improve the health of everyone in the community. Increased public knowledge of the negative impact of $PM_{2.5}$ on health in the FNSB could contribute significantly to decreasing cold season $PM_{2.5}$ emissions by residents.

The SCT has been widely used in public health research. A study by Heydari, Dashtgard, and Moghadam (2014) examined implementation of the SCT on research in patients with addictions who were referred to the addiction-quitting clinic at the Imam Reza Hospital. The results of the study revealed that patients in the experimental (test) group were significantly more successful than those in the control group in quitting their addiction, and that patients' self-efficacy scores in the experimental group were improved using the SCT approach.

Other theoretical frameworks that I considered included the social ecological model and the integrated behavioral model. The social ecological model is closely related to the SCT. However, the social ecological model is more appropriate for qualitative studies such as the study by Salihu, Wilson, King, Marty, & Whiteman (2015). They used this model as the framework to overcome challenges in attaining and maintaining high rates for recruitment of participants as well as high rates of retaining participants for their study of minorities and the effect of folic acid on fetal brain size in pregnant smokers.

The integrated behavioral model, which considers constructs from the theory of reasoned action and is also referred to as the theory of planned behavior, was also a possible theoretical basis for this study. However, this model considers a person's attitude toward perceived norms and the ultimate pressure on individuals as a major part of this theory. Theorists believe that a person's attitude comprises both cognitive and affective dimensions (Conner, Godin, Sheeran, & Germain 2013; French et al., 2005). The problem with this is that in the FNSB, perceived norms are deeply integrated into the culture, and it is therefore critical to educate the population about the adverse effects of $PM_{2.5}$ on their health before significant change can occur. This is one of the reasons that the SCT is a strong theoretical foundation for this study.

Nature of the Study

This research is a retrospective, quantitative study. I used quantitative data from secondary data sets for the study. A quantitative methodology was most appropriate to this research issue, allowing an examination of the relationship between breathing high levels of $PM_{2.5}$ as a potential causal factor for all cancer types. This type of methodology emphasizes objective statistical measurements using existing data.

Engaging community partners in this study was critical. The Cancer Center at Fairbanks Memorial Hospital (FMH) has provided support through the provision of data from the tumor registry through the FMH Cancer Center. Data from cancer subjects were de-identified by FMH prior to my receiving the data. Additionally, only the zip codes that could accurately be used for the geographical distribution of subjects and for the determination of area hot spots in which $PM_{2.5}$ spikes significantly during the cold season

were used for this study. The Alaska Department of Environmental Conservation's Division of Air Quality provided $PM_{2.5}$ data for the study. Data came from three EPA-approved air monitors. Two of the monitors are located in downtown Fairbanks and one is located in North Pole. Two local organizations, Citizens for Clean Air Fairbanks and the Fairbanks Climate Action Coalition were also valuable resources for providing a historical, political, and cultural perspective to the air pollution issue in the FNSB.

The dependent variable was incidence of all cancer types other than lung cancers. Using all cancer types (collectively) rather than individual cancer types provided for a more than adequate number of subjects for the study. Because the primary focus of this study was to consider the extent to which exposure to high levels of $PM_{2.5}$ influences all-type cancer incidences in the FNSB area, and the population in this area is relatively small at slightly less than 100,000 (U.S. Census Bureau, 2017), I did not break down data into specific types of cancers beyond lung cancer. The independent variable for this study was the FNSB $PM_{2.5}$ levels, which included both the cold season $PM_{2.5}$ levels (> 35micrograms/m^3/24 hours during the months November through March in area Zip Codes that represent hot spots and are areas with significantly increased cold season $PM_{2.5}$ levels), along with area Zip Codes that are outside of the hot spot Zip Codes (non-hot spot areas) in which the $PM_{2.5}$ levels are generally less than the 35 micrograms/m^3/24 hours. The non-$PM_{2.5}$ hot spots were used as controls. In addition, it must be noted that non cold-season $PM_{2.5}$ levels are generally due to wildfires in and around the FNSB and also are expected to influence this study. However, wildfires in the FNSB are varied in

geographical locations, so therefore, the inclusion of specific wildfires and their potential effects on $PM_{2.5}$ levels in various Zip Codes was not included in this study.

In order to prevent a spurious conclusion about the association between exposure to high levels of $PM_{2.5}$ and cancers, controlling for the effects of confounders is the most ideal approach for quality research. A major confounder in this study was tobacco smoking. However, the dataset provided by the FMH Tumor Registrar only would have been able to provide about a two- year period of smoking data for cancer patients within the 10 year time frame of this study (this data was collected for a previous study). Because this limited data is only about 20% of the total number of study participants, I was unable to control for smoking as a potential confounder. Another confounder that I considered in this study was the latency/lag time period that exists between exposure and the onset of symptoms of various cancers. The latency/lag period is the time period between exposure to the presumed cancer-causing agent and the first signs or symptoms of the particular type of cancer. Latency periods are also generally related to the age of patients. For example, Nadler and Zurbenko (2014), reported that for acute lymphocytic leukemia, which is much more common in young people, the time from onset to diagnosis is 35.7 years with a median age at cancer onset of 8.3 years. However, for chronic lymphocytic leukemia, which is almost exclusively a cancer type occurring in older and elderly people, the time from onset to diagnosis is 2.2 years with a median age at cancer onset of 67.8 years. While age is an important confounder for cancer research, it was beyond the scope of this study to control for age associated with each individual type of cancer reported.

Data from subjects were not identified beyond the subject's residential Zip Code, each subject's specific type of cancer upon initial diagnosis, and the year of diagnosis (which was included to confirm that this study only recognized data between January 1, 2008, and December 31, 2017). Accessibility to the data was established by the FMH Cancer Center Committee. The stipulation was that before I have access to the patient data, I receive necessary Institutional Review Board (IRB) approval from Walden University, and that once my study is completed, that I give a presentation with the results from this study to the FMH Cancer Committee. IRB approval from Walden University was granted on 3/9/2020. The IRB approval number for this study was 03-09-20-0621354

Literature Review

Introduction

It is important to recognize that knowledge of the adverse health effects of breathing high levels of $PM_{2.5}$ is evolving. This literature review will confirm that studies have proven a link between inhaling high levels of $PM_{2.5}$ to lung cancer. Other studies linking breast cancer to $PM_{2.5}$ exposure have also been reported (Andersen et al., 2017; Parikh & Wei, 2016; Wong et al., 2016). In addition, there have been few studies that suggested the possible link between $PM_{2.5}$ and other non-lung cancers beyond breast cancer (Andersen et al., 2018; Wong et al., 2016; Yeh et al., 2017). However there has yet to be a study linking non-lung cancers to high $PM_{2.5}$ levels in a high latitude community that repetitively experiences extreme cold during a long cold season and where the burning of wood is a common source of heat. Thus, this literature review

included studies that have specifically linked wood smoke as the primary source of $PM_{2.5}$ to cancers as well as other adverse outcomes in human health.

Wood smoke emits particularly hazardous $PM_{2.5}$, including carcinogens that are carried on the $PM_{2.5}$, and it is increasingly suspect in significantly contributing to adverse health effects, including cancers. The specific carcinogens that have been identified on $PM_{2.5}$ include the following: hydrocarbons (PAHs, benzene, styrene, 1, 3 butadiene); oxygenated organics (aldehydes such as formaldehyde and acrolein, and phenols), and other possibly carcinogenic agents such as quinones and semiquinones (Loomis et al., 2013). Because high levels of $PM_{2.5}$ become trapped at breathing level during severe temperature inversions that occur during the cold season, the particulates and the toxins that they carry pose a serious health threat (Krapf et al., 2017; Marabini et al., 2017; Montes de Oca et al., 2017; Oudin, Segersson, Adolfsson & Forsberg, 2018; Weichenthal et al., 2017). Fine particulates emitted from wood smoke also pose a particular threat to the unborn and to children (Lai et al. 2017; Rodriguez-Villamizar, Magico, Osornio-Vargas & Rowe, 2015). The residential burning of wood in the FNSB area is a common practice and is estimated to contribute to between 60%-90% of the $PM_{2.5}$ spikes in the FNSB area during the cold season (Huff, 2017). $PM_{2.5}$, which is primarily due to wood smoke, carries a number of known carcinogens, and $PM_{2.5}$ from summer wildfires also poses a serious health concern in the FNSB.

The major health conditions addressed in this literature review included the following: lung cancer, cancer types other than lung cancer, adverse cardiovascular events, adverse respiratory events other than lung cancer in adults and children, adverse

cerebrovascular events, and adverse outcomes for the fetus and during pregnancy. It is important to introduce all potential adverse physiological effects of $PM_{2.5}$ because many of the mechanisms of harm have common characteristics to cancer. Fine particulates have the ability to induce reactive oxygen species mediated oxidative stress within cells, which can alter intracellular proteins and lipids, altering cellular permeability. Reactive oxygen species is also involved in signaling pathways that regulate gene expression of substances that are related to inflammation, apoptosis, and fibrosis (Cachon et al., 2014). Fine particulates also contain PAHs and metals that can induce oxidative stress and are considered to be strong carcinogenic and mutagenic agents that may increase cancer frequency in humans (Falcon-Rodriguez, Osornio-Vargas, Sada-Ovalle, Segura-Medina, 2016). A brief history of $PM_{2.5}$ and its effects on disease is also presented in the literature review.

Because a quality literature review should provide evidence of research into other adverse health effects from exposure to $PM_{2.5}$ resulting from mechanisms similar to those that initiate cancer, as previously explained, in this section I also review select studies that have confirmed the serious cardiovascular, cerebrovascular, and respiratory effects of inhaling high levels of ambient $PM_{2.5}$. It is important to illustrate that $PM_{2.5}$ induces similar physiological and immunological mechanisms that occur in triggering cancers as well as other adverse effects on the cardiovascular system (particularly the heart endothelium and arterial inflammation), the brain, the respiratory system, and other systems of the body, predominantly with regard to inflammation (Li, Zhou, & Zhang, 2018; Lin et al., 2016).

Literature Search Strategy

For this literature review, a number of databases were used in the discovery of articles pertinent to the topic. They included Medline Plus, CINHAL, Pubmed, Semantic Scholar, Google Scholar, and Directory of Open Access Journals.

The strategy for literature discovery included searching for peer-reviewed articles published less than seven years previous with the exception of articles providing an historical perspective on the $PM_{2.5}$ issue as it relates to disease and those studies cited in more recent articles used for this research. Select articles must address one or more of the following: impact of $PM_{2.5}$ on human health; sources of $PM_{2.5}$ with an emphasis on cold season, high latitude air pollution; wood smoke fine particulates and their components; and the various major health conditions that can result in increased morbidity and premature mortality in the population, with an emphasis on cancer. Articles must be published in English by the original author(s) or translated into English.

Medical Subjects Headings (MeSH) terms used for the literature review included the following: ambient $PM_{2.5}$; cold season $PM_{2.5;}$ cold season air pollution; wood smoke; ambient air fine particulates; $PM_{2.5}$ and cancer, $PM_{2.5}$ and lung cancer, cardiovascular diseases, cerebrovascular diseases, respiratory conditions, and adverse pregnancy and fetal outcomes; $PM_{2.5}$ and children; $PM_{2.5}$ mortality and morbidity rates; EPA.

History of Air Particulate Matter

Air particulate matter was first observed experimentally, in the early18th century (Ramazzini & Porzio, 1703). Ramazzini and Porzio observed air particulates with the use of a primitive optical microscope and were able to relate particle counts to a number of

different respiratory conditions in people from 52 different occupations. However, it was not until 1963 that the Clean Air Act enabled the establishment of standards for environmental air pollution control in the United States. In 1970, the Clean Air Act Extension allowed for the creation of the EPA and directed the EPA to launch the NAAQS. The indicator for particulate matter at that time was total suspended particulates. In 1977 another Clean Air Act Amendment mandated that the EPA review and make necessary revisions to the NAAQS every 5 years based on the most recent scientific evidence. In 1987, the total suspended particulates was replaced with an indicator that took into account air particle's aerodynamic equivalent diameter less than or equal to 10 microns (PM_{10}). In 1997 another indicator for NAAQS was incorporated to account for particulate matter with an aerodynamic equivalent diameter less than or equal to 2.5 microns ($PM_{2.5}$; EPA, n.d.).

An important historical example of the dramatic effects of severe air pollution is from 1952. While air pollution in urban environments had long been considered a public health threat, the dense smog covering London in December, 1952, brought heightened awareness globally to the consequences of breathing air that was extremely thick with particulates due primarily to coal burning. The serious air pollution event lasted 5 days and mortalities from this ambient air disaster ended up being close to 12,000 people (Bell & Davis, 2001). Studies from this naturally occurring event continue today. For example, Bharadwaj, Zivin, Mullins, and Neidell (2016) studied the long-term effects of exposure to high levels of air pollution early in life with an emphasis of the development of asthma later in life.

$PM_{2.5}$ and Effects on Lung Cancers

Lung cancer is known to be the world-wide leading cause of deaths from cancers in men and women (Horn, Pao, & Johnson, 2012) and in 2012 alone was responsible for approximately 1.59 million deaths worldwide (International Agency for Research on Cancer, 2012). While inhalation of tobacco smoke is the leading cause of lung cancer, inhalation of particulates from the incomplete combustion of wood or coal also induces lung cancer (Reid et al. 2012).

It has been established from numerous studies that inhaling high levels of $PM_{2.5}$ is a risk factor for lung cancer. In 2013, WHO's International Agency for Research on Cancer classified $PM_{2.5}$ in air pollution as a group 1 lung carcinogen. A study by Harrison et al., (2004) looked at data from the American Cancer Society (ACS) study that compared $PM_{2.5}$ levels containing several known chemical carcinogens with lung cancer incidence between 1979 and 1983 and between 1999 and 2000 and found a positive correlation between $PM_{2.5}$ levels and lung cancer. This was one of the earlier studies linking $PM_{2.5}$ to cancer, but only to lung cancer. Further studies on the effects of $PM_{2.5}$ on lung cancer incidence successfully built on this and other early studies on the topic.

Huang et al. (2017) conducted a meta-analysis that found a relationship between $PM_{2.5}$ exposure and incidence of lung cancer and lung cancer mortality. There were 17 studies meeting the author's criteria for inclusion in the analysis. An interesting aspect to the findings from this study was regarding lung cancer mortalities in developing countries compared to developed countries. Mortality estimates in developed countries was 1.14 (95%CI: 1.06, 1.23) compared to developing countries (1.03 [95%CI: 1.00, 1.07]).

However lung cancer incidences that were associated with $PM_{2.5}$ exposure were highest in Asia (1.09 [95% CI: 1.03, 1.15]), compared to North America (1.06 [95% CI: 1.01, 1.11]), and then Europe (1.03 [95% CI: 0.61, 1.75]). Other studies suggest that lung cancer mortalities associated with $PM_{2.5}$ are lower in developed countries compared to lung cancer mortality levels in developing countries. (Huang et al., 2017).

Fu et al. (2015) explored the relationship between $PM_{2.5}$ and lung cancer mortalities in China using a geographical weighted regression model. They compared the number of cancer mortalities based on long-term exposure to fine particulates. They compared the number of deaths from lung cancer, according to both the WHO air quality guidelines and the ACS. The WHO air quality guidelines found that over a 3 to 4 year period there were between 531,036 and 532,004 deaths from lung cancer associated with $PM_{2.5}$. The ACS found that the number of $PM_{2.5}$ related lung cancer deaths was 614,860. This study concluded that there is a positive relationship between $PM_{2.5}$ and lung cancer mortalities in China. This study however only considered long-term exposure. While this research contributed to the limited studies published on the impact of $PM_{2.5}$ exposure over a 3 to 4 year period and lung cancer deaths in China, the authors were only able to estimate lung cancer mortality rates from the data. Therefore, it should be noted that this could lead to bias when interpreting the relationship between lung cancer mortalities and exposure to high levels of $PM_{2.5}$ over a long term.

It is estimated that there are over 400,000 premature deaths each year in the European Union due to $PM_{2.5}$ exposure, with Poland having the greatest concentration of $PM_{2.5}$ among all countries in the EU. A study between 2007-2011 found that Poland had

unusually high death rates due to lung cancer and cardiopulmonary diseases, both attributable to elevated $PM_{2.5}$ in eleven of Poland's largest cities (Badyda, Grellier, & Dabrowiecki, 2017).

The effect of biomass smoke on health has been reported in a number of studies reviewed by Rajendra, Shukla, Gautam, Hansbro, and O'Toole (2018). For example, for lung cancer, a meta-analysis considering 28 epidemiological investigations found that there is a much greater risk of developing lung cancer in women (OR 1.81, 95% CI, 1.54-2.2; p = .034) compared to men (OR 1.16 95% CI 0.79-1.69). The conclusion was that this is likely due to women having smaller lung sizes than men, so women's exposure to the same level of $PM_{2.5}$ would have a greater impact than it would in men, and that women might have been exposed to the smoke for greater periods of time.

PAHs have been observed to be released when biomass fuel is incompletely combusted. PAHs can cause the formation of active carcinogens such as radical cations, diol-epoxides, and *o*-quinones, which ultimately result in mutations in DNA, tumorigenesis, and gene expression alterations. PAHs can also alter tumor-suppressor genes such as $_{p}53$. PAHs have been shown to increase the susceptibility to developing cancer in all age groups, ethnicities, and genders. Consequently, PAHs are considered important carcinogens found in biomass smoke and inhaling PAHs is known to increase lung cancer risk (Eom et al., 2013; Osgood et al., 2013; Tsay et al., 2013).

Wei et al. (2017) sought to explain the role that $PM_{2.5}$ plays in lung cancer etiology. They described the carcinogenic means of $PM_{2.5}$ by considering properties of cancer stem cells and epithelial-mesenchymal cells in non-small cell lung cancer cells.

They found that $PM_{2.5}$ exposure, both acute and chronic, increased the migration and invasion of cancer cells. The study also implicated microRNAs as potential biomarkers for predicting the carcinogenicity of $PM_{2.5}$.

Hystad, Demers, Johnson, Carpiano, and Brauer (2013), considered $PM_{2.5}$ exposure over a 3 year period and found that lung cancer incidence, for each 10 microgram/m_3 increase in $PM_{2.5}$ concentration in ambient air, the odds ratio was 1.29 (CI, 95% [0.95-1.76]). They also included covariates such as smoking in their model. Additionally, the study by Turner, Krewski, Pope, Chen, Gapstur, and Thun (2011) that showed that lung cancer mortality risk increases by 8% for every 10 microgram/m_3 increase in the concentration of $PM_{2.5}$. This association was much stronger amongst people who had never smoked (never smokers). In never smokers lung cancer mortality risk increased by 15%-27% for each 10 microgram/m_3 increase in exposure to $PM_{2.5}$.

Li et al. (2018), illustrate a number of epidemiological studies that illustrate the pathogenesis of chronic inflammatory diseases of the respiratory system, as well as lung cancer, when exposed to high levels of $PM_{2.5}$. There are many diseases that contribute to early mortalities from exposure to $PM_{2.5}$, including strokes (40.3%), ischemic heart disease (26.8%), lung cancer (23.9%), and chronic obstructive pulmonary disease (COPD; 18.7%; Song et al., 2017).

There are a number of physiological mechanisms that are common to all of these diseases. $PM_{2.5}$ has the capability of using micro RNAs to activate oncogenes, which can lead to lung cancer. Micro RNAs are tiny non-coding RNA strands that help to regulate post-transcription gene expression (Fabian, et al., 2010). Li et al. (2018), point out

however, that just how lung cancer is induced, following the introduction of $PM_{2.5}$ into cells is not yet clear, although there are other studies into the specific role of micro RNAs in inducing cancer. p53 is a gene that regulates cell growth and proliferation, damage repair, and cell apoptosis. $PM_{2.5}$ can cause mutations in p53 that can lead to non-small cell lung cancer (Deben et al., 2017). $PM_{2.5}$ can also increase the release of immunological cytokines and cells associated with inflammation. Inflammatory cytokines are linked to inflammatory diseases of the respiratory system as well as the proliferation of lung tumor cells (Vendramini-Costa, & Carvalho, 2012). When $PM_{2.5}$ stimulates inflammation, it also causes oxidative stress responses that are linked to a number of respiratory diseases, including COPD, as well as lung cancer (Rahman & Adcock, 2006).

Cao, Rui, and Liang (2018) studied the relationship between ambient $PM_{2.5}$ and lung cancer in China based on a geographical model. They studied the number of lung cancer deaths over a 5 year period from 2004-2008 in all provinces in China. They found a statistically significant relationship between ambient $PM_{2.5}$ levels and lung cancer mortality ($r = 0.0052$, $p = 0.036$). In addition, lung cancer morbidities increased with increasingly longer $PM_{2.5}$ exposure times. The study also showed that lung cancer mortalities rose by 13.73% over the 5-year period. In 2004, the average $PM_{2.5}$ concentration was 37.48 micrograms/m_3 and mortality rates from lung cancer were 0.27/million. In 2008 the average $PM_{2.5}$ was 41.36 micrograms/m_3 and mortality rates from lung cancer were 0.53/million, indicating a rising trend in rates of lung cancer mortalities in China. The study concluded that in 2004, $PM_{2.5}$ was responsible for 23.23%

of lung cancer deaths, and in 2008, $PM_{2.5}$ was responsible for 26.42% of deaths due to lung cancer in China.

The studies that are summarized above indicate that exposure to increased levels of $PM_{2.5}$ can be definitively linked to lung cancer. However, the question remains whether or not exposure to higher levels of $PM_{2.5}$ can be linked to cancers other than lung cancer.

$PM_{2.5}$ and Cancer Types Other Than Lung Cancer

There have been relatively few studies on the relationship between exposure to high levels of $PM_{2.5}$ and cancers other than lung cancers. Turner et al. (2017) conducted a large prospective study using data from the Cancer Prevention Study II (CPS-II) to determine whether there is an association between ambient fine particulate air pollution and deaths due to non-lung cancers in general. Over 600,000 U.S. adults participated in the study. The participants were followed from 1982-2004. The CPS-II team studied cancer mortalities from 29 sites where participants had long-term exposure where they lived, to $PM_{2.5}$, ozone (O_3), and nitrogen dioxide (NO_2). There were over 43,000 deaths from non-lung cancers. Ambient $PM_{2.5}$ was associated with deaths due to bladder and kidney cancer. For each 4.4 microgram/m_3 increase in $PM_{2.5}$ there was a 13% increase in bladder cancer and a 14% increase in kidney cancer. Colorectal cancer mortalities were associated with NO_2 exposure. Mortalities from other types of non-lung cancers were not statistically significant in this study. The authors concluded that ambient fine particulate air pollution was not associated with mortalities from the majority of non-lung cancers, but that there needs to be further studies to investigate a possible association between air

pollution due to $PM_{2.5}$ and colorectal, bladder, and kidney cancer mortalities. Again, my study seeks to contribute to the impact of $PM_{2.5}$ on cancers other than lung cancers, and to contribute to this area of research that is lacking knowledge on this important subject.

In one of the few studies published on the relationship between $PM_{2.5}$ and its link to cancers beyond lung cancer, Wong et al. (2016), found strong associations between $PM_{2.5}$ and the upper gastrointestinal tract, and digestive accessory organs, as well as hematopoietic and lymphatic organs and the breast. The authors looked at the long-term effects of $PM_{2.5}$ exposure on all type cancers in 66,820 Hong Kong residents who were enrolled in the study from 1998-2001, and followed up for mortality outcomes due to all type cancers until 2011. They used satellite data and fixed-site monitors with sampler inlets that met the electronic code of federal regulations (e-CFR) for neighborhood special scale $PM_{2.5}$ sites. For those sites the sampler inlet probe or at minimum 80% of the monitoring path is required to be positioned between 2 and 15 meters above ground to meet vertical location standards. For microscale $PM_{2.5}$ sites, the inlets must be between 2 and 7 meters above ground for vertical location standards. For horizontal locations, if either the inlet probe or a significant part of the monitoring pathway is near a wall, such as the side of a building, it must be on the windward side, relative to the direction of the prevailing winds during the season in which the potential for highest concentration of $PM_{2.5}$ occurs (Cornell Law School, n. d.; EPA, 2008). In this study, the Cox regression model was used to determine the HR of cancer mortality for each 10 microgram/m^3 increase in $PM_{2.5}$. $PM_{2.5}$ was linked to an increase in risk of mortality for all cancers (HR 1.22[95% CI: 1.11, 1.34]); for upper digestive tract cancers (1.42 [95% CI: 1.06, 1.89]),

for accessory organs of the digestive tract in male participants (1.135 [95% CI: 1.06, 1.71]), for female breast cancer (1.80 [95% CI: 1.26, 2.55]); and for lung cancer in males (1.36 [95% CI: 1.05, 1.77]). This study illustrates the increased risk of cancers other than lung due to $PM_{2.5}$ exposure and further substantiates the need for my study in the FNSB region of the impact of $PM_{2.5}$ on all type cancers.

Parikh and Wei (2016) examined the relationship between both $PM_{2.5}$ and PAHs and incidence of breast cancer in women living in rural versus metro Georgia (Atlanta). They used data from the EPA, the End Results Program, and epidemiological and surveillance studies to determine whether $PM_{2.5}$ and PAHs increased breast cancer in women and if there was a difference in the city versus the rural areas. Both $PM_{2.5}$ and PAHs increased breast cancer incidence in all women, but in Atlanta there was a considerably higher incidence in breast cancer compared to rural areas in Georgia (132.6 vs 113.7 per 100,000) respectively, from 1992-2011. In metro Atlanta, breast cancers associated with $PM_{2.5}$ emissions were (adjusted *beta* = 2.964 [95% CI: 0.468, 5.459] p = 0.023), and for emissions of PAHs (adjusted *beta* = 0.568 [95% CI: 0.209, 0.927] p = 0.004). They concluded that living in particular metro areas have an impact on breast cancer incidence in women due to $PM_{2.5}$ and PAHs exposure. The results also indicate that $PM_{2.5}$ exposure poses more of a threat to developing breast cancer than exposure to PAHs. This particular study is significant to my proposed study because the $PM_{2.5}$ hot spots are located in the urban-like areas of the FNSB. The outlying areas/zip codes (non-hot spots) are all rural. Therefore, the probability of seeing an increase in breast cancers

in residents living in the FNSB hot spots is likely greater than the probability of seeing an increase in breast cancer in residents living in the FNSB non-hot spot areas.

A study by Yeh et al. (2017) found a relationship between air pollution and bladder cancer in males living in the north of Taiwan, and women living in the majority of townships in Taiwan. According to the authors, this was the first evidence-based study that linked $PM_{2.5}$ exposure to bladder cancer. The study was based on data that was obtained from a geographically available 13-year mortality rate in Taiwan, due to bladder cancer linked to $PM_{2.5}$ air pollution. There has been intensive regulatory attention in $PM_{2.5}$ in Taiwan since 2000. The mortality rate for bladder cancer in males slowly declined from 3.66 to 3.01 per 100,000 between 2000 and 2012. In females the mortality rate for bladder cancer decreased from 1.69 to 1.49 per 100,000 between 2000 and 2012. Reductions such as these are examples of what may occur following the research that I am proposing in the FNSB region. This study illustrates how intensive regulation can lower cancer incidents due to $PM_{2.5}$ exposure, with the ultimate goal being to reduce mortalities and morbidities related to exposure to high levels of $PM_{2.5}$ in those areas of the world where this is of great concern.

The possibility that pancreatic cancer might be associated with fine particulate matter in high concentrations in ambient air, was addressed by Wang et al. (2018), in a study that was conducted using data from a China database from 1991-2009, as part of the National Disease Surveillance Point System. In this study the relative risks of death from pancreatic cancer due to a 10 microgram/m_3 increase in $PM_{2.5}$ were 1.16 (95% CI: 1.13, 1.20) for the entire population, 1.21 (1.17, 1.25) for ages 65-84, 1.08 (1.05, 1.13)

for ages 40-64, 1.19 (1.14, 1.24) for females, 1.14 (1.10, 1.18) for males, 1.29 (1.22, 1.37) for the rural population, and 1.23 (1.16, 1.30) for the urban population. The authors were able to conclude from this study that ambient $PM_{2.5}$ pollution has the potential to increase the risk of death from pancreatic cancer due to exposure to $PM_{2.5}$. The results of this study further highlight how ubiquitous the threat of developing cancer from $PM_{2.5}$ exposure is. Therefore, control of $PM_{2.5}$ pollution is most imperative, as is the need for further studies on the effects of exposure to high levels of $PM_{2.5}$ on all non-lung cancers.

My study provided additional knowledge in the evolving research on $PM_{2.5}$ exposure and incidents of cancers other than lung cancers, and was able to contribute to existing (yet weak) public education programs regarding this threat to the health of Fairbanks residents and visitors.

$PM_{2.5}$ and Adverse Respiratory Events Other Than Lung Cancer

Adverse respiratory events primarily seen in adults. Adverse respiratory events in susceptible individuals are generally expected when breathing polluted air. However, polluted air, particularly air that is high in $PM_{2.5}$, is increasingly being recognized as contributing to a number of different respiratory conditions such as asthma (Nachman & Parker, 2012), and COPD, and pneumonia (Pun et al., 2017). Additionally, when the primary source of $PM_{2.5}$ is from the burning of biomass, such as wood and animal dung, risk of adverse respiratory conditions, including COPD, are significantly higher than when fine particulates come from combustion of other sources such as gasoline and diesel. For example, a study conducted by da Silva, Saldiva, Saldiva, and Dolhnikoff (2012), there was an increase in the odds ratio (OR) for dyspnea, wheezing,

and cough in adults exposed to outdoor biomass (OR= 1.80, 1.78, 1.78, respectively) compared to gasoline exposure.

According to the WHO (2018), there are nearly 4 million premature deaths globally, due to health issues and illnesses that develop from exposure to residential biomass smoke. It is estimated that about 55% of those deaths are due to diseases of the respiratory system, which include lung cancer, COPD, and pneumonia. Tobacco Smoking is a well-established risk factor for developing serious lung diseases. Globally, there are about 1.1 billion tobacco smokers, however close to 3 billion individuals are exposed to smoke from biomass combustion. In epidemiological research conducted in Europe, Asia, Africa, and South America, it has been consistently demonstrated that exposure to smoke from biomass combustion is associated with serious lung diseases, even after tobacco smoking, as a confounder, has been controlled in the studies (Rajendra et al., 2018).

Pun et al. (2017) considered cardiovascular and respiratory events, and cancer in older adults in the United States due to exposure to $PM_{2.5}$. This was a very large study of the Medicare population with a cohort of 18.9 million. Between 2000 and 2008 there were 4.2 million fatalities in the contiguous United States associated with $PM_{2.5}$ exposure. The study revealed that there were statistically significant positive associations of PM2.5 respiratory conditions, COPD, and pneumonia deaths associated with $PM_{2.5}$ exposures per 10 microgram/m3 increases, with the risk ratios varying between 1.10 to 1.24. They also found that lung cancer and cardiovascular mortality increases with longer $PM_{2.5}$ exposure. A 60 month moving average of exposure to $PM_{2.5}$ had a relative risk (risk ratio) of 1.33 for lung cancer (95% CI: 1.24, 1.40), compared to a relative risk of

1.13 (95%CI: 1.11, 1.15) for a 12 month moving average of exposure to $PM_{2.5}$. While this study provides evidence that long-term exposure to $PM_{2.5}$ can significantly increase mortalities from lung cancer, cardiovascular disease, and respiratory disease in patients 65 years of age and older, it is not conclusive with regard to lung cancer mortalities. This is due to a number of European and United States cohort studies in which null associations between $PM_{2.5}$ and lung cancer, have been described (Carey et al., 2013; Cesaroni et al., 2013; Lipsett et al., 2011).

In a meta-analysis conducted by Hu, Zhou, Tian, Yao, Li, Li, … and Ran (2010), a strong association was found between exposure to biomass smoke and development of COPD, compared to those who were unexposed to biomass smoke. Their study revealed that individuals who are exposed to smoke particulates from biomass have an OR of 2.44 (CI: 1.9-3.33) for developing COPD, relative to individuals unexposed to biomass smoke.

A study conducted by Krall et al. (2017) considered emergency room admissions to determine associations between specific sources of $PM_{2.5}$, such as wood smoke, vehicle gasoline, vehicle diesel, coal, metals, and dust, and respiratory disease in four cities in the United States. Coal and metal sources varied significantly across the four cities. They concluded that $PM_{2.5}$ from gasoline and diesel combustion had less impact on health than did $PM_{2.5}$ burning of biomass, and there was also limited evidence that dust, as a source of $PM_{2.5}$, was associated with respiratory disease. However, the study made clear that biomass burning such as wood was most intensely associated with diseases of the respiratory system and was associated with increases in emergency room visits. This

research may contribute significantly to understanding potential dangers of $PM_{2.5}$ coming from the burning of wood.

Xing et al. (2016) conducted a study focusing on the epidemiological and experimental evidence of the impact that $PM_{2.5}$ has on the respiratory system, looking at evidence from areas around the world. They summarized the established mechanisms of how $PM_{2.5}$ causes damage to lung tissue, confirming the results from multiple studies previously discussed in this literature review. They illustrated how fine particulates are linked to a wide variety of lung conditions including asthma, multiple cardiopulmonary abnormalities, lung cancer, pneumonia, and others. Finally, their detailed guidelines to limit ones exposure to high levels of $PM_{2.5}$ during serious smog alerts, provide both scientists and the lay community, practical ways to protect their own health as well as those populations at greater risk.

Using cell culture models from donors, Krapf et al. (2017) were able to illustrate the adverse impact on respiratory tract epithelium that combustion of different types of wood can cause. The cell models were clearly differentiated as normal human epithelium from bronchi, and epithelium from diseased bronchi such as those with asthma and cystic fibrosis. They looked at both atmospherically aged wood, and primary wood sources in hopes of identifying significant chemical fractions in the different particulates. Cell death and inflammatory processes were significantly increased in all cell models except for the asthma models. The authors were unable to identify a particular chemical fraction from the particles as a primary cause, but both the aged and primary wood sources caused bronchial epithelial cell disease.

Another study that considered the exposure to $PM_{2.5}$ due to both wood smoke and traffic pollution in residents living in Vancouver, Canada over a 5 year period (*n*=467,994) and who did not exhibit a baseline COPD, found that both exposure to wood smoke and traffic pollution causes an increased risk of developing COPD. However the authors of the study found that wood smoke $PM_{2.5}$ exposure more than doubled the number of hospitalizations due to COPD than did traffic-related $PM_{2.5}$ exposure (CI: 95%). There was a 15% (2-29%) increase in hospitalizations due to COPD attributed to pollution from woodsmoke compared to a 6% (2-10%) increase in traffic carbon emissions (Gan, FitzGerald, Carlsten, Sadatsafavi & Brauer, 2013).

Adverse respiratory events other than lung cancer seen primarily in children. Asthma in children has long been a concern, but the underlying cause is not yet fully understood. Using emergency room visits as a way to determine the extent of acute exposure to high levels of ambient $PM_{2.5}$, a study conducted by Fan, Li, Fan, Bai and Yang (2016), was able to conclusively determine that such exposure significantly increases emergency room visits due to acute asthma symptoms. The study concluded that children are at a higher risk than adults for such emergencies. Children showed an increased risk of emergency room visits at 3.6%/10 microgram/m_3 increase in $PM_{2.5}$ air concentrations (95% CI 1.8, 5.3%) where the adult population showed an increased risk of 1.7%/10 microgram/m_3 increase in $PM_{2.5}$ (95% CI 0.5, 6.9%).

A Canadian study by Rodriguez-Villamizar et al. (2015) on the impact that ambient air pollution has on the health of children, considered twenty seven heterogeneous studies with regard to air pollution exposure (particularly $PM_{2.5}$),

population, study design, and respiratory consequences. They evaluated epidemiological research between 2004 and 2014 and found that children are exceptionally susceptible to disease when exposed to air pollution, because their immune systems are immature and there is significant potential for developmental disturbances. Children also exhibit a higher volume of air exchange in relation to their body mass index as compared to adults.

Bateson and Schwartz (2008) also considered the effects of air particulates on children. Since lungs in children of all ages are still developing, air pollution has the potential to cause serious respiratory harm. Furthermore, children, inhale relatively more air pollutants than do adults. This is because of their smaller size, their minute volume of respiration (pulse/minute X tidal volume) per body weight unit is higher than adults, as is their basal metabolic rate. Furthermore, people in the United States tend to spend more time indoors compared to people in other countries (Klepeis et al., 2001). Consequently, the level of indoor air pollution and its components, particularly pollution due to indoor cooking using wood as fuel, is an increasing concern, particularly for the respiratory health of children. It is estimated that more than 3 million U.S. children live in homes that use wood stoves as a primary means of heating (Noonan, Ward, & Semmens, 2015).

Burning wood emits significant amounts of harmful $PM_{2.5}$. Using wood stoves results in incomplete combustion of firewood, yielding smoke particulate emissions that are heterogeneous, consisting of significant amounts of $PM_{2.5}$, with organic compounds and elemental carbon such as PAHs, organic carbon, inorganic materials such as salts, and acids, all of which condense on the surface of the fine particulates, and since these particulates go deep into the alveoli and cross into the blood, they are particularly

harmful (Badyda et al., 2017). $PM_{2.5}$ emissions increase when burning moist wood, when burning wood in unregulated and poorly functioning stove, and when burning certain types of wood (EPA, 2013). The more incomplete the combustion of the wood when burning, the more $PM_{2.5}$ is emitted, and the more harm it can cause to human health. Ambient pollution from wood smoke in developed countries poses a significantly greater threat to childhood health than in-home wood smoke. This is based on the fact that correctly installed modern wood stoves that properly vent to the outside can significantly decrease in-home exposure to $PM_{2.5}$. (EPA, 2013). Ward et al. (2012) found that up to 80% of wintertime ambient $PM_{2.5}$ in Fairbanks, Alaska comes from residential burning of wood.

The above studies reflect the broad range of respiratory conditions that can be caused by or exacerbated by increased $PM_{2.5}$ exposure. This information, together with increased knowledge of how $PM_{2.5}$ affects other systems and potentially all types of cancer, is expected to significantly contribute to the efforts to decrease $PM_{2.5}$ exposure in the FNSB region.

$PM_{2.5}$ and Cardiovascular Events

Many studies have indicated that the heart may be susceptible to the adverse influences of $PM_{2.5}$ and the toxic effects of exposure to $PM_{2.5}$. For example, Du et al. (2016) explain the two established pathways, direct and indirect, that link fine particulates to CVD. In the direct pathway, $PM_{2.5}$ crosses from the alveoli directly into lung capillaries and are carried to target organs such as the heart. The presence of $PM_{2.5}$ in the vascular system damages endothelium directly, through aggravation of localized

inflammation and oxidative stress. This can intensify plaque instability. Fine particulates have also been shown to have cardiotoxic effects, which can directly impact heart performance. The indirect pathways include cascading pulmonary inflammation and oxidative stress, which increases pro-inflammatory cytokines, which are linked to increased blood coagulation, further disrupting endothelial function. This contributes to atherosclerosis, arrhythmias, and myocardial damage. Additionally, particulates have been linked to altered autonomic balance, in favor of an increase in sympathetic tone. This increases adverse cardiovascular events by inducing vasoconstriction and hypertension.

With the link between CVD and $PM_{2.5}$ established, being able to identify individuals who are more at risk for CVD from long or short term exposure to $PM_{2.5}$ could benefit higher risk individuals by alerting them to their increased susceptibility to the adverse cardiovascular effects from $PM_{2.5}$. Since there have been no recent studies that considered the relationship between $PM_{2.5}$ and inflammatory biomarkers for the risk of CVD, Dabass et al. (2015) examined this relationship in a large population of adults, using the National Health and Nutrition Examination Survey from the 2001-2008 cycle. They linked data on air pollution in the contiguous United States with participant's addresses from the National Health and Nutrition Examination Survey study. Considering the effects of both long and short term $PM_{2.5}$ exposure on C-reactive protein, homocysteine, fibrinogen, and leukocytes would provide insight into the CVD risk from $PM_{2.5}$ exposure in different individuals. However, no association between cardiovascular biomarkers and $PM_{2.5}$ exposure was found, except in specific sensitive groups of

individuals: diabetics, smokers, and those with multiple risk factors for CVD. It would be interesting to conduct a similar study on the FNSB population. Being able to screen known sensitive groups for CV biomarkers following $PM_{2.5}$ spikes during the cold season could alert health care providers and patients in these groups to impending adverse cardiovascular events. For example, the Dabass et al. (2015) study found that for each 10 micrograms/m^3 increase in $PM_{2.5}$, a 39.6% increase (95% CI: 0.1%, 87.2%) in C-reactive protein levels occurred in diabetics. In smokers, for each 10 micrograms/m^3 increase in $PM_{2.5}$, a 2.6% increase in homocysteine levels occurred (95% CI: 0.1%, 5.1%) at lag 0.

Burning organic biomass is a known source of ambient air $PM_{2.5}$ and has been linked to numerous diseases in humans (Gan et al., 2013; Krapf et al., 2017; Montes de Oca et al., 2017; Rokoff et al., 2017). Perhaps the most significant impact of $PM_{2.5}$ on the human body is adversely affecting heart function. The anatomy and physiology of this has previously been discussed in the introduction section of this paper.

$PM_{2.5}$ and Cerebrovascular Events

The effects of $PM_{2.5}$ on the brain is only beginning to be understood. Cerebrovascular accidents (strokes) are known to be the second leading cause of death and the leading cause of morbidities in the world (Leiva, Santibanez, Ibarra, Matus & Seguel, 2013). The Leiva et al. (2013) study found that for every 10 micrograms/m^3 increase in $PM_{2.5}$, emergency admissions due to cerebrovascular accidents increased by 1.29% (95% CI 0.552%–2.03%) in metropolitan Santiago.

A study by Oudin et al. (2018), has found a relationship between the incidence of dementia (declined cognition and memory due to Alzheimer's disease or vascular

dementia), and exposure to the residential burning of wood from residents living in Northern Sweden. There were 1806 participants in the study who were followed from the time they entered the study (1993-1995) until the study ended in 2010. They found a hazard ratio of 1.55 for each 1 microgram/m^3 increase in the level of ambient $PM_{2.5}$ (95% CI: 1.00-2.41, p=.05), suggesting more than just a casual association between $PM_{2.5}$ and dementia. Additionally, participants in the study who lived in an area with $PM_{2.5}$ due to burning wood were in the highest quartile, and who also had a wood stove, had an increased likelihood of developing Alzheimer's disease or vascular dementia than those who lived in the lower three quartiles and didn't have a wood stove (hazard ratios of 1.74, 95%CI: 1.10-2.75, p value 0.018).

$PM_{2.5}$ and Effects on Pregnancy and the Fetus

Stieb et al. (2016) studied the association between exposure to fine particulates and outcomes from pregnancy in women living near air pollution monitors in both rural and urban areas. This was a large Canadian study on nearly three million pregnancies and their outcomes, using single, live births only. Adjusting for socioeconomic status and individual covariates of the mother, the authors of the study found that a 10 microgram/m^3 elevation in $PM_{2.5}$ over the course of the pregnancy increased the risk of the newborn weighing less than 5.5 pounds (low birth weight), and small for gestational age (odds ratio = 1.04; CI 95% 1.01, 1.07). The authors reported that there were variations among subgroups in this study that were based on the time period (1999-2003 versus 2004-2008) and the mother's place of birth.

The relationship between inhaling fine particulates during pregnancy and premature births was investigated in a study by Sun et al. (2015). The authors conducted a meta-analysis to summarize quantitatively, the association between $PM_{2.5}$ exposure during pregnancy and pre-term births, and to consider sources and reasons for heterogeneity in past findings on this issue. After the search process, which used PUBMED, MEDLINE, and databases from Embase, Wanfang, and China Biological Medicine, 18 studies were included in the author's final analysis. Using a random-effects model (for studies with heterogeneity) and a fixed-effects model (for studies with no heterogeneity), the association between premature births associated with each 10 micrograms/m_3 increase in exposure to $PM_{2.5}$ was calculated. The odds ratio of exposure to $PM_{2.5}$ during the first, second and third trimester of pregnancy were 1.08 (95% CI: 0.92, 1.26), 1.09 (95% CI: 0.82, 1.44), and 1.08 (95% CI: 0.99, 1.17) respectively. Although these ORs were slightly above 1.00, which could indicate a positive relationship between PM2.5 exposure and negative pregnancy outcomes, the margin of error results (95% CI) indicate that since each were not entirely above or below 1.0, then $PM_{2.5}$ exposure does not affect the odds of experiencing negative pregnancy outcomes. Therefore these results are not statistically significant. The authors also considered the impact of $PM_{2.5}$ exposure at the regional level, the semi-individual level, and the individual level. The three classifications used to assess exposure were centered on residential level of exposure. Individual-level was determined using particulate dispersion models that were based on meteorology, traffic, geometry of roadways, air quality monitoring, vehicle emission and land use databases, which together allowed highly

accurate estimations of each of the subject's daily exposure level to $PM_{2.5}$. Semi-individual level was determined by using 24 hour ambient $PM_{2.5}$ concentrations from a monitoring station that was located closest to the subject's residence. Regional-level was determined by calculations that used the average concentration of $PM_{2.5}$ in a region or by using a low-resolution grid. The results yielded the following odds ratios for regional-level, semi-individual level, and individual level of exposure: 1.07 (95% CI: 0.94, 1.23), 1.14 (95% CI: 0.97, 1.35) and 1.11 (95% CI: 0.89, 1.37), respectively. The use of the semi-individual level in this study allows for individual $PM_{2.5}$ studies with ecological (group) exposure assignment. These odds ratios indicated that exposure to $PM_{2.5}$ at the semi-individual level did have a slightly greater impact on negative pregnancy outcomes than exposure at the individual and ecological level (1.14 for semi-individual-level versus 1.07 and 1.11 for regional and individual levels, respectively [CI:95%]). However a statistically significant association is not indicated by these results since the margins of error bracket 1.0 and the 95% CI doesn't state a measured value's statistical significance.

In the Zhang et al. 2016 cohort study, there were 105,998 infants that were born alive, fetal deaths, and stillbirths. Mothers in the two-year study (June 2011 to June 2013) lived in Wuhan district. The authors studied both $PM_{2.5}$ and PM_{10} exposure during the first trimester of pregnancy. There were only 2 ambient air quality monitoring stations for $PM_{2.5}$ in Wuhan so the district was divided into two areas for $PM_{2.5}$ study, compared to 9 monitoring stations for PM_{10} and thus 9 areas for PM_{10} study. Using multivariate logistic regression to odds ratios and 95% CIs for the association between both congenital heart defects and Ventricular Septal Defect (VSD), and ambient $PM_{2.5}$, the authors found a

statistically significant risk of the baby developing both congenital heart defects and VSD during the second and third months of pregnancy. The effect estimate during the second month was an adjusted OR of 1.10 per 10 microgram/m^3 increase in $PM_{2.5}$ (95% CI: 1.03-1.08) and for the third month it found an adjusted OR of 1.08 (95% CI: 1.01-1.06). No statistically significant association to congenital heart defects was found during the first month of exposure to $PM_{2.5}$ nor anytime during the first trimester for exposure to PM_{10}. The association between $PM_{2.5}$ and VSD was found to be statistically significant during the first trimester. The association between PM_{10} and VSD was not found to be statistically significant during the first trimester. It is interesting to note that $PM_{2.5}$ levels in the Wuhan district were significantly higher than in other areas of the world, with the mean concentration of $PM_{2.5}$ over the two year study period documented to be 65.61 micrograms/m^3, with only 12% of the daily $PM_{2.5}$ levels in Wuhan achieving the WHO guidelines of a maximum of 25 micrograms/m^3.

The impact of $PM_{2.5}$ on embryonic and fetal development continues to illustrate the importance of research in this area. The Wuhan study in particular, highlights the impact of very high levels of $PM_{2.5}$ on health. In the FNSB, the cold season spikes in $PM_{2.5}$ are likely having a significant impact on health of people living in the FNSB. My study on the impact of $PM_{2.5}$ on all-type cancers is hoped to add to the growing body of knowledge on the influence of $PM_{2.5}$ on human health.

While the focus of my study is on the impact of $PM_{2.5}$ on non-lung cancers as well as lung cancer, it is important to recognize that it has already been established, as noted in the representative samples of studies above, that exposure to high levels of fine

particulates can also cause serious non-cancer related adverse respiratory, cardiovascular, cerebrovascular, and pregnancy events, and that many of the underlying adverse physiological mechanisms from the influences of $PM_{2.5}$ is the same for cancers as well as for a large number of non-cancer adverse effects.

Conclusion

The select studies reported above have shown that exposure to high levels of ambient $PM_{2.5}$ has a significant negative impact on health. Studies have repeatedly shown that $PM_{2.5}$ increases the risk of lung cancer and other various negative respiratory health outcomes in both adults and children, as well as negative cardiovascular outcomes. Additionally, negative cardiovascular, non-cancer respiratory illnesses and cerebrovascular outcomes such as strokes, due to $PM_{2.5}$ exposure have been revealed. Studies on cancers other than lung cancers are only beginning to emerge. Those few studies that have been reported have shown a likely link to various types of non-lung cancers and merit further studies in this important area, particularly in high latitude cold climates. Thus, my study on the impact of $PM_{2.5}$ on non-lung cancer incidences in the FNSB region added to the body of knowledge in this relatively new area of concern.

Definitions

Dependent Variable: The dependent variable is incidents of all cancer types. The independent variable for this study is the frequent FNSB ambient $PM_{2.5}$ levels >35micrograms/m^3/24 hours in area zip codes that represent hot spots, (areas with significantly increased cold season $PM_{2.5}$ levels), and area zip codes that are less exposed to cold season $PM_{2.5}$ levels. The hot spot zip codes are the two zip codes in which EPA

regulated air quality monitors are strategically located (99701 and 99705) and are designated by the EPA as "serious non-attainment areas."

Assumptions

There are several assumptions that guided this study and that impacted the study's design and statistical approach. $PM_{2.5}$ levels will constantly vary due to climatic and unpredictable weather conditions. The three EPA-approved ambient air monitors in the FNSB are strategically located in the hot spot areas of the Borough, since these locations consistently experience the highest cold season, inversion-induced $PM_{2.5}$ levels in these two areas. These include the ambient air monitor in North Pole (zip code 99705), and two ambient air monitors in downtown Fairbanks (zip code 99701) (FNSB Air Pollution Control Commission Air Quality Comprehensive Plan, 2016). For this study, it was assumed that data from these air monitors accurately represent cold season $PM_{2.5}$ levels in the zip code areas of greatest concern. It is also assumed that the zip code areas outside of 99705 and 99701 consistently experience lower levels of ambient $PM_{2.5}$ during strong atmospheric inversions. These zip codes include the following: 99702, 99703, 99709, 99712, 99714, 99775, and 99790. It should be noted that within the 99709 zip code area, there are several micro hot spots. These were addressed in the section on scope and delimitations.

It is assumed that the data from the FMH Cancer Center and the EPA-approved ambient air monitors are reliable since both the Cancer Committee and the EPA-approved monitors must continually meet established quality control standards. FMH has accreditation by the Commission on Cancer of the American College of Surgeons and

notably, is the only hospital in Alaska that has also obtained accreditation by the National Accreditation Program for Breast Cancer of the American College of Surgeons.

Scope and Delimitations

The scope of the proposed study is limited to ambient $PM_{2.5}$ data from the three main EPA approved monitors in the FNSB; two in downtown Fairbanks (99709) and one in North Pole (99705), with both zip codes considered to be hot spots for $PM_{2.5}$ during the cold season. This study is also limited to the cancer registry data from the FMH J. Michael Carroll Cancer Center. The registry only provided data on the year and type of primary cancer diagnosis for cancer patients; the zip code of residence in the FNSB of cancer patients, and the specific histology of the cancer type diagnosed. Military patients living in Fort Wainwright and Eielson Air Force Base zip codes were not considered in the study. This was due to the inability to access military cancer patient data, and the fact that military patients are more transient, and thus would become a threat to the external validity of the study.

Not being able to control for the two major confounders in this research (tobacco smoking and the latency period for each cancer type are significant limitations to this study. Future studies with more comprehensive patient information included in the data set, such as smoking, and being able to analyze each cancer type latency period with other data on cancer latency such as age, will provide even more information.

Another limitation to this study that deserves mention is exposure to radon. Radon is known to be one of the leading causes of lung cancer. A study by Grundy et al. (2017), reported that in Alberta in 2012, 16.6% of lung cancer cases were due to radon exposure,

and is an example of the importance of considering radon as another contributing factor to developing cancer. However it was beyond the scope of this study to consider radon exposure in the FMH cancer patient dataset. This is a potential area of focus for future studies on environmental causes of cancers.

An additional consideration in this study is the impact of random and unpredictable periods of summertime wildfires that typically expose residents in all areas of the FNSB to short-term high-level $PM_{2.5}$. The effects of $PM_{2.5}$ exposure due to wildfires is an area of intense interest in this field, however it is beyond the scope of this study to address the impact of wildfire $PM_{2.5}$ on cancer incidences in the FNSB.

This study was able to provide preliminary data on the relationship between ambient $PM_{2.5}$ exposure and all-type cancer incidences, as well as lung cancer incidences. This generalizable data could be used for the development and guiding of future prospective research and studies in this area.

Significance, Summary, and Conclusions

It was the intent of this research to advance our knowledge of the impact of exposure to high levels of $PM_{2.5}$ with regard to cancer incidences that include both all-type cancers as well as lung cancers, in a high latitude, cold climate environment. There have been many studies confirming that high levels of $PM_{2.5}$ is a risk factor for lung cancer, as select studies in the literature review section revealed. No study such as this has been conducted in the FNSB. As residents of the FNSB struggle to improve the long cold season air pollution problem, having more knowledge on the adverse health effects can further encourage policy makers as they work to bring the FNSB $PM_{2.5}$ levels to

within mandated EPA standards. Additionally, medical and health providers will be able to better counsel patients on the carcinogenic effects of inhaling high levels of $PM_{2.5}$. As more of the public becomes educated on this critical issue, the strong differences in opinion that socially divide the community on air quality regulations should fade and the community will hopefully come together to reduce cold season $PM_{2.5}$ emissions with the goal of improving health for everyone.

The relationship between $PM_{2.5}$ exposure and non-lung cancers remains more elusive. Some of the more recent studies looking into this include Turner et al. (2017), who found a 13% and 14% increase in bladder and kidney cancers, respectively, for each 4.4 micrograms/m^3 increase in ambient $PM_{2.5}$. Yeh et al. (2017) demonstrated a relationship between ambient air pollution and bladder cancers in Taiwan. Parikh, and Wei (2016), discovered a relationship between $PM_{2.5}$ and breast cancer, and Wang et al. (2018), found that $PM_{2.5}$ exposure may increase the risk of death from pancreatic cancer, and as with these and other non-lung cancer studies, the authors recommend future studies on ambient $PM_{2.5}$ and its link to non-lung cancers.

My study added to the limited body of knowledge on the relationship between ambient $PM_{2.5}$ and non-lung cancers. Furthermore, since there have yet to be any studies of cold climate ambient $PM_{2.5}$ due primarily to biomass burning, my study filled this gap in the research on this topic and contributed to our knowledge in the field of oncology and its relationship to human exposure to high levels of ambient $PM_{2.5}$.

Acronyms and Abbreviations

ACS American Cancer Society

ALA	American Lung Association
CCA	Citizens for Clean Air Fairbanks
CHD	Congenital Heart Defects
CoC	Commission on Cancer
COPD	Chronic Obstructive Pulmonary Disease
CPS II	Cancer Prevention Study II
CVA	Cerebrovascular Accident (Stroke)
CVD	Cardiovascular Disease
DEC	Department of Environmental Conservation
EPA	Environmental Protection Agency
FCAA	Federal Clean Air Act
FCAC	Fairbanks Climate Action Coalition
FEV	Forced Expiratory Volume
FMH	Fairbanks Memorial Hospital
FNSB	Fairbanks North Star Borough
FVC	Forced Vital Capacity
Micro RNA	Micro Ribonucleic Acid
NAAQS	National Ambient Air Quality Standards
NAPBC	National Accrediting Program for Breast Cancer
NQMBC	National Quality Measures for Breast Cancer Program
O_3	Ozone
PAHs	Polycyclic Aromatic Hydrocarbons
PELL	Pregnancy to Early Life Longitudinal (study)
$PM_{2.5}$	Particulate Matter less than or equal to 2.5 microns in diameter
PM_{10}	Particulate Matter less than or equal to 10 microns in diameter
ROS	Reactive Oxygen Species

Section 2: Research Design and Data Collection

Introduction

This study's purpose was to determine if there is a significant difference in the incidence of both lung cancer and all type cancer incidences in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in the FNSB areas that are non-hot spots. In Section 2, I address the design of the research and the rationale for that design, as well as the study's population and sampling procedures used. I also present the plan for data analysis and ethical considerations.

Research Design and Rationale

This study was a quantitative retrospective cohort study in which I considered the incidence of new cancer diagnoses in the FNSB population during a 10-year period from January 1, 2008, to December 31, 2017. Both the number of lung cancer and non-lung cancer diagnoses in the two hot spot Zip Codes (99701 and 99705) were compared to the number of lung cancer and non-lung cancer diagnoses in the six outlying (non-hot spot) residential Zip Codes (99706, 99709, 99712, 99714, 99775, and 99790).

In determining the most appropriate design for this study, I considered the value of a retrospective review of the data provided to me by the FMH Cancer Committee. I accessed the following data from de-identified cancer patient information that is included in the cancer registry at the FMH Cancer Center: patient's type of cancer, Zip Code of residence of cancer patients, and year of initial diagnosis. Patient's names and addresses were not made available to me, and if there was any way in which a single cancer patient

could be identified based on Zip Code of residence or any other data, that patient was omitted from the study.

The dependent variable was incidents of all cancer types. The independent variable for this study was the frequent FNSB ambient $PM_{2.5}$ levels >35 micrograms/m^3/24 hours in area Zip Codes that represent "hot spots," (areas with significantly increased cold season $PM_{2.5}$ levels) and area Zip Codes that were less exposed to cold season $PM_{2.5}$ levels. The hot spot Zip Codes were the two Zip Codes in which EPA regulated air quality monitors are strategically located (99701 and 99705). The major confounders in this study were age, tobacco smoking, and the latency period that occurs between carcinogen exposure and onset of symptoms.

There were no resource constraints with this choice of study design, as this doctoral student study was not funded by outside sources, rather only by me, the author of this study. I expected that because this study was basically a community service effort on my part, that the Cancer Committee would provide the requested data as part of service to their community.

Methodology

Population

The target population included all patients in the FNSB initially diagnosed with cancer at FMH from January 1, 2008, through December 31, 2017. There are a total of 41,563 residents living in the hot spot Zip Codes and 46,365 residents living in the non-hot spot Zip Codes (Zip-codes.com, n.d.). On average, there are approximately 300 new cancer diagnoses each year at FMH (FMH Cancer Committee Annual Report, 2017).

Sampling and Sampling Procedures

The type of sampling procedure that I used for this study was nonprobability, purposeful sampling. All patients living in the FNSB, excluding those living at Fort Wainwright and Eielson Air Force Base, who were initially diagnosed with any type of cancer between January 1, 2008, and December 31, 2017, were included in the study, unless the patient was able to be identified by Zip Code of residence (such as if there were only one diagnosis in a Zip Code). I obtained data on cancer patients from the tumor registrar at FMH. I obtained $PM_{2.5}$ data from the Alaska Department of Environmental Conservation Division of Air Quality and the EPA. Data from subjects was not identified beyond the subject's Zip Code of residence and diagnosis.

The procedure for accessing the data set included getting both verbal and written permission from the FMH Cancer Committee to access the data. A permission letter is attached in an appendix at the end of this document. Additionally, I was in regular contact, both in person and online, with the FMH Tumor Registrar for the past year to ensure that we both had a clear understanding of the process I was to follow in obtaining and using the data set.

Because the FMH Cancer Committee uses patient information including chart reviews, I have thus referred to "chart reviews." I did not personally review patient charts, only the compilation of data obtained by the Cancer Committee and submitted to the licensed Tumor Registrar at FMH. The chart inclusions and exclusions were recognized to ensure that patient confidentiality was well established and also that the coders for patient cancers were appropriately ascertained.

FMH maintains its accreditation by the Commission on Cancer of the American College of Surgeons. FMH has maintained Commission on Cancer accreditation since 1976. The Commission on Cancer accreditation is maintained by American College of Surgeons on-site surveys performed every 3 years to make certain that FMH continues to enhance patient quality of care and meets or exceeds national standards (American College of Surgeons, Commission on Cancer, n. d.)

FMH is currently the only hospital in Alaska that, since 2009, also maintains accreditation through the ACS's National Accreditation Program for Breast Cancers. This requires cancer centers to undergo rigorous on-site evaluations every 3 years to determine the breast cancer center's compliance with National Accreditation Program for Breast Cancer Standards (https://www.facs.org/quality-programs/napbc). In 2014, the breast cancer center at FMH was given a distinguished honor when it was recognized by the National Quality Measures for Breast Centers Program as a Certified Quality Breast Center of Excellence (http://www2.nqmbc.org/).

In order to determine the sample size for this study, I performed a G* power analysis using G* Power 3.1.9.2 for Macs. I used the following input parameters: test family = *z* test; statistical test = logistic regression; tails = 2; *OR* = 1.2; correlation = 0.3; alpha = 0.05; power = 0.80. The output parameters were as follows: critical *z* = 1.96; total sample size needed = 1138; actual power = 0.80. Given approximately 3,000 cancer cases over the 10-year period of study, there was a more than adequate sample size for this study.

Operationalization

Cancer patient Zip Codes representing hot spots (99701 and 99705), and non-hot spots (99706, 99709, 99712, 99714, 99775, and 99790) were the independent variables. All type cancers composed the dependent variable for the first research question, and lung cancers constituted the dependent variable for the second research question. Hot spots are areas within the FNSB that frequently exceed the NAAQS maximum allowable 24 hour ambient $PM_{2.5}$ levels of 35 micrograms/m^3 (EPA, 2006). There are about 300 new cancer cases/year (all-type cancers), so there were about 3,000 new cancer cases over the 10-year period of data that I used. As an initial estimate, I computed that if there are 40,000 people living in the hot spot areas, and 40,000 people living in the non-hot spot areas, then there would be 80,000 residents overall. This computes to an average new cancer rate among all residents to be about 4%. The question was to determine if there is a higher rate of cancer diagnosis among residents living in the hot spot areas versus those living outside the hot spot areas. Therefore, a two by two table was constructed by which I considered the following: a = the number of people in the hot spot areas diagnosed with any type of cancer; b = the number of people in the hot spot areas that are not diagnosed with cancer; c = number of people in the non-hot spot areas that are diagnosed with cancer; d = number of people in the non-hot spot areas that are not diagnosed with cancer. An odds ratio was determined using the following formula: *OR*= a/c divided by b/d (ad/bc), and the relative risk was determined using the following formula: *RR*= a/a+b divided by c/c+d.

Data Analysis Plan

The software used for this study was SPSS version 24. The research questions and hypotheses were:

RQ1 Quantitative: Is there a significant difference in the incidence of all cancer types other than lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots?

$H_0$1: There is no significant difference in the incidence of all cancer types other than lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots.

H_a1: There is a significant difference in the incidence of all cancer types other than lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB that are non-hot spots.

RQ2: Quantitative: Is there a significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots?

$H_0$2: There is no significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots.

H_a2: There is a significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots.

Because I had two categorical variables and a very large sample size, I determined the Chi-square statistic to be most appropriate for this quantitative study. Additionally, there was insufficient data to control for smoking as a confounder because smoking data on cancer patients was not part of the 10-year dataset that was provided by the FMH Tumor Registrar. The same was true for determining the potential confounder of latency period for specific types of cancers.

Regarding the interpretation of results, I considered that those Zip Codes that are further above the population Mean would be assumed to have more cancer incidences. If the two hot spot areas are above the population Mean in cancer incidences compared to those in the non hot spot areas, and the p value obtained is < 0.01, then the results were considered to be statistically significant and the null hypothesis could be rejected. The final Chi-square output and computed *OR*s and *RR*s are located in the results section of this paper.

Threats to Validity

Threats to external validity in this study were limited. This is because the cancer data is factual information from patients and medical staff based on absolute results from highly controlled medical testing. With regard to this study being reproducible by other researchers in the future, and because $PM_{2.5}$ levels in the hot spots areas could be affected by climate change and even changing air quality laws, policies, and enforcement, future results could vary significantly in either direction. An additional threat to external validity was the omission of FNSB residents who live at Ft. Wainwright Army Base and

Eielson Air Force Base. This was due to the inability to access patient data from the military sites.

Threats to internal validity included the inability to control for the two major confounders: tobacco smoking and latency period for different types of cancers in different age groups. These were limitations to this study that the data either doesn't include (smoking), or that is beyond the scope of this study (evaluation of each cancer type and each age of the patient).

Threats to construct validity for this research doesn't apply, since all variables are already well-defined. Statistical conclusion validity is reported in the results section of this paper.

Ethical Procedures

Since this study involved the collection of patient data, a Walden University Institutional Review Board (IRB) application was submitted and approved prior to obtaining the dataset. The Walden University IRB approval number for this study is 03-09-20-0621354. Following IRB approval on March 9, 2020, the dataset was obtained from FMH and analyzed.

The FMH Tumor Registrar made certain that no patient names were included in the data set and that the researcher did not have access to patient identification codes. If there was only one case of a cancer patient in one Zip Code, that might enable identification of a patient, it was to be omitted from the study. There were no such cases with this study. Following completion of the study, the dataset will be destroyed after a period of five years. The data is stored in a password-protected laptop computer.

A signed letter from the FMH Tumor Registrar is attached to this document and can be found in Appendix A.

Summary

This study was a quantitative retrospective cohort study that considered the incidence of new primary all-type cancer diagnoses and primary lung cancer diagnoses in the FNSB population over a ten-year period from January 1, 2008 to December 31, 2017. The relationship between the number of cancer diagnoses in patients living in the two hot spot Zip Codes (99701 and 99705) was compared to the number of cancer diagnoses in the 6 outlying residential zip codes (99706, 99709, 99712, 99714, 99775, and 99790). Cancer data was obtained by the FMH Tumor Registrar and was analyzed using the Chi-square statistic and SPSS software. The *OR* and *RR* were computed manually. The independent variable was Zip Code (hot-spot versus non-hot spot) of residence of cancer patients and non-cancer residents. The dependent variables in this study are all-type cancer diagnosis and lung cancer diagnosis.

In section 3 the study's results and findings were presented. In addition, the implications and impact on positive social change in the FNSB was presented, as well as recommendations for future research in this area of study.

Section 3: Results

The purpose of this study was to determine if there is a significant difference in both lung cancer and, particularly, all other types of cancer incidences in people who live in areas of the FNSB, which see frequent episodes of high levels of ambient $PM_{2.5}$ (area hot spots) compared to people living outside the hot spot areas of the FNSB. The following research questions guided this study:

RQ1: Is there a significant difference in the incidence of all cancer types other than lung cancer, in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots?

RQ2: Is there is a significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots?

RQ2 served as a validation study question because $PM_{2.5}$ is already recognized as a cause of lung cancer. (Huang, et al., 2017; Poirier, et al., 2017; Wei et al., 2017).

In this section, I present the study demographics, the statistical results, and an overall summary of the results and conclusions.

Data Collection of Secondary Dataset

The number of new primary site cancer diagnoses in the FNSB between January 1, 2008, and December 31, 2017, excluding lung cancers, was 1,526. The number of lung cancers diagnosed in the same 10-year period was 214. This data is based on cancer diagnoses in patients residing in the following postal Zip Codes: 99701 and 99705 (hot spot zip codes), and the five FNSB areas located outside of the hot spot areas (99709,

99712, 99714, 99775, and 99790). The Zip Codes 99702 (Eielson Air Force Base), and 99703 (Fort Wainwright) were omitted from this study because complete data on military residents could not be obtained. Additionally, all Zip Codes for P.O. box addresses were omitted because population data in these zip codes was either reported as zero or a number negligibly small and the fact that many residents with secure P.O. boxes often have postal mailbox Zip Codes for their actual residence or live out of State during the cold season.

Table 1

Population of Hot Spots and Non-Hot Spot Zip Codes

Hot spots		Non-hot spots	
Zip Codes	Population	Zip Codes	Population
99701	19,019	99709	29,830
99705	22,544	99712	13,866
		99714	1,385
		99775	1,251
		99790	*20
Total	41,563	Total	46,352

*No cancer cases

Table 2

Total Number of Primary Site Diagnoses in the Hot Spot and Non-Hot Spot Areas

	All types of cancers excluding lung cancers.	Lung cancers
Hot spots	838	134
Non-hot spots	688	80

According to zip-codes.com (2010) and the United States Census Bureau (2019), the total population of the FNSB in 2010 was 97,581, with 47.3% of the population living within the hot spot areas and 52.7% of the population living outside of the hot spot areas. Males make up 52.8% of the population and females make up 47.2%. The median age of the FNSB population is 31 years. Additionally, the following demographics regarding race are as follows: 77% white, 7% Native Alaskan and Indian, 6% Hispanic, 5% African American, 3% Asian and 2% other races. These demographics are important to consider in understanding and evaluating cancer diagnoses in the population. While detailed analysis of each of the above demographics with regard to $PM_{2.5}$ exposure and cancer diagnoses is beyond the scope of this study, these demographics may shed some light on the existing study. It is also important to note that the population within the FNSB is relatively well educated with 94.5% of residents 25 years of age and older having graduated from high school or higher, and 32.6% of the population having a bachelor's degree or higher. Also of note is that 13.2% of the population under 65 years of age have no health insurance (U.S. Census Bureau, 2019).

Results

SPSS version 24 was selected for the chi-square analysis for this study. For the first research question, the chi-square result of 36.35 was significant at an alpha level set at 0.001. Therefore, I can reject the null hypothesis of RQ1 and conclude that there is a significant difference in the incidence of all cancer types other than lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots. The odds ratio (*OR*) and the relative risk (*RR*) values were *OR* = 1.37, *RR* = 1.36. Both also reflect an association of living in hot spot areas and having an increased incidence in all types of cancer other than lung cancer.

Table 3

All Cancers Other Than Lung Cancers in Hot Spot Areas Vesus Non-Hot Spot Areas (Research Question 1)

	Value	*df*	Asymptotic significance (2-sided)
Pearson chi-square	36.35[a]	1	.000
N of valid cases	87915		

Note: a 0 cells (0.0%) have expected count less than 5. The minimum expected count is 721.44.
$x^2(1, N = 87915) = 36.35, p < 0.001$

The chi-square result for the second research question was 20.25 and significant at an alpha level set at 0.001. Therefore, I can reject the null hypothesis of RQ2 and conclude that there is a significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are $PM_{2.5}$ non-hot spots. Additionally, the *OR* = 1.87 and the *RR* = 1.88, indicating a

strong association between living in a hot spot area and increased incidence of lung cancer.

Table 4

Lung Cancers in Hot Spot Areas Versus Non-Hot Spot Areas (Research Question 2)

	Value	*df*	Asymptotic significance (2-sided)
Pearson chi-square	20.25a	1	.000
N of valid cases	87915		

Note: a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 101.7.
$x^2(1, N = 87915) = 20.25, p < 0.001$

Interpretation of Findings

The chi-square statistic is computed from expected frequencies and observed frequencies and applies effectively to determine the association between variables that make up a table's rows and columns in order to determine whether or not to reject the null hypothesis. Thus, the chi-square statistic was appropriate for this study, the variables of which composed a two by two table. The alpha level of the analysis of both RQ1 and RQ2 was set at 0.001. The consequent *p*-values for both RQs were extremely low. For all cancers other than lung cancers in hot spot areas versus non-hot spot areas, I can confidently say that the chi-square value of 36.35 is statistically significant and can reject the null hypothesis. Therefore, the alternative hypothesis can be accepted and answered, that there is a significant difference in the incidence of all cancer types other than lung cancer, in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB that are non-hot spots. Likewise, I can confidently conclude for RQ2 that the chi-

square value of 20.25 is statistically significant and the null hypothesis can be rejected. Again, the alternative hypothesis can be accepted and answered, that there is a significant difference in the incidence of lung cancer in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in FNSB areas that are non-hot spots.

The odds ratio of 1.37 for the first RQ indicates that the odds of a cancer diagnosis other than lung cancer in people living in the $PM_{2.5}$ hot spots is 37% greater than those living in non-hot spot areas. The relative risk of 1.36 indicates that residents in a $PM_{2.5}$ hot spot have a 36% higher risk of a cancer diagnosis other than lung cancer than residents in non-hot spot areas.

The *OR* of 1.88 indicates that the odds of a lung cancer diagnosis in people that live in a $PM_{2.5}$ hot spot is 88% greater than those living in a non-hot spot area. The *RR* of 1.87 indicates that residents in a $PM_{2.5}$ hot spot area have an 87% higher risk of a lung cancer diagnosis than those living in non-hot spot areas.

The results for RQ1 provide new knowledge for understanding the relationship between exposure to high levels of $PM_{2.5}$ and incidences of all cancer types beyond lung cancer, particularly in a high latitude, cold climate. While other studies have provided information on specific types of cancers and $PM_{2.5}$ exposure, such as the study done by Wong et al. (2016), who found strong associations between $PM_{2.5}$ and cancers of the upper gastrointestinal tract and other digestive accessory organs, as well as cancers of lymphatic organs, bone marrow, and the breast. A recent study by Wang et al. (2018), found a link between $PM_{2.5}$ and pancreatic cancer. Another study by Yeh et al. (2017) provided the first evidence-based study linking exposure to $PM_{2.5}$ and bladder cancer in

both men and women. While these studies have provided valuable information in this area, they are limited to only specific types of cancer and do not consider cold-climate $PM_{2.5}$ due primarily to biomass burning.

As I expected to see a relationship between $PM_{2.5}$ exposure and lung cancer because this has been confirmed in numerous studies (Badyda, et al., 2017; Cao et al., 2018; Rajendra et al., 2018), I was surprised for my study to reveal such a strong association between $PM_{2.5}$ and lung cancer. Therefore, a future study to consider what effect inhaling ice fog containing high levels of $PM_{2.5}$ compares to inhaling warmer air with high levels of $PM_{2.5}$ on the incidence of lung cancer is advised.

These findings can clearly support how the concept of reciprocal determinism on which the social cognitive theory is based, can lead to positive personal choices among residents of the FNSB with regard to how to safely heat homes and businesses. Ultimately, the public's knowledge of the significant health risks due to biomass burning and inhalation of $PM_{2.5}$, will expectantly lead to changes in behavior that result in a healthier environment for everyone, and thus, more positive public health outcomes.

Overall Summary and Conclusions

The first RQ reflected the primary intent of this study. Determining if exposure to high levels of $PM_{2.5}$ in the type of climate and geographical location of the FNSB influences the incidences of cancers other than lung cancer is an important question in cancer and air pollution research. The statistically significant chi-square result (at an alpha level of 0.01) indicated that there is an association between $PM_{2.5}$ exposure and an

increase in all types of cancers beyond lung cancer. The *OR* and *RR* for the first RQ also support the statistically significant chi-square result.

The second research question was a validation study because many previous studies have demonstrated an association between exposure to high levels of $PM_{2.5}$ and development of lung cancer. However, regarding the second research question, and as previously stated, few studies have considered $PM_{2.5}$ exposure in an extremely cold climate with very long cold seasons and strong weather inversions. As with the first RQ, the chi-square result was statistically significant at an alpha level of 0.01. The *OR* and *RR* for the second RQ also supported the statistically significant chi-square result.

Section 4 provides a detailed interpretation of the results of this study. I also consider limitations of the study as well as recommendations for future studies in this area. I also address the implications that this study will have on positive social change in the FNSB, followed by a final conclusion.

Section 4: Application to Professional Practice and Implications for Social Change

This study's purpose was to determine if there is a significant difference in the incidence of both lung cancer and all type cancer incidences in people living within the FNSB area $PM_{2.5}$ hot spots compared to those living in the FNSB areas that are non-hot spots.

This research was a retrospective quantitative study. I used quantitative data from secondary data sets for the study. A quantitative methodology was most appropriate to this research issue, allowing an examination of the relationship between breathing high levels of $PM_{2.5}$ as a potential causal factor for all cancer types. This type of methodology emphasizes objective statistical measurements using existing data.

Engaging community partners in this study was critical. The Cancer Center at FMH has provided support through the provision of data from the tumor registry through the FMH Cancer Center. Data from cancer subjects were de-identified by FMH prior to my receiving the data. Additionally, only the Zip Codes that could accurately be used for the geographical distribution of subjects and for the determination of area hot spots in which $PM_{2.5}$ spikes significantly during the cold season were used for this study. The Alaska Department of Environmental Conservation's Division of Air Quality provided $PM_{2.5}$ data for the study. Data came from three EPA-approved air monitors. Two of the monitors are located in downtown Fairbanks and one is located in North Pole. Two local organizations, Citizens for Clean Air Fairbanks and the Fairbanks Climate Action Coalition were also valuable resources for providing a historical, political, and cultural perspective to the air pollution issue in the FNSB.

The positive associations between cancer diagnoses and exposure to ambient fine particulates revealed by the results of this study can provide a basis for future expanded research in this area, further justify the need for strengthened and enforced policies to reduce air pollution levels in the FNSB during the long cold season, and significantly increase public awareness of the serious adverse health effects from exposure to high levels of $PM_{2.5}$, particularly during the cold season. In this final section I interpret the results of the study and discuss the study's limitations, including significant unmeasured confounders. I detail further recommendations and the positive impact on social change.

Limitations of the Study

There were several limitations to this study. One limitation was the lack of continuous monitoring of air pollutants by an EPA regulated monitor in the areas outside of the hot spot Zip Codes to give a more precise comparison of $PM_{2.5}$ levels in each Zip Code in the FNSB. Another limitation was the lack of data from the two military bases located within the FNSB, Fort Wainwright and Eielson Air Force Base. Because Fort Wainwright is a $PM_{2.5}$ hot spot zip code (99703) and has a larger population than Eielson Air Force Base, which is a $PM_{2.5}$ non-hot spot zip code (99702; U.S. Census Bureau, 2019, and zipcodes.com, 2010), it is possible that cancer data from these populations could have made an even stronger case for rejection of the null hypothesis.

Limitations of this study also included two unmeasured potential confounders. The first was the latency period (the elapsed time period between exposure to a carcinogen and the initial signs or symptoms of cancer) for all of the cancer types, including lung cancer, and the second limitation of the study was cancer patients'

smoking habits. With regard to latency period for cancers, it is important to note that latency periods vary for different cancer types (Nadler & Zurbenko, 2014). Therefore, it would be necessary to consider each specific type of cancer. The cancer dataset for this study included over 135 different types of cancer, and of those cancer types counted, no cancers such as breast, colon, or lung were subdivided into the specific type of breast, colon, or lung cancer. Thus, for a study to consider cancer latency periods, it would be necessary to have a well-funded study that included a team of researchers, each with their own specific expertise in cancers who were also familiar with current studies on latency periods in their area of expertise. Furthermore, it is known that for many cancer types, latency period is also influenced by age (Nadler & Zurbenko., 2014).

The second limitation and potential confounder to this study was the lack of enough data on cancer patients' tobacco smoking history and habits. There was some limited data on cancer patients' tobacco smoking habits that was collected for a previous study, but there were not enough data to be statistically significant for this study.

Recommendations

The first recommendation for future studies on this topic would be to advise the FMH Cancer Committee to consider including data on patient's smoking history and current smoking habits. Tobacco smoking has been well established as contributing to the development of many different diseases, including respiratory and CVDs, and lung, oral, pharyngeal, and laryngeal cancers, among others (West, 2017). Most certainly, future studies similar to this study will be using the FMH Cancer dataset, and having smoking

data will provide researchers with valuable information and enable researchers to quantify the impact of smoking on their subjects.

Ideally, there will be improved air quality monitoring in strategic areas of $PM_{2.5}$ non-hot spot Zip Codes. This would provide valuable data for future research. Future studies could also include specific dates and lengths of weather inversions during the cold season, as well as locations, dates, and lengths of time for wildfires in the summer.

Because this study resulted in a very strong association between inhaling high levels of $PM_{2.5}$ in a very cold climate area and increased lung cancers, a study considering the effect on lung cancer incidences from inhaling high levels of $PM_{2.5}$ embedded in tiny ice fog crystals when the temperature drops way below zero as compared to inhaling high levels of $PM_{2.5}$ in warmer air would be useful.

Finally, in the aftermath of the coronavirus disease (COVID-19) pandemic, I would recommend future research that considers mortality rates during the COVID-19 pandemic at strategic areas around the world: those that have demonstrated historically high levels of ambient $PM_{2.5}$ and those areas that have had historically low levels of ambient $PM_{2.5}$. It would be interesting to see if there is a difference in mortalities in people who presumably have already had some lung damage from chronic exposure to fine particulates versus those who have not. Additional research following the COVID-19 pandemic could follow individuals who have recovered from a severe case of the disease to see what kinds of lung problems develop in the future in these individuals.

As of the final writing for this study, I discovered that indeed there has already been research published on the impact of chronic $PM_{2.5}$ exposure and mortality rates from

COVID-19, based on data thus far into the pandemic. Wu, Nethery, Sabath, Braun, and Dominici (2020) revealed that only a $PM_{2.5}$ increase of 1 microgram/m^3 is associated with an increase in COVID-19 mortalities by 15% (95% CI: 5%, 25%). Their research found that only a small increase in fine particulate exposure over time leads to a sizeable increase in COVID-19 mortality rates, with a scale of escalation 20 times greater than what is observed for $PM_{2.5}$ exposure and all causes of $PM_{2.5}$ mortalities. This study emphasizes the importance of enforcement of current regulations to control air pollution both now, during the pandemic, and after the pandemic crisis is over. In the FNSB, both current regulations on air pollution control and their enforcement remains weak.

Implications for Professional Practice and Social Change

The statistically significant results of this study provide cause for concern with regard to the $PM_{2.5}$ hazards in the FNSB, and indicate the serious need for changes in the way people heat their homes and provide for their other energy needs. As the residents of the FNSB learn more about the dangers of biomass burning, and in particular that there is a relationship between $PM_{2.5}$ exposure and incidences of cancers of all types, it is expected that more and more people will take responsibility for their energy practices. Bandura's SCT has been used extensively in public health research, particularly research similar to this study, and has been shown that as an individual's cognition on a topic or problem improves, so does their behavior. Heydari et al. (2014) demonstrated how effective the application of the SCT was in their study on addictions. While the practice of burning biomass for heat and other energy needs in the FNSB is seen as an economic and somewhat efficient way to provide heat during the long cold season, I believe the

practice to also be a form of addiction. On a bitter cold winter day, the warmth and ambience of a wood fire is most soothing. However, with an increased understanding of the vast number of serious adverse health effects in people of all ages due to $PM_{2.5}$ exposure, positive social change should occur in the FNSB. With knowledge that a healthier environment will directly lead to a healthier population, biomass burning will hopefully significantly decrease. Just as people have come together to decrease COVID-19 exposure by social distancing, in order to decrease mortalities and preserve health for the masses and themselves, residents in the FNSB should come together to improve their air quality for their own health, their children's health, and for the health of the population. I expect that using cleaner forms of energy and keeping biomass burning to a minimum will become the "new normal" in the FNSB.

It is also important that health care providers recognize the dangers of $PM_{2.5}$ exposure and take measures to educate their patients on the issue, just as they educate their patients on other ways to achieve optimum health. Providers should also be aware of disease processes in their patients that could be the result of high levels of $PM_{2.5}$ exposure and take appropriate clinical measures to address the issue. The Public Health Department (PHD) can play a major role in an educational offensive for the purpose of decreasing biomass burning and promoting the use of cleaner energy. The PHD should have the tools necessary to implement educational programs designed to improve the air quality. The PHD should also have the expertise to appropriately market the movement away from biomass burning and toward promoting clean energy.

In summary, education is our greatest tool for improving public health, and in the case of the practice of biomass burning in the FNSB area, it provides an opportunity to change the way people think about their energy needs and what they can individually do to help improve the health of the community as a whole.

Conclusion

This study considered the impact of $PM_{2.5}$ exposure and incidences of all types of cancers other than lung, and lung cancer separately, and found that that in both cases, there is an association between $PM_{2.5}$ exposure and increased incidences of cancers. This study may contribute to the existing body of knowledge on the relationship between cancers and $PM_{2.5}$ exposure and in particular the limited research on non-lung cancers and $PM_{2.5}$ exposure. It is hoped that this study can contribute to social changes in the FNSB that result in greatly improved air quality and significantly lowering $PM_{2.5}$ by decreasing the number of residents who currently practice the burning of biomass for heat and other energy needs. The ultimate goal is improved health outcomes for the entire FNSB community in the near and distant future.

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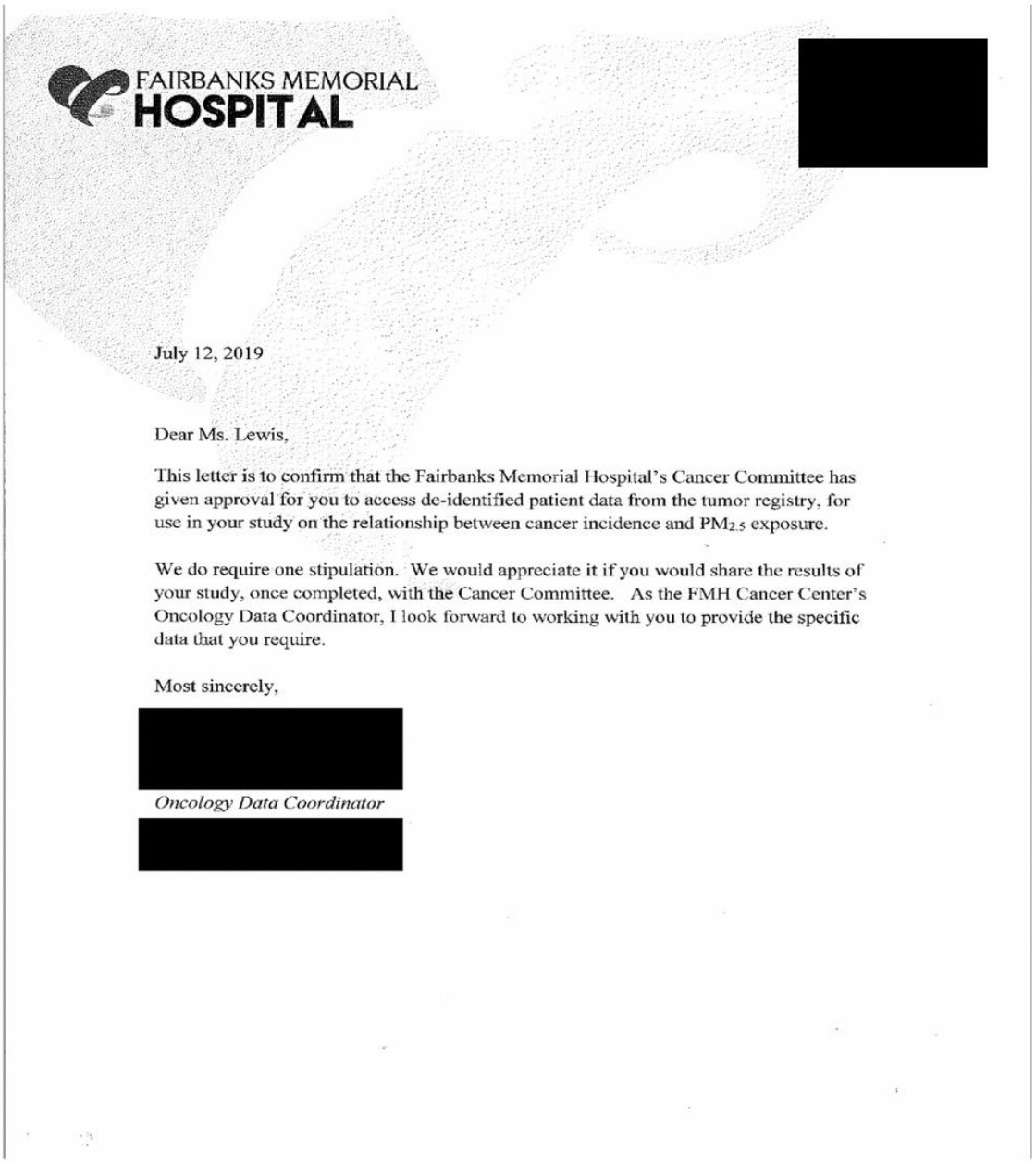
Appendix



FAIRBANKS MEMORIAL HOSPITAL

[redacted]

July 12, 2019

Dear Ms. Lewis,

This letter is to confirm that the Fairbanks Memorial Hospital's Cancer Committee has given approval for you to access de-identified patient data from the tumor registry, for use in your study on the relationship between cancer incidence and $PM_{2.5}$ exposure.

We do require one stipulation. We would appreciate it if you would share the results of your study, once completed, with the Cancer Committee. As the FMH Cancer Center's Oncology Data Coordinator, I look forward to working with you to provide the specific data that you require.

Most sincerely,

[redacted]

Oncology Data Coordinator

[redacted]